The neurological aspects of multiple myelomatosis

Edwin Clarke

C O N T E N T S

APPENDIX I

There are twenty-six cases in the present series and they have been described in detail and in a standard fashion. When these cases are referred to in the text, the number is always spelt out so as to distinguish them from the cases of other authors, where a numeral is employed.

Much uncertainty and confusion has been caused in the literature by the publication of doubtful or unproven cases of multiple myelomatosis. All the cases described below were adequately diagnosed, but to substantiate this a reproduction of the histological appearances is provided in all but six of them.

References to other pages invariably allude to the first volume and not to the appendices.

CONTENTS

CASE ONE

Female, 61. 4 years of diplopia, right visual impairment and bilateral deafness. One year of nasal obstruction and tingling right face. Involvement of right 2nd, 5th, 6th and 8th cranial nerves and left 8th. Nasopharyngeal mass shown by biopsy to be a plasma cell myeloma. Extensive destruction of skull base with evidence elsewhere of multiple myeloma. Treatment with deep X-rays and urethane with considerable improvement. Survival 6 years after first symptom.

Mrs. E.E.W. (Hospital No. 32835), a housewife aged 61 was admitted to the National Hospital, Queen Square, on 9th August 1951, under the care of Sir Charles Symonds.

HISTORY.

Her family had no ancestral taint and she herself had suffered no illnesses of note in the past.

Four years before admission, she experienced a brief episode of diplopia, and over the next year she had several similar attacks. Two years before admission, it returned again and continued intermittently for 5 months, but again disappeared. One year later (one year prior to admission) she

noticed the vision in the right eye was gradually failing, and when she reached hospital she could only distinguish shadowy outlines with it. The left eye was normal. Four years before admission she rapidly became deaf in the right ear, and for one year the hearing in the left ear had been similarly, but less severely, affected. There was also loud tinnitus in both ears. Bilateral loss of smell had been present for 1 year, and she had recently noticed a vague tingling all over the right face. At no time had she suffered any pain.

EXAMINATION.

She was a healthy-looking, active woman who was so deaf that satisfactory contact could only be made by writing. Her mental state was normal, as was the skull, but there was slight proptosis of the right eye. The nasal septum was deviated to the left and in the right posterior nares there was a soft, purplish, polypoid mass which seemed to be growing from the roof of the nasopharynx. She appreciated none of the test odours, but there was complete nasal obstruction. Visual acuity in the right eye was reduced to hand movements in the upper nasal field only, and vision on the left was J.14, with correction.

Cerebrospinal Fluid. Pressure, 100 mm., Cells, 3. Protein, 50 mgm. per cent. Lange, 0001110000; Wassermann reaction (W.R.), negative.

Electroencephalogram. Gave no evidence of an intracranial space-occupying lesion.

Left percutaneous carotid angiogram. (fig. 6) The carotid siphon was elevated and in the lateral views the soft tissue shadow previously noted was seen to contain many pathological vessels and the internal maxillary artery was unusually large.

OPERATION. 29th August, 1951.

Mr. C.P. Wilson at the Middlesex Hospital made a biopsy of the nasopharyngeal neoplasm, and microscopic examination revealed a typical plasma cell myeloma (fig. 7).

ADDITIONAL INVESTIGATIONS.

Further X-rays revealed myelomas of femoral shafts, humeri and radii, as well as doubtful areas of erosion in the right second and left ninth ribs.

Blood. Picture: Haemoglobin, 79 per cent. Red cells, 4.1 million per cmm. White cells, 12,600 (differential count normal):

Erythrocyte sedimentation rate (E.S.R.), 62 mm. (Westergren) (Corrected to 38 mm.) in the first hour.

W.R., negative.

Serum proteins: Total proteins: 9.3 g. per 100 ml. Albumin 2.7 g. per 100 ml. Globulin 6.3 g. per 100 ml. Fibrinogen 0.34 g. per 100 ml.

Bone-marrow examination (sternum) showed a slight increase in the number of plasma cells but no conclusive evidence of myelomatosis.

Urinalysis. No Bence Jones proteinuria was found on repeated testing.

PROGRESS.

She was given a course of deep X-ray irradiation (total dose 4,900 r.) directed to the base of the skull, and a course of 78 gms. of urethane. When discharged home on 8 November 1951 there had been improvement in her nasal airway, and the right sixth nerve weakness was less marked.

On 20 March 1952, 5 months later, she reported that the vision in the right eye had increased and that the airway was better, but hearing was unchanged. Her general condition was good, and her weight had not changed. The sense of smell was now normal on both sides, the original defect having been due to nasal obstruction. The acuity in the right eye, although better, was still less than 6/60. The left visual field was normal and on the right the lower temporal quadrant was principally involved. The left 6th nerve palsy had almost disappeared, but other cranial nerve lesions were unchanged. The rest of

the central nervous system and the other systems were still clinically normal. X-rays showed no change in the skull lesion, but there were additional foci in the femoral shafts. There was no Bence Jones protein in the urine and the blood count was normal. The serum proteins had now only a slight excess of globulin. No further therapy was given.

In August, 1953, 2 years after investigation and treatment in hospital, she was examined again. She was continuing to improve and her general condition was excellent. Diplopia had disappeared and vision, particularly in the left eye, was better. Charting optic visual fields revealed an almost normal field on the left but a dense central and paracentral scotoma in the right eye (Fig. 8) She could now hear a shouted voice and the sense of smell was normal. X-rays revealed that new bone was forming at the base of the skull but the long bone myeloma persisted. The naso-pharyngeal mass was still present. Apart from slightly increased total serum protein, the blood was entirely normal and there was no Bence Jones proteinuria.

She has thus survived for 6 years.

COMMENT.

The cranial lesion in this case was thought to

be a nasopharyngeal carcinoma, and other possibilities considered were a chordoma or a metastatic deposit. After the biopsy, further investigations revealed ample evidence of a much more widespread disease process, despite the fact that all the symptoms and signs were referable to the skull lesion. If these had not been carried out, it would have been easy to style this myeloma as 'solitary'. The disease has now been present for 6 years and the case is an example of the slowly progressive type of multiple myeloma, the usual pain, short history, fractures and general debilitation being absent.

The erosion of the skull base was a striking feature in this case and the lesions probably corresponded closely with that described by Wright (1953) in his case, and mentioned already (p. 24).

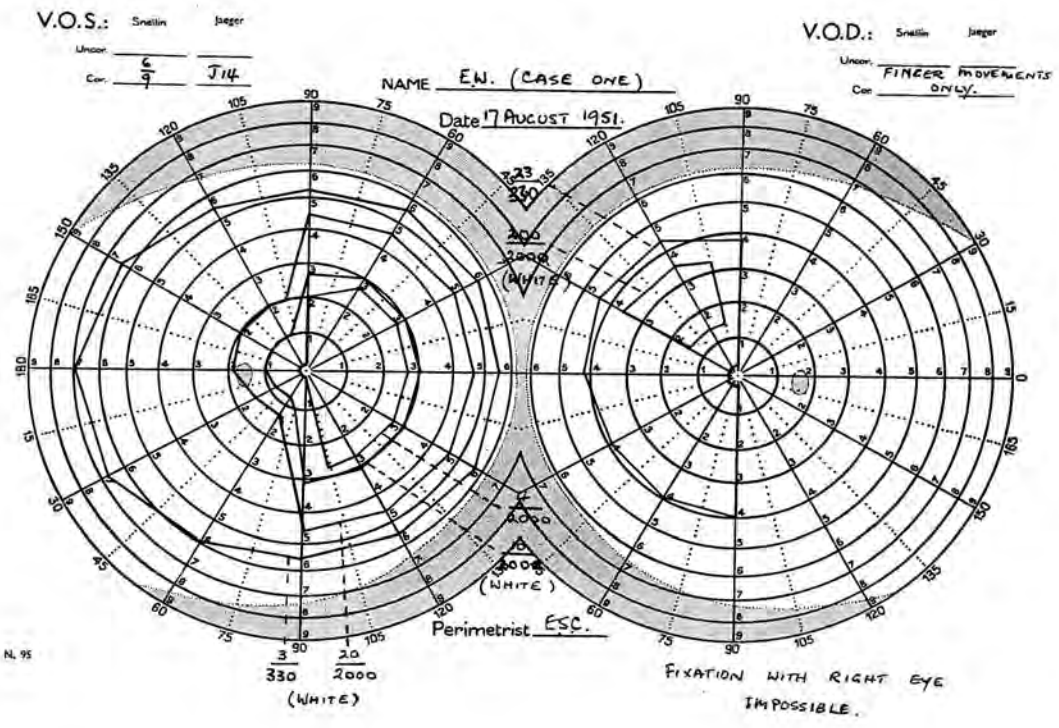

Fig.3. CASE ONE. Visual fields charted before treatment was begun.

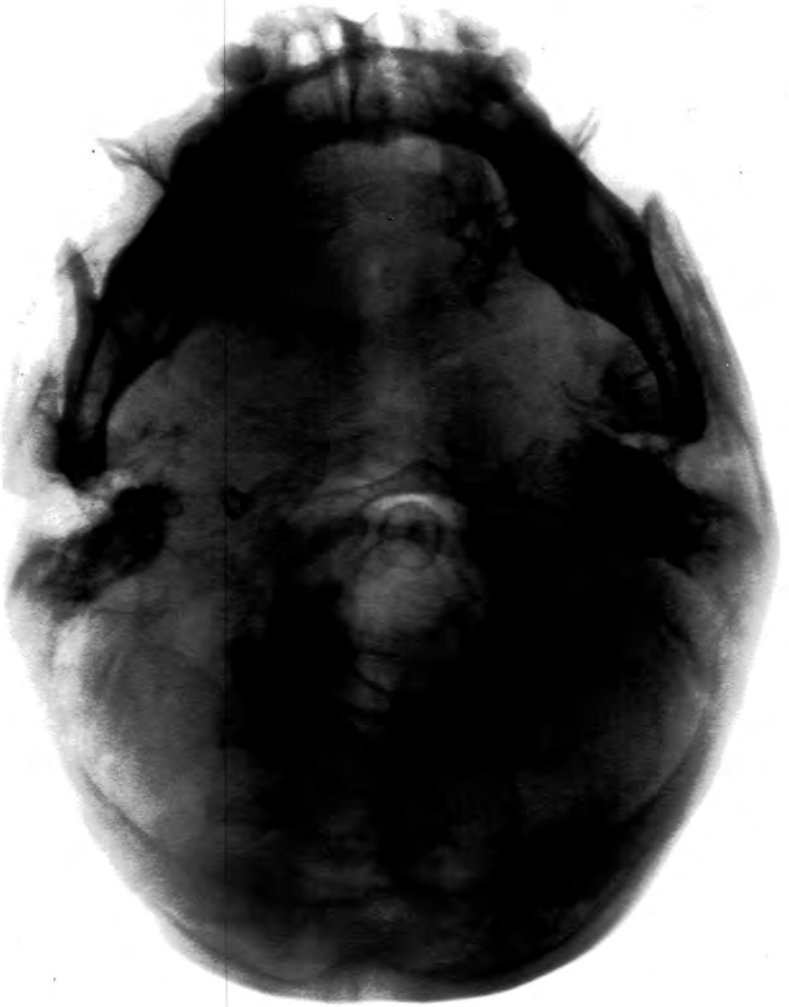

Fig.4. CASE ONE. X-ray of skull, full axial view. The extensive bony erosion produced by the myeloma is shown.

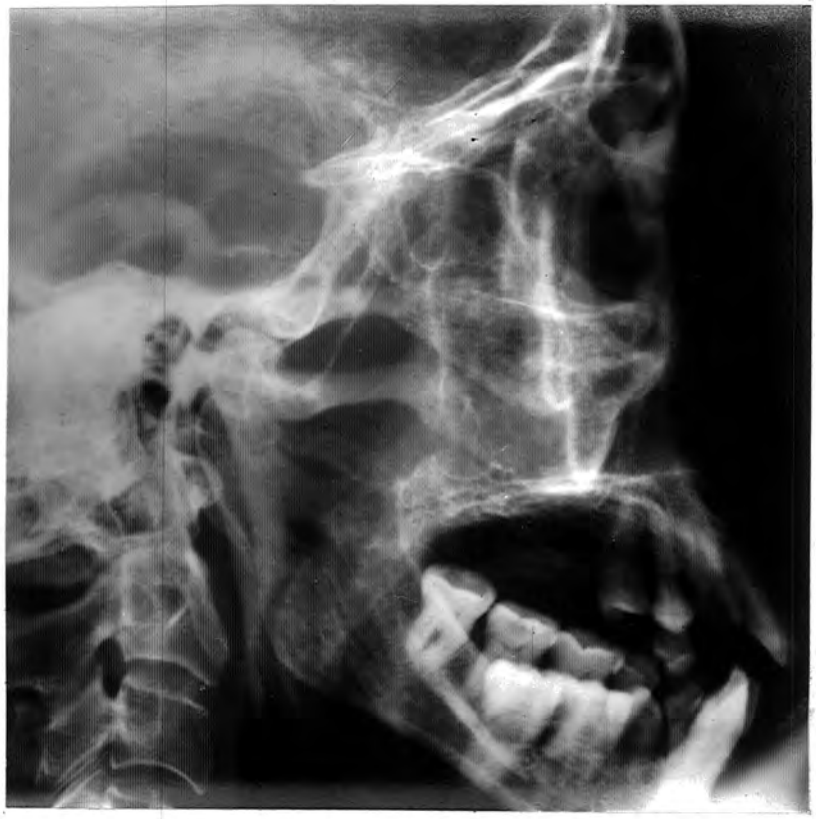

Fig.5. CASE ONE. X-ray of skull, lateral view. Erosion of base is shown.

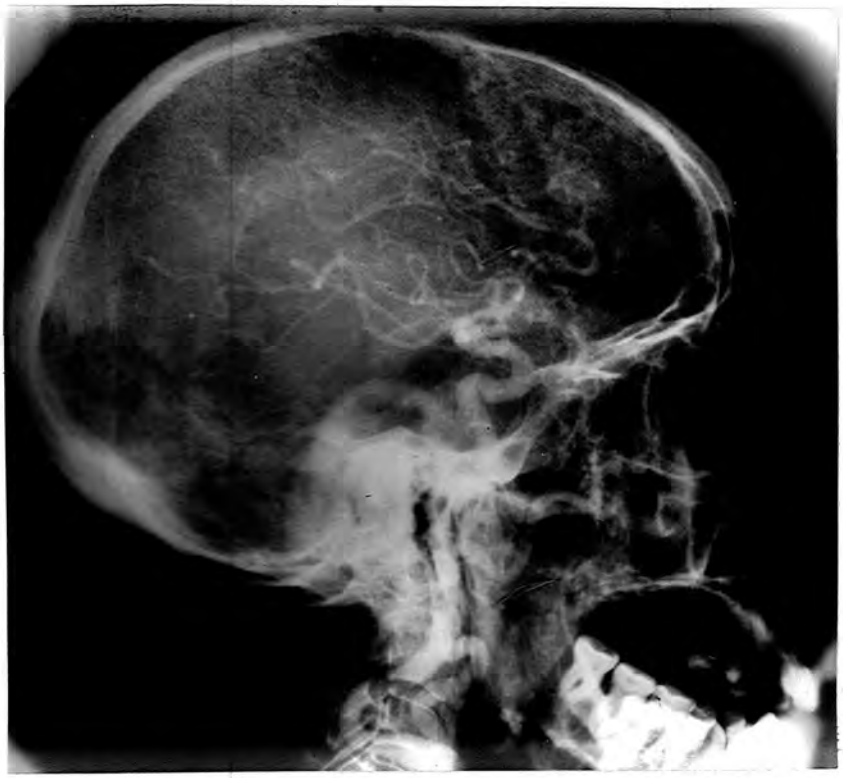

Fig.6. CASE ONE. Right carotid arteriogram, lateral view. The carotid siphon is elevated and the internal maxillary artery is enlarged. There are abnormal vessels in the region of the basal myeloma.

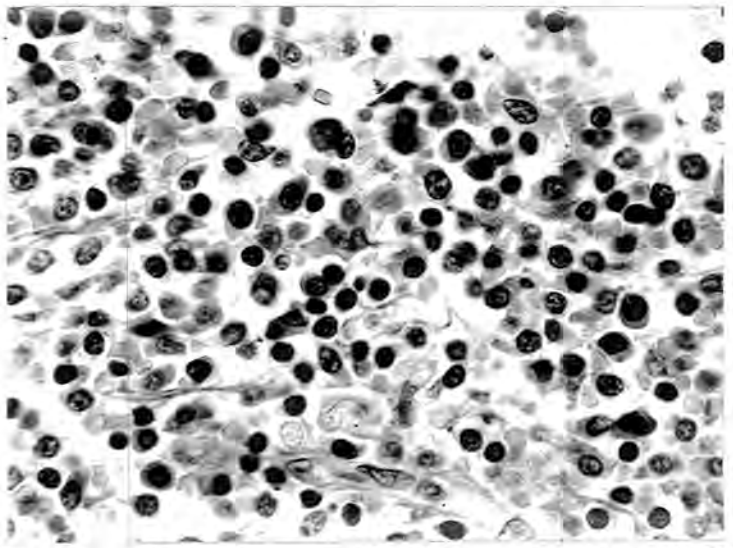

Fig.7. CASE ONE. Myeloma of the skull base, formed mainly of well-differentiated plasma cells (x 450).

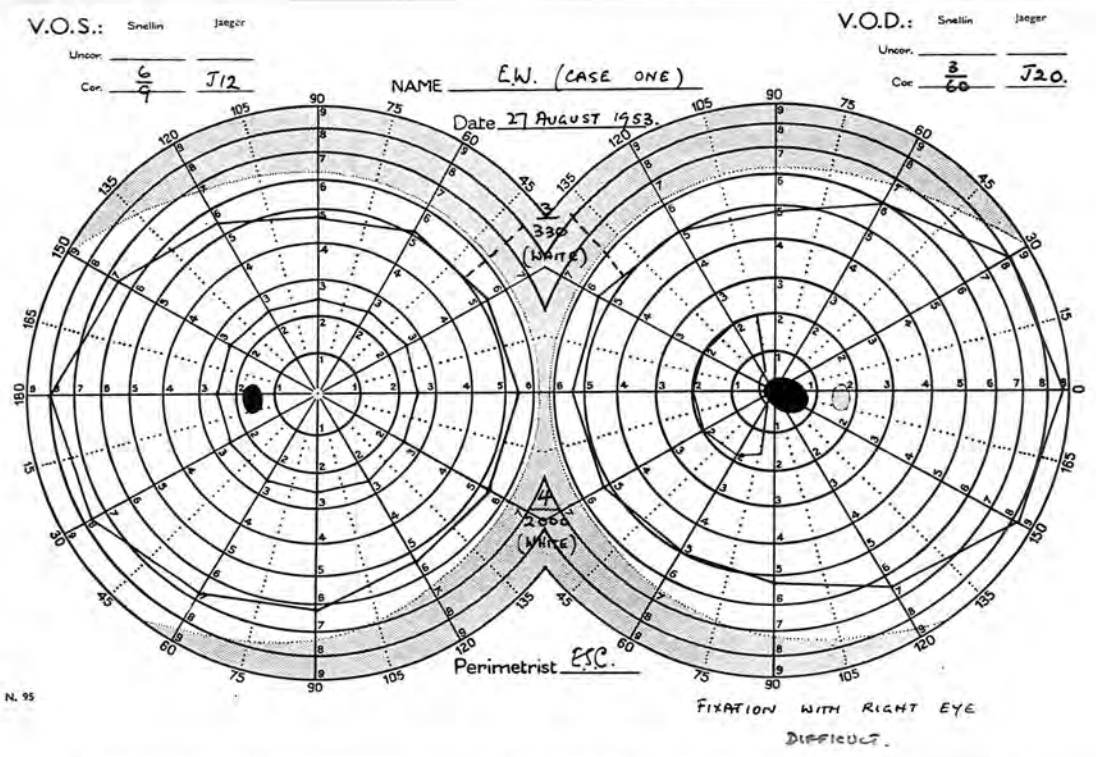

Fig.8. CASE ONE. Visual fields charted 2 years after treatment.

CASE TWO

Female, 76. 2 years of backache, loss of weight and pallor. 2 weeks of diplopia. Poor general condition and right 6th nerve palsy. Osteolytic areas in all bones, including skull, but base not examined. Improvement in palsy before death. Duration about 2 years. No autopsy.

Mrs. A.M. (Hospital No. 87739), a housewife aged 76, was admitted to Hammersmith Hospital on 9th September 1948, under the care of Dr. W.W. Brigden.

HISTORY

The history was difficult to obtain, but it appeared that she had suffered severe backache for 2 years and for one year had been bed-ridden. During this latter period, she lost a stone in weight and became progressively more pallid. 2 weeks before admission, she awoke to find that she had diplopia, accompanied by intermittent headache. Her past and family histories contributed no relevant information.

EXAMINATION

Her general condition was poor and there was a complete right external rectus palsy, which was responsible for the diplopia. There was some blurring of the vision bilaterally. The rest of the nervous system was normal, as were the other systems, and the blood pressure was 180/90.

INVESTIGATIONS.

X-rays. Skull: There were multiple osteolytic areas in the vault. The base was not examined.

Other bones: All the flat and long bones contained similar lesions.

Blood. Picture: Haemoglobin, 64 per cent. Red cells, 3.1 million per c.mm.

Urea: 300 mgm. per cent.

Urinalysis. No Bence Jones Proteinuria.

Bone marrow biopsies (sternum and iliac crest). These gave some support to the diagnosis of myelomatosis but were not diagnostic of it.

PROGRESS.

Her condition deteriorated steadily, although paradoxically, the cranial nerve palsy became less and abduction of the right eye was returning when she died in uraemia on 20 October 1948, six weeks after admission to hospital. An autopsy was not permitted.

COMMENT.

It is reasonable to suppose that the abducens palsy in this patient was produced by a myeloma of the skull base. She can be compared with the patients of Wright (1900), Bloodgood (1906), Meyerding (1925) and Hellner (1938), in whom there were single ocular nerve palsies producing diplopia, but no autopsy verification of a basal myeloma, except in the last patient, was obtained.

The orbit was not obviously involved, there was no evidence of increased intracranial pressure, and no arteriosclerosis, or any alternative aetiological agent responsible for the nerve paralysis. Unfortunately the presence of a basal lesion was not verified. The improvement of the palsy which occurred as death approached, and which was not due to therapy, is difficult to explain, but it was also reported by Hammer (1894) and Sparling et al. (1947, case 21).

CASE THREE

Female, 55. 3 months of back and pelvic pain. Multiple myelomatosis with involvement of all bones, pathological fractures, and death. Survival 9 months. Autopsy. Multiple myelomas of skull base but no clinical evidence of them.

L.H. (Hospital No. 143373), a housewife of 55, was admitted to Hammersmith Hospital on 1 February, 1953, under the care of Dr. C.A.P. Wood.

For three months, she had suffered from pain in the back and right iliac crest. X-rays showed multiple osteolytic areas in the pelvis, femora and ribs. The bodies of T9 and T10 were collapsed. The E.S.R. was 74 mm. in 1 hour (Westergren) and the bone marrow contained 20 per cent of plasma cells.

She was given radiation therapy to the painful areas and a course of urethane. Despite these measures, however, the clinical course was progressively downhill. Multiple fractures of long bones occurred and a tumour grew on the left side of her head. Head pain was a prominent symptom but there was no true headache and no signs of increased intracranial pressure; the C.S.F. was normal in pressure and content. She died on 14 July, 1953, about nine months after the disease began. At no time did she have any cranial nerve or cerebral disorders.

POST MORTEM. (Dr. C.V. Harrison).

The malignant process was widespread throughout the body. In the skull, there was a myeloma of 5-6 cm. diameter in the left parietal bone and many others scattered throughout the vault. The base was similarly affected, but none of the lesions were larger than 1.0 cm. in diameter. They were present in most of the bones but were more numerous in the sphenoid and petrous temporals (Fig. 9). The brain was normal.

COMMENT.

This case illustrates the diffuse involvement of the skull base which is probably not uncommon. As in this instance, the process is symptomless.

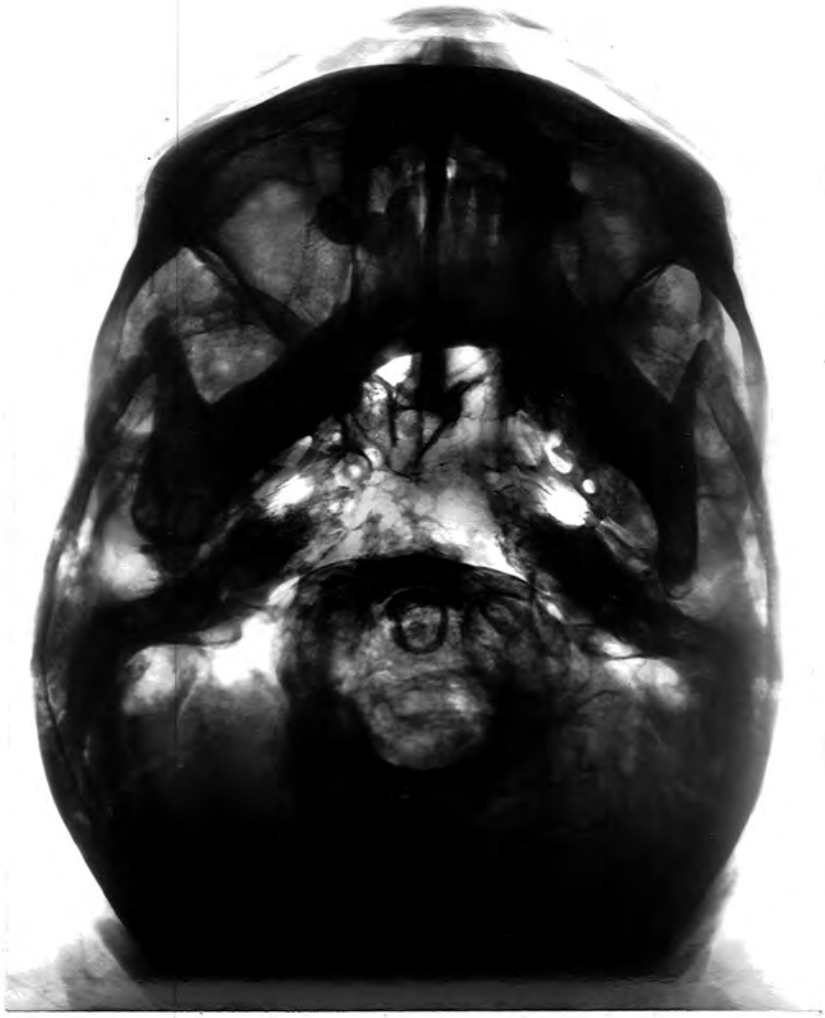

Fig.9. CASE THREE. X-ray of skull, full axial view. Multiple osteolytic lesions.

CASE FOUR

Male, 53. Lump on left side of head for 4 years, gradually increasing in size. Weak left arm and leg, headaches and giddiness for 2 months. Left sided cranial tumour 17 x 17 x 8 cms. with minimal left hemiparesis. Partial removal of myeloma and treatment with radiation. Tests for multiple myeloma not done. Death after fits, aphasia and paralyses had appeared. 6 years survival. No autopsy.

H.H. (Hospital No. 22991/44), cafe proprietor aged 53 was admitted to the Radcliffe Infirmary on 18 February 1944, under the care of the late Sir Hugh Cairns.

HISTORY.

In the past he had suffered no illnesses of note and his family history yielded no relevant information. He was right handed.

For four years he had noted a pulsating, painless lump in the left parietal region which had gradually increased in size, but more rapidly over the preceding four or five months. Soon after its appearance an attempt was made to excise the tumour, but it was found to be very vascular. He also complained of postural vertigo, occasional headaches, and for two months the left arm and

leg had been getting progressively weaker.

EXAMINATION.

There was a large bilobular tumour of the skull mainly fronto-parietal in location, measuring 17 cms. in diameter and protruding 8 cms. from the skull surface. (Fig. 10). There was no pulsation and no bruit could be heard over it.

In the central nervous system the only abnormalities were slight weakness of the left lower face, arm and leg, and an equivocal plantar response on that side. There was no aphasia, papilloedema, visual field defect, or sensory impairment. Other systems were normal.

INVESTIGATIONS.

X-rays. Skull: Almost the whole of the left side of the cranium had been eroded by the tumour and in the soft tissue shadow there were multiple flecks of calcification. Large vascular channels could be seen grooving the bone close to the tumour (Fig. 11).

Cerebrospinal Fluid. Pressure, 265 mm. Cells, 2 lymphocytes. Protein, 15-20 mgm. per cent. Lange, no change. W.R., negative.

Blood. Picture: Haemoglobin, 70 per cent. Red cells, 3.9 million per c.mm. White cells, 18,000 per c.mm. (Neutrophils, 87 per cent, lymphocytes, 11 per cent and

monocytes 2 per cent).

No other investigations were carried out.

OPERATION. 24 February, 1944. (Mr. J.B. Pennybacker).

An attempt was made to excise the tumour but his condition throughout the operation was very precarious and only a small portion of it could be removed. The dura was seen only in the occipital region and it appeared normal.

HISTOLOGY. (Dr. A.H.T. Robb-Smith)

The tissue had the characteristics of a "plasmacytoma". Typical plasma cells were lying in sheets without any pattern and amongst them was a material thought to be amyloid. (Fig. 12).

PROGRESS.

His post-operative recovery was uneventful and 3 months later he was given a course of radiation therapy (5000 r) with some slight diminution in the size of the tumour.

One year later his general condition and the skull tumour were much the same and he was given further radiation treatment. After this the mass became harder and X-rays showed the presence of an increased amount of calcification.

Two years after the operation, he was not suffering headache and there was no evidence of increased intracranial

pressure. The postural vertigo was still present, and the left sided signs were unchanged. Three months later, however, he had transient attacks of aphasia and on 23 December 1946 he died, six years after he first noted the skull tumour. Before his death he had suffered from epileptiform seizures and there had been limb paralyses two weeks earlier. Unfortunately, additional information could not be obtained and autopsy was not carried out.

COMMENT.

This case cannot be considered as an example of solitary myeloma of the skull as a search for evidence of myeloma elsewhere was not made and a post-mortem was not performed. It would seem, however, that the clinical picture and his death were produced by the cranial lesion alone.

The cranial myeloma was single and massive and the resultant appearance approximated to that of Batt's (1939, p. 811, figure 2) patient. The few neurological signs were ipsilateral to the skull tumour and it is suggested that they were due to pressure on the displaced right cerebral peduncle by the free edge of tentorium cerebelli. The terminal attacks of aphasia, however, indicated direct left cerebral hemisphere involvement, and no doubt the convulsions were also caused by this. Details concerning

the limb paralyses are not available. There was never any evidence of increased intracranial tension, although it may have been present terminally; the initial raised C.S.F. pressure is of doubtful significance as it was only found on one occasion. The neoplasm was relatively insensitive to irradiation for it grew despite the therapy, but progress of the disease may have been delayed thereby. He died six years after first noting the calvarial lesion. Surgery was hazardous in this case, but the reason was not obvious; it was not apparently due to massive blood loss, although the tumour was very vascular.

The calcification within the tumour is an unusual feature, but has been described by Krainin et al (1949), and the intercellular amyloid substance is of considerable interest, for the occurrence of primary amyloidosis with myeloma is well-known.

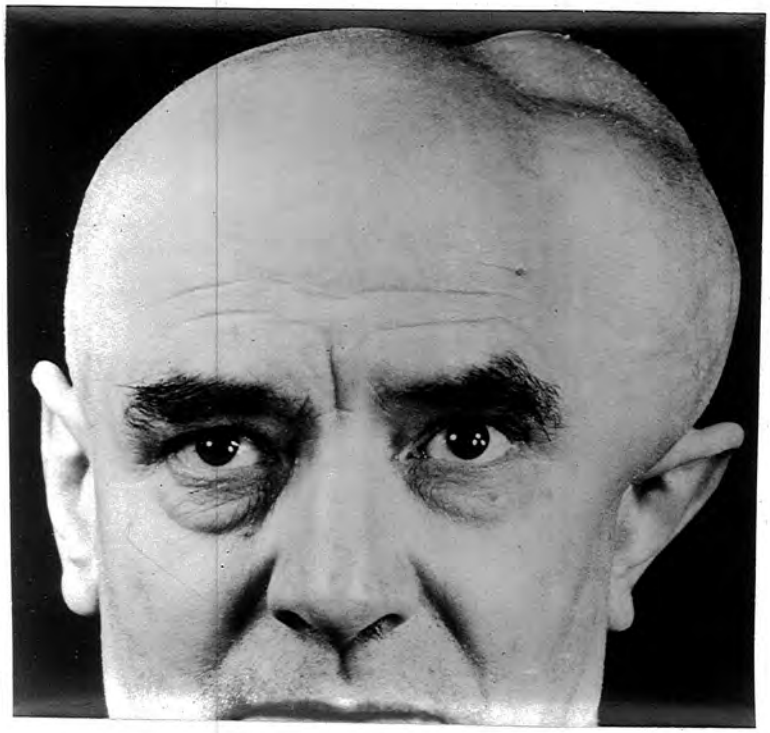

Fig.10. CASE FOUR. Photograph of patient showing cranial tumour.

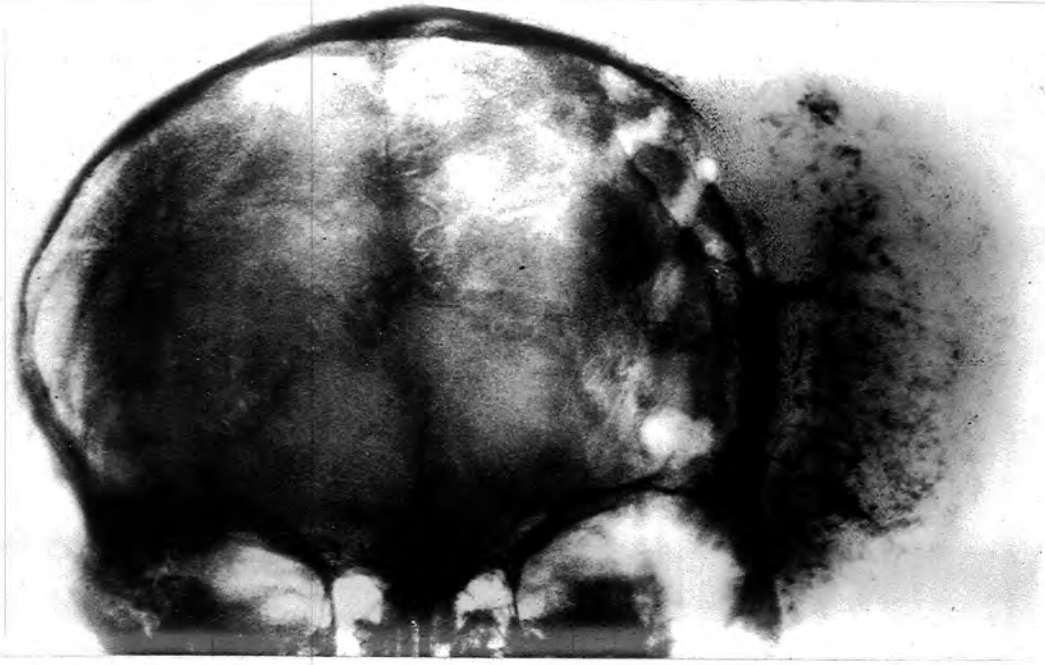

Fig.11. CASE FOUR. X-ray of skull, axial view. Note calcification within soft tissue shadow and the enlarged vascular channels.

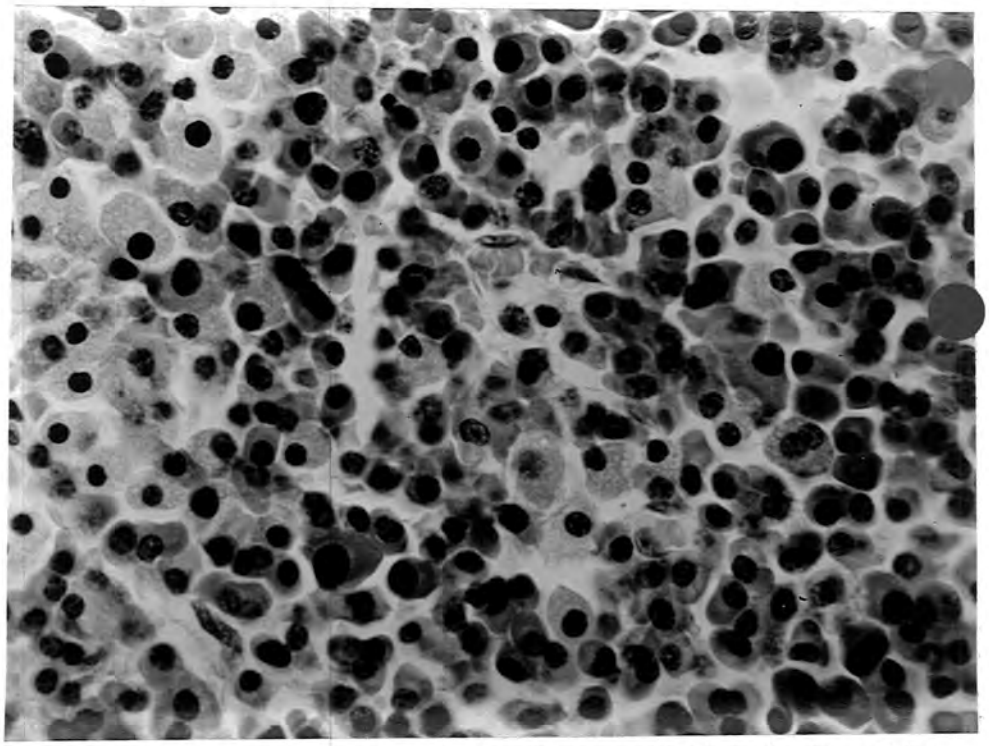

Fig.12. CASE FOUR. Myeloma of the left side of the calvarium. Most of the cells are typical plasma cells (x 580).

CASE FIVE.

Female, 58. 2 years of intermittent occipital headache worse for 3 months and with vomiting, drowsiness and periodic breathing. Signs of increased intracranial pressure and minimal left arm weakness and hypertonia. B.P. 190/110 and heart enlarged. Ventriculogram and operation revealed an extracerebral plasma cell myeloma of the dura of the tentorium cerebelli. Death. Autopsy.

Miss W.M.U. (Hospital No. 32516) a school teacher aged 58, was admitted to the National Hospital on 25 July 1951, under the care of Dr. J. St. C. Elkington.

HISTORY.

There were no significant features in her family history, and until the onset of her symptoms she had been quite healthy. She was right handed.

For about two years she had experienced intermittent occipital headaches, diagnosed as migraine and treated as such with relief. However, three months before admission these headaches became more severe and about six weeks before she entered hospital she began to suffer from a severe stabbing pain in the right temporal region spreading to the occiput. Over a few days, this pain subsided but did not disappear and five or six days

later it again grew worse and was now accompanied by vomiting, drowsiness and Cheyne-Stokes' respiration. Again improvement occurred but there were two further spells of head pain before the final episode three days prior to admission. Now as well as suffering severe headache, she was confused and semiconscious.

EXAMINATION.

She was very drowsy, but could be roused to answer questions, and there was well-marked Cheyne-Stokes' breathing. The optic discs were bilaterally swollen to an equal degree and there were arteriosclerotic changes in the retinal blood vessels. The visual fields seemed to be full to menace. The left pupil was slightly larger than the right, but its reactions were normal. In the left arm there was hypertonia and slight distal weakness, but motor functions of the legs were intact. The tendon reflexes were brisk and equal and the plantar responses flexor. The rest of the central nervous system was normal, as were other systems, except for a blood pressure of 190/110, and some enlargement of the heart, confirmed by X-ray.

INVESTIGATIONS.

X-rays. Skull: Erosion of the dorsum sellae due to raised intracranial pressure was demonstrated, but

there were no other abnormal features.

Electroencephalogram (Dr. W.A. Cobb) was thought to be consistent with a right frontal tumour, either large and infiltrating or surrounded by widespread oedema.

Ventriculogram (26 July 1951). Mr. L.S. Walsh. There was a shift of 1.0 cm. of the septum pellucidum to the left and the floor of the right occipital horn was elevated, indicating a right sided tempero-occipital space-occupying lesion. (Fig. 13).

FIRST OPERATION (26 July 1951). Mr. L.S. Walsh.

Through a right temporal burr hole and at a depth of 4.0 cm. a brain canula encountered abnormal tissue, which Dr. W. Blackwood thought was typical of a plasma cell myeloma.

FURTHER INVESTIGATIONS.

X-rays. Unfortunately, she was too ill to be X-rayed again, but a review of the skull and chest films showed no myelomas.

Blood. Picture: Haemoglobin, 108 per cent. Red cells, 5.34 million p. c.mm. White cells, 6,200 p. c.mm. (differential count normal).

Serum proteins: Total, 7.3g.per 100 ml. Albumin, 4.1g.per 100 ml. Globulin, 3.2g. per 100 ml. A:G ratio, 1.3:1.

Cerebrospinal Fluid. Cells, 3. Protein, 50 mgm. per cent. Lange, no change. W.R., not done.

PROGRESS.

Two days after the ventriculogram and biopsy, she was a little more drowsy and ventricular drainage was established with an improvement in her condition.

SECOND OPERATION (30 July 1951). Mr. W. McKissock.

A reddish coloured extracerebral tumour which appeared to be arising from the floor of the middle fossa and extending towards the free edge of the tentorium was seen and its removal begun. The deepest part of the tumour had to be left because of troublesome haemorrhage, but 6.26 gms. were extracted.

She remained deeply unconscious and died thirty six hours after the second operation.

POST MORTEM REPORT (Dr. W.G.P. Mair).

Skull: The cranium was normal except for the operation flap, and the bones of the base, after the dura had been removed, were healthy and there were no myelomas.

Dura Mater: On the convexity, apart from surgical trauma, the dura mater was intact. At the base it was readily removed from the middle fossa and was normal everywhere except for the right half of the tentorium cerebelli, most of which had been removed at operation.

Only the thickened medial part, comprising the free edge, remained; this was thickened, and fixed to it was a small portion of the tumour that had been left behind at operation.

Brain: At the site of operation there was no evidence of tumour tissue having invaded the brain. The right cerebral hemisphere was considerably swollen, and there was mid-brain distortion and herniation of cerebellar tonsils.

Except for the heart, which was slightly enlarged, and the liver, which was large and very pale, other organs and tissues were normal. There were no myelomas of the lumbar vertebrae, femora or humeri.

HISTOLOGY.

The biopsy diagnosis of plasma cell myeloma was confirmed (Fig. 14). The cerebral tissue adjoining the lesion was normal, and so were all other structures examined. Several samples of bone-marrow from a number of bones were normal and there was no plasma cell infiltration of the petrous bone.

COMMENT.

This is a most unusual case. There were no distinctive features, for it presented as a space-occupying

lesion, and as with many other brain tumours there were no clues to its pathology until the biopsy examination.

Reconstructing the appearances of the tumour from the operation and autopsy findings, it arose from the right half of the tentorium cerebelli and extended medially up to the free edge. It was impossible to say from which layer of dura mater it had arisen for both were thickened and infiltrated. However, the bulk of it was growing from the superior surface and when seen at operation it had the appearance of a myeloma and there was no dural covering. It distorted the brain but, as with all other intracranial myelomas, there was no actual invasion of brain tissue, despite the absence of the dural barrier. The bone of the base of the skull was normal everywhere, including the petrous portion of the temporal bone, which showed no abnormality on section. Thus it can definitely be stated that the myeloma originated from the dura and not from the bone. This case is therefore unique.

Unfortunately, investigations to establish other evidence of myeloma were not completed. She was too ill to be fully X-rayed, but no deposits in lumbar vertebrae, femora or humeri could be found at post-mortem. The bone-marrow was not examined microscopically during life,

although at autopsy it was normal in sternum, vertebrae, ribs and both femora; as it was not fresh, however, abnormalities cannot be entirely excluded.

There is no doubt that this was a true myeloma allied to multiple myeloma but it is not possible to say whether it was solitary or not. It is, however, reasonable to speculate that when she died, it was the only manifestation of a disease that would later become more widespread. Her early death was due entirely to the situation and not to the malignancy of the myeloma, and had it been in a less nocuous position she might have survived for generalization to take place at a later stage. It would, however, be difficult to conceive of a more solitary tumour and perhaps this case supports Christopherson and Miller (1950) and their concept of a solitary myeloma as a distinct entity, both clinically and pathologically.

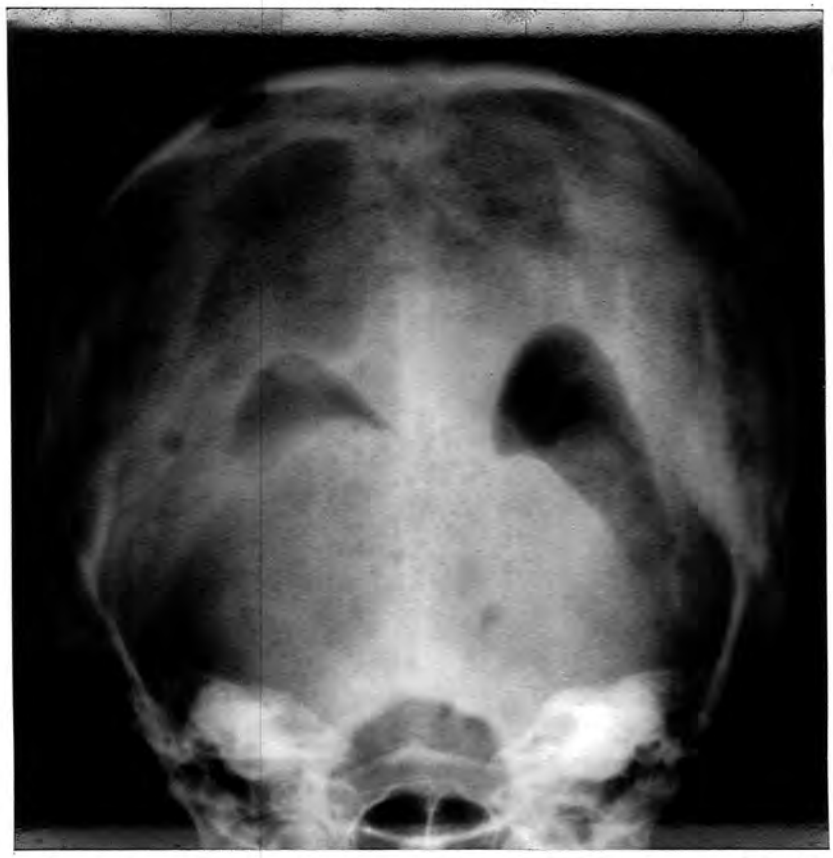

Fig.13. CASE FIVE. Ventriculogram, half axial view, A.P., indicating a right temporal space-occupying lesion.

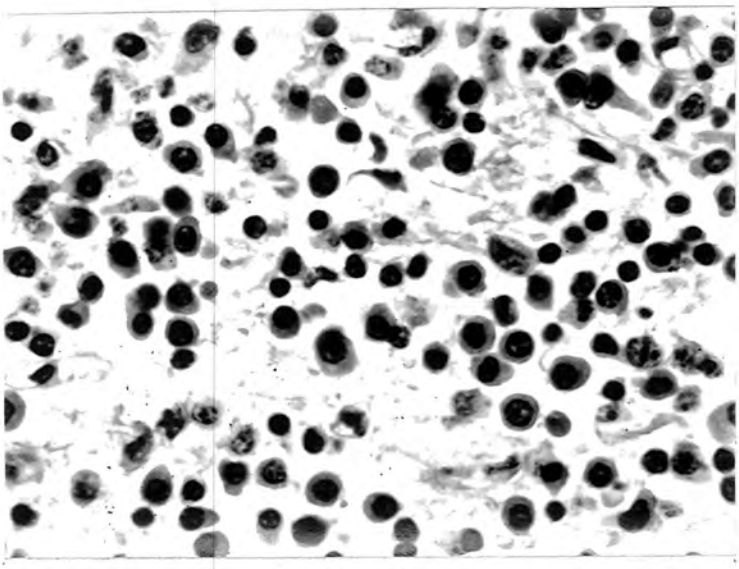

Fig.14. CASE FIVE. Myeloma of the tentorium cerebelli, consisting mainly of plasma cells. (x450).

CASE SIX

Male, 67. One year of diplopia, 2 months of left ptosis and proptosis. Left supraciliary mass and X-rays showed osteolytic lesions in this and other regions. Partial removal of left orbito-frontal tumour (verified as myeloma) and radiation therapy given, but generalization and local recurrence occurred. Death. Total survival 3½ years. No autopsy.

T.B. (Hospital No. 295/43), a butcher aged 67, was admitted to the Radcliffe Infirmary Oxford, on 18 May 1949, under the care of the late Sir Hugh Cairns.

HISTORY.

In the past he had enjoyed good health and there was no relevant information extracted from his family history.

One year before admission, he noticed double vision which was constantly present and most marked when he looked downwards. For two months there had been progressive drooping of the left upper eyelid and slight protrusion of the eye. His general health had been excellent and he had no other symptoms.

EXAMINATION.

His general condition was good. There was slight proptosis of the left eye, the globe being pushed downwards and slightly laterally. In the left supraciliary region, there was a firm non-tender mass, and a similar lesion was palpable in the right occipital region.

Visual acuity in the right eye, J 1 and in the left eye J 2 (both uncorrected). Optic fundi, visual fields and pupils normal. Upward movement and adduction of the left eye were slightly limited with the production of diplopia in all directions. The central nervous system and other systems were normal.

INVESTIGATIONS.

X-rays. Skull: A large area of bone destruction was found in the left frontal region, extending to the orbit, and similar but much smaller areas elsewhere (Fig. 15 and 16).

Urinalysis. No Bence Jones proteinuria.

OPERATION. 26 May 1949 (Mr. J.B. Curtis).

A soft vascular tumour was found in the left supraciliary region. Much of the orbital roof on this side had been destroyed and tumour tissue was invading

the orbit. Only partial excision was possible.

HISTOLOGY. (Dr. F.D. Bosanquet).

The material removed was very cellular and many of the cells were plasma cells. No mitroses were seen and there was no necrosis. The microscopical appearances were those of a plasma cell myeloma (Fig. 17).

PROGRESS.

The patient made a good post-operative recovery and was given three courses of deep X-ray therapy directed to the left orbital region. The proptosis and diplopia disappeared and he was discharged on 3 June 1949. A year later, he was found to have a myelomatous deposit in the sixth thoracic vertebral body, and six months after this noted the return of proptosis, ptosis and diplopia. He was given another course of radiation therapy but after six months his condition had deteriorated further. He now had evidence of left cerebral hemisphere compression and he died on 8 August 1951, three and one quarter years after the onset of the disease. It was not possible to carry out an autopsy.

COMMENT.

This was a typical case of multiple myeloma presenting with ocular features due to an orbital myeloma

that had presumably spread to the frontal bone. Its exact site of origin cannot be determined but may have been the contents or roof of the orbit. Partial removal and irradiation produced only temporary improvement and the classical course of the disease was observed.

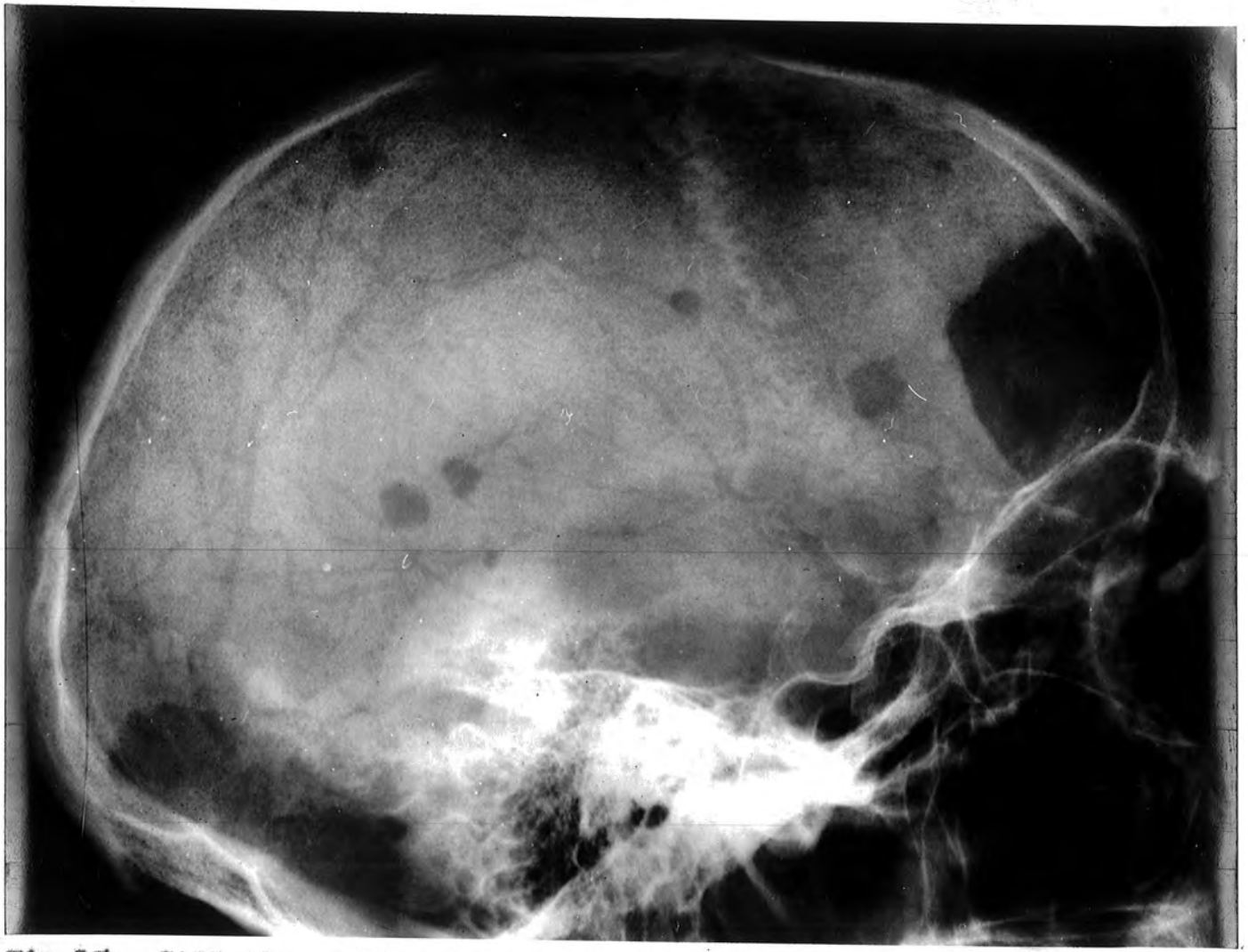

Fig.15. CASE SIX. X-ray of skull, lateral view. Large left fronto-orbital myeloma with smaller osteolytic areas elsewhere in the vault.

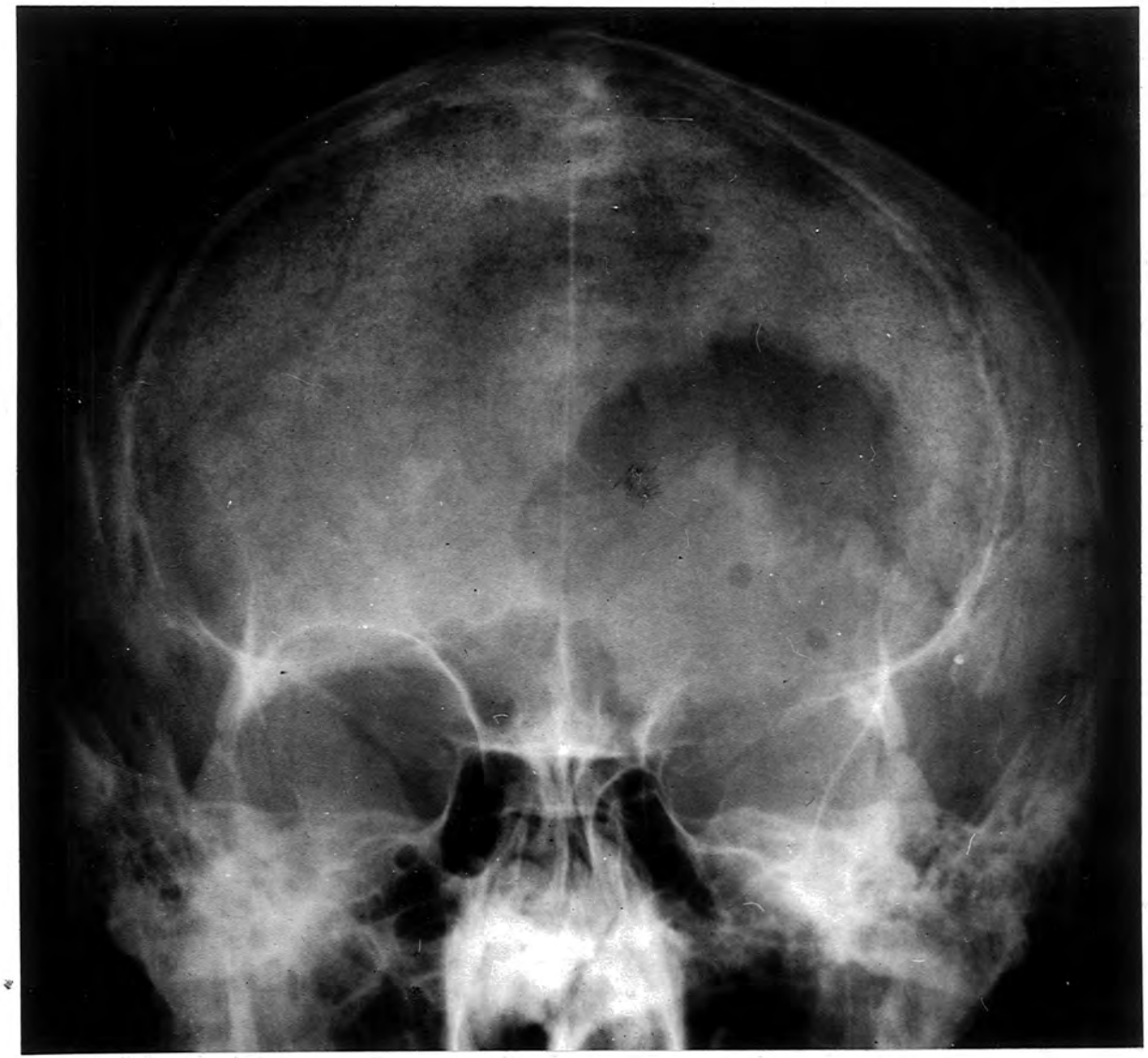

Fig.16. CASE SIX. Skull X-ray, A.P. view. Large left fronto-orbital myeloma.

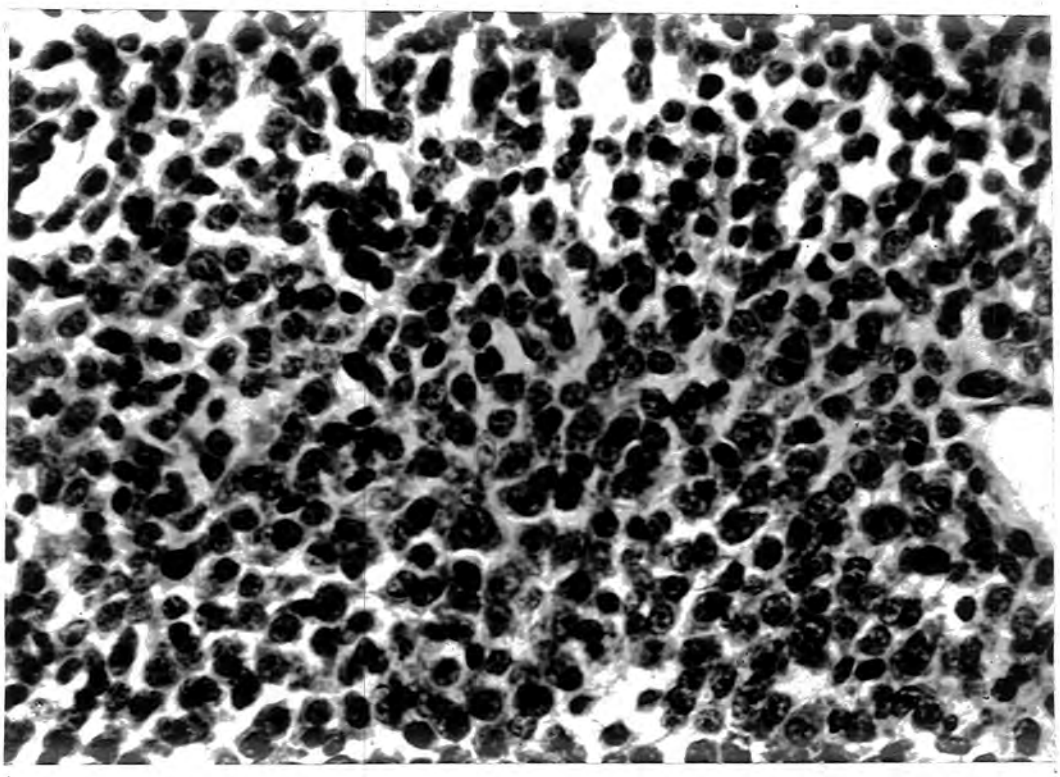

Fig.17. CASE SIX. Left fronto-orbital plasma cell myeloma. (x580).

CASE SEVEN.

Female, 60. 9 months of headache following left frontal injury. 3 or 4 months of left frontal tumour with left ptosis and proptosis. Biopsy revealed a plasma cell myeloma. Bence Jones proteinuria. Partial removal with development of coma and right hemiplegia, not influenced by further decompression. Death. Total survival about 9 months. Autopsy. Myeloma involved sinuses and orbital roof.

L.C., a housewife aged 60, was admitted to the London Hospital on 24 March, 1938 under the care of the late Sir Hugh Cairns.

HISTORY.

Nine months before admission she had fallen and struck the left side of her head but had not lost consciousness. Thereafter she suffered headaches which were mainly left frontal and which became progressively more severe. For three or four months there had been a swelling of the left forehead, the left eye was slightly more prominent and the upper lid was drooping. Recently she had been less alert mentally but had noted no other symptoms.

EXAMINATION.

A slightly obese, cheerful woman in no apparent distress. A mass 11.0 cm. in diameter occupied the left frontal bone. Its elevation above the skin surface was slight but it extended down to involve the supra orbital region and the upper orbit. It was slightly tender, fluctuant and a distinct systolic bruit, which could be obliterated by pressure on the ipsilateral carotid artery, was heard over it. The irregular edge of a cranial defect could be felt beneath. There was slight proptosis and ptosis on the left and a fullness above the eye. (Fig 18).

Visual acuity, both eyes J 1 and 6/18 (corrected). Optic discs and fields normal. The left pupil was slightly smaller than the right but had normal reactions. Upward and lateral movements of the left eye were restricted.

The central nervous system and other systems were normal.

INVESTIGATIONS.

X-rays. Skull: There was extensive destruction of the left frontal region extending to the left orbit (Fig 19).

Chest: Normal.

Long bones: Normal.

Blood. Picture: Haemoglobin, 94 per cent. White cells, 8,960 (differential count normal).

Cerebrospinal fluid. Pressure, 140 mm. Cells, 1. Protein, 25 mgm. per cent. Lange, no change. W.R., negative.

Urinalysis. Bence Jones protein present.

Biopsy. 30 March, 1938 (Mr. J.B. Pennybacker). Tissue removed from the skull tumour was reported by Professor D.S. Russell as being diagnostic of a myeloma. (Fig. 20).

FIRST OPERATION. 5 April, 1938 (Sir Hugh Cairns and Mr. J.B. Pennybacker).

The tumour although a product of the bone was firmly attached to the dura mater which was intact except for two areas at the centre of the tumour where the myelomatous tissue had extended through it. An attempt was made to remove the tumour, but partly because of its vascularity (ligation of the ipsilateral common carotid artery did not help) and partly because of its adherence to the dura, this was only partially successful.

PROGRESS.

The following day the patient was comatose and had a right hemiplegia, and as there was no improvement a second operation was carried out on 7 April 1938. The left frontal lobe was very oedematous and a portion of it was removed. There was some temporary improvement,

but she did not regain consciousness and died two days later.

AUTOPSY. (J.R.C.)

The remnants of the myeloma were found and it was seen that tumour tissue had invaded the left frontal, left ethmoidal, and right frontal sinuses, and that there was a defect in the roof of the orbit, with growth on the surface of the orbital fascia displacing the contents. The bone marrow was normal to macroscopical examination in the sternum, vertebrae, one humerus, ribs, and other bones. No other abnormal features were detected.

COMMENT.

The myeloma in this case had grown from the frontal bone to involve the orbit secondarily, and although it was single, the presence of Bence Jones proteinuria indicated a more widespread process. Nevertheless it was felt that surgical intervention was justified, but the difficult operation illustrates the hazards of attempting complete excision of these neoplasms. As the cases of Morax (1919), Meyerding (1925) and Fuerste and Zuckerman (1950), there was a close relationship with trauma.

This patient shows several of the features that were described by Lecène (1919) in his case; the localization was the same, a bruit was audible in both, and

in each, the ethnoid and frontal sinuses had been invaded. Although cerebral compression had occurred, no clinical evidence of it was present. The post-mortem findings in Case Seven were probably similar, but less extensive, to those figured by Morax (1926, Planche IV, Figure 3).

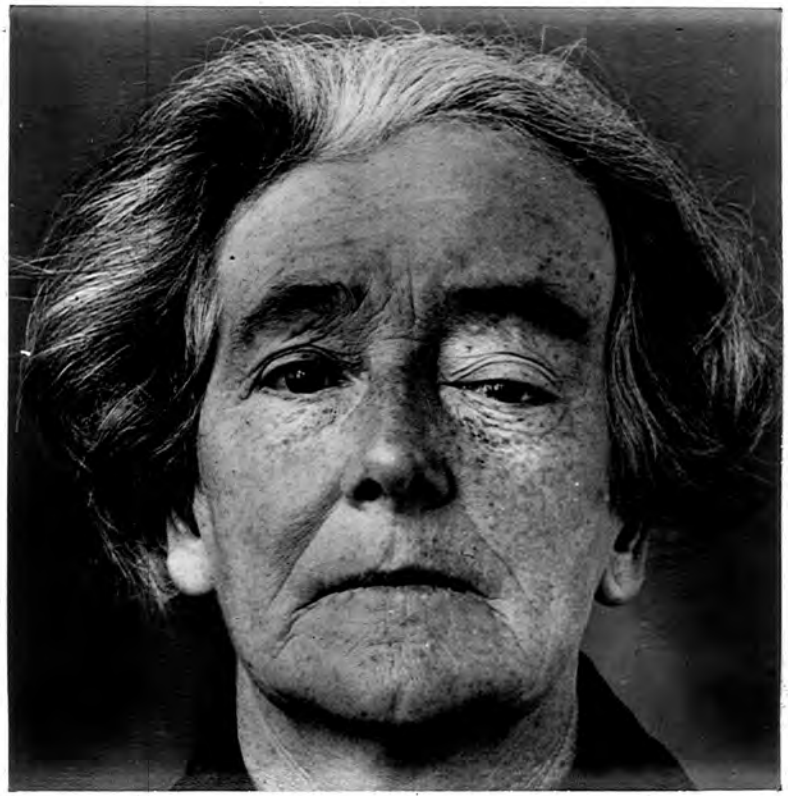

Fig.18. CASE SEVEN. Left frontal myeloma invading orbit to produce ocular displacement and slight proptosis.

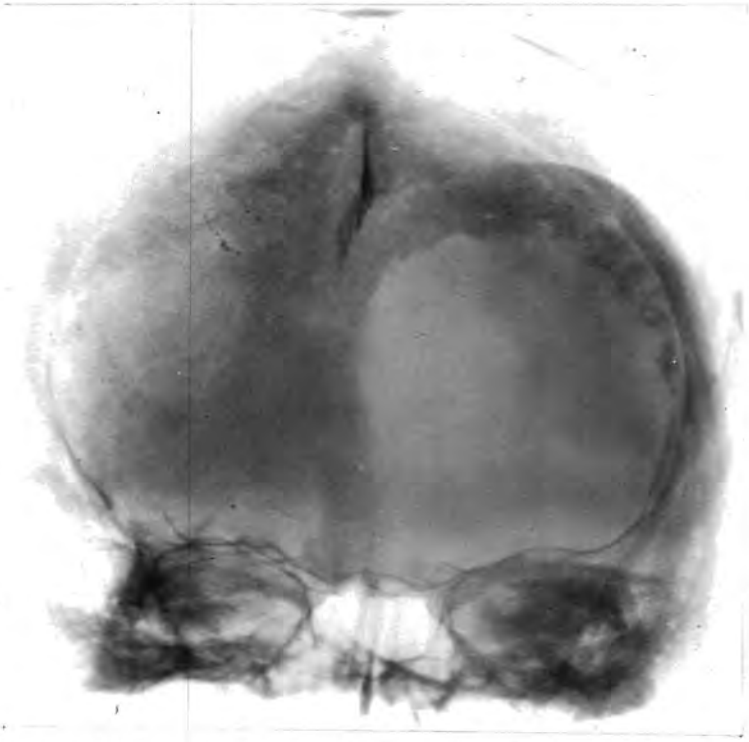

Fig.19. CASE SEVEN. X-ray of skull, A.P. view, showing large left frontal myeloma.

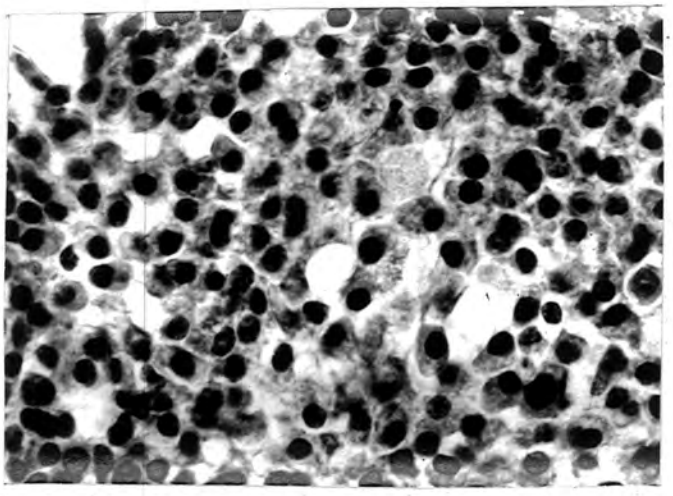

Fig.20. CASE SEVEN. Plasma cell myeloma of frontal bone (x580).

CASE EIGHT.

Male, 37. 9 weeks of increasing leg weakness and sensory loss. Severe spastic paraplegia with T5 sensory level. Increased C.S.F. protein. Collapsed body of T6 and changes in T4 and left 9th rib. Decompression of cord with good functional recovery. Tumour was a plasma cell myeloma. Survival of at least 3½ years. Fate unknown.

W.C., a male clerk aged 37, was admitted to the National Hospital, Queen Square on 11 November 1927, under the care of Dr. S.A. Kinnier Wilson.

HISTORY.

His past and family histories were not relevant. Nine weeks before admission, he noticed a heaviness of the legs and at the same time a loss of sensation over his thighs. The latter spread rapidly to involve all the lower extremities and up over the trunk to the level of the costal margins. The weakness of the legs was gradually progressive and eventually he could only walk with great difficulty.

There had been no pain and no other complaints.

EXAMINATION.

His general condition was good and above his wrist

the central nervous system was normal. There was, however, marked generalized leg weakness with slight increase of tone and these findings were more prominent on the left. He could not sit up unaided, but there was no umbilical deviation. The abdominal reflexes were all absent, tendon reflexes in the legs were increased and both plantar responses were extensor. At T5 there was a sharp sensory level to all modalities, and vibration and joint position sense were impaired in the feet.

The other systems were normal.

INVESTIGATIONS.

X-rays. Thoracic spine: The body of T4 vertebra was opaque, suggesting neoplastic infiltration and on the left side there was an extravertebral mass. The body of T6 was partially collapsed.

Chest: There was a bony tumour in the head of the left ninth rib.

Cerebrospinal Fluid. Manometrics, not described. Cells, none. Protein, 300 mgm. per cent. Lange, 0000122221. W.R., negative.

Blood. Picture: Haemoglobin, 105 per cent. Red cells, 4.54 million per c.mm. A film showed no abnormalities.

W.R.: Negative.

Urinalysis. Bence Jones protein was looked for on two occasions, but was not found.

OPERATION. 6 January, 1928 (Sir Percy Sargent).

The lamina of T4 vertebra was considerably enlarged and the bone in parts was softer than normal. The spinal canal had been invaded at this level by soft vascular tissue which was entirely extradural. The cord was compressed and this was relieved by partial removal of the tumour-like material.

HISTOLOGY. (Dr. J.G. Greenfield).

This tissue was made up of medium-sized cells that had many of the characteristics of plasma cells. There was no intercellular tissue except in the vicinity of blood vessels. The tumour was thought to be a plasma cell myeloma. (Fig. 21).

PROGRESS.

Power began to return to the legs soon after the operation and the defects in sensation regressed six weeks later, there had been marked increase in leg power and impairment of sensation was now patchy. On discharge from hospital two months post operatively, he could walk with only slight assistance and his general condition was excellent.

One year and ten months after the operation, however, all his symptoms reappeared. He was given deep X-ray irradiation at King's College Hospital with the same improvement. There was, however, an enlarged lymph node in the right posterior triangle of the neck and section showed it to be similar in nature to the spinal tumour. Bence Jones proteinuria appeared and X-rays showed multiple deposits in the vertebrae and ribs.

This patient's case was described by Wakeley (1931) and he had survived three years and nine weeks at that time. His subsequent fate is unknown.

COMMENT.

This patient was suffering from spinal cord compression which was the first clinical evidence of myelomatosis. However, even in the early stages, evidence of a more widespread process was present (rib tumour and two vertebral tumours). The onset of symptoms was rapid and relief from them was equally so. When last seen, he had survived 3 years but the generalized disease was established and further survival would almost certainly be limited. He improved with both surgery and radiation therapy alone and should therefore have been expected to respond well to a combination of both. The entire absence of pain was most unusual.

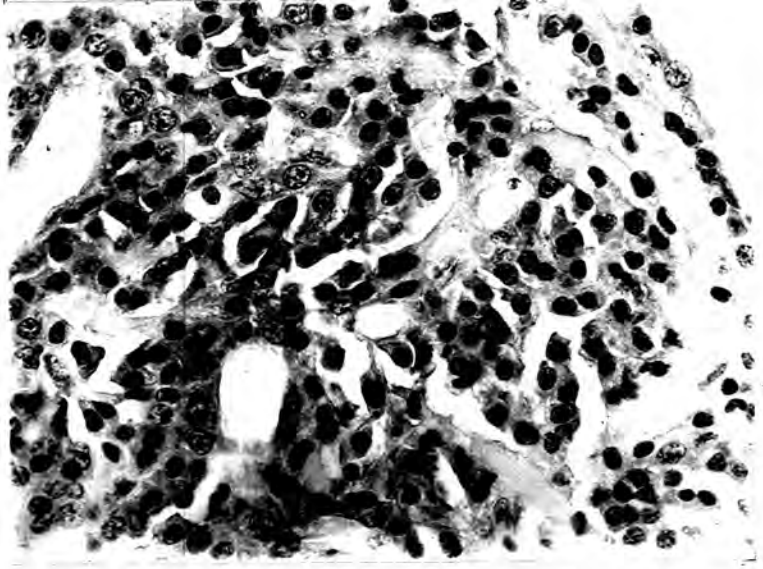

Fig.21. CASE EIGHT. Spinal myeloma. There are many typical plasma cells (x450).

CASE NINE.

Male, 37. 5 months of upper thoracic back pain terminating in complete flaccid paraplegia with T5 sensory level. T4 body partially collapsed. Death. Survival 6 months. Autopsy: no spinal canal tumour but cord compressed by collapsed T4 body. Other laminae involved. Histology, plasma cell myeloma.

H.H., a male supervisor aged 37, was admitted to the National Hospital, Queen Square, on 31 July, 1930, under the care of Sir C.P. Symonds.

HISTORY.

His past and family histories were not contributory.

Five months before admission, he experienced severe and constant pain in the centre of the back at the level of the lower angle of the scapulae. It was aggravated by coughing. One month later, he noticed paresthesiae in the legs and then found that his legs were gradually becoming weak. Over a period of four to six weeks, he became completely paraplegic and all sensation was lost in the legs. The back pain persisted. In addition he now had difficulty controlling urination and had been constipated for several months. He was losing weight and his appetite was poor.

EXAMINATION.

His general condition was poor and there was evidence of recent weight loss. Respirations were laboured and coughing defective.

The central nervous system was normal above the upper thorax. He could not sit up and neither the abdominal nor the lower thoracic muscles moved with respiration; the abdominal reflexes were absent. The legs were in a state of complete flaccid paralysis with absent tendon reflexes. Plantar responses were also absent. The sensory level to pin prick loss was at T5 and other modalities were severely affected in the legs. He was doubly incontinent.

The liver was slightly enlarged to palpation.

There was a depression between the third and fourth thoracic dorsal spinous processes with tenderness to palpation in this area.

INVESTIGATIONS.

X-rays. Thoracic spine: The body of T4 was mottled, and partial collapse had taken place.

Cerebrospinal fluid. Partial manometric block. Cells, 3. Protein, 350 mgm. per cent. Lange, 0000001212. W.R., negative.

PROGRESS.

A marked kyphosis of the thoracic spine developed and the sternum "buckled" to accomodate this. Respiratory embarrassment thus became increasingly severe and his death on 1 September, 1930, six months after his first symptom, was due to respiratory failure.

POST MORTEM. (Dr. J.G. Greenfield).

The laminae from the fourth thoracic vertebrae downward were abnormally soft and could be cut easily with a knife. At the level of T4, haemorrhagic material was infiltrating to muscle, just external to the inter-vertebral formina. There was no tumour tissue within the spinal canal but the cord was compressed by the collapsed body of T4.

The lungs were emphysematous and congested. The liver was pale and fatty and the thyroid was slightly enlarged. No other evidence of myelomatosis was obtained, but examination was not complete.

HISTOLOGY. (Dr. J.G. Greenfield).

The haemorrhagic growth in the bone was composed of small round cells, many of which were plasma cells. This tissue was typical of a myeloma (Fig. 22).

COMMENT.

This patient died rapidly of a myeloma of the

fourth thoracic vertebra. From the facts given above, it might be considered that this was a solitary lesion but as investigations, both clinical and pathological, were limited, this conclusion cannot be accepted. No doubt there was other evidence of myelomatosis and he died of this as well as spinal cord compression. In fact, the softness of the laminae of the vertebra other than the one known to be affected, suggests that the disease was extensive in the spine. The collapsed vertebral body was sufficient to damage the cord without the presence of tumour tissue in the spinal canal.

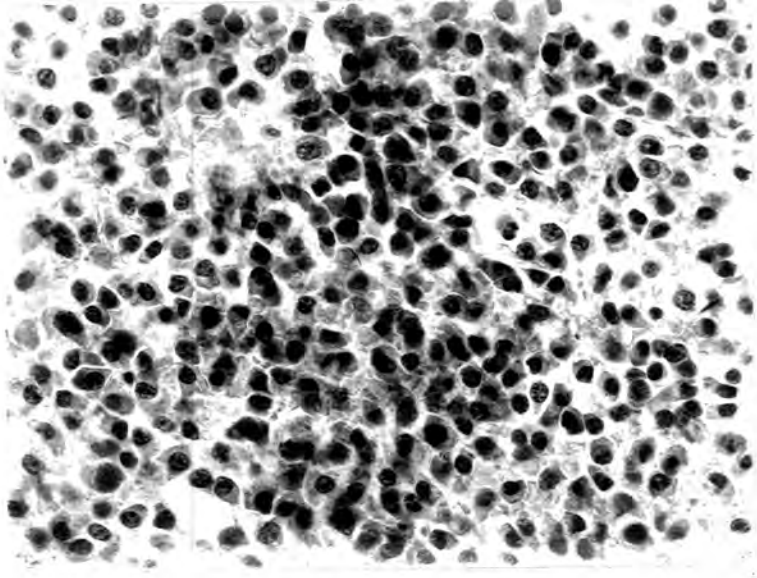

Fig.22. CASE NINE. Spinal myeloma. A very cellular tumour containing many plasma cells (x450).

CASE TEN

Male, 67. 3 months of upper thoracic back pain. 5 weeks of complete paraplegia with T9 sensory level. Erosion of T10, T11, T12 and lesion in left 11th rib. Complete manometric block. Death. Survival 3½ months. Autopsy, plasma cell myeloma arising from T8 lamina and compressing spinal cord.

J.D., a clergyman aged 67, was admitted to the National Hospital, Queen Square on 17 January, 1935 and died there 13 days later. He was under the care of Sir Gordon Holmes.

HISTORY.

His past and family histories were not relevant.

Three months before admission, he experienced severe upper thoracic back pain which was persistent. Five weeks before, there was a rapid onset of "numbness" and weakness of the left leg and two days later the right leg was similarly affected. He now found that all sensation below the waist was absent. Four days after this, complete urinary retention developed. There were no other complaints.

EXAMINATION.

His general condition was poor and he was doubly

30 January, 1935 two weeks after admission and three and one half months after the onset of his fatal illness.

POST MORTEM. (Dr. J.G. Greenfield).

Spinal cord. At the level of the eighth thoracic body, there was a mass of soft fleshy tissue surrounding the cord. It appeared to arise from the laminal arch and extended out of the intervertebral foramina, more so on the right side. The cord was surrounded by it. The vertebral body itself was found to be healthy.

Apart from early bilateral bronchopneumonia, the other organs and tissues were normal.

HISTOLOGY. (Dr. J.G. Greenfield).

The tumour tissue had the characteristics of a plasma cell myeloma, containing many plasma cells. A few mitotic figures were seen. (Fig. 23).

In the cord, at the level of the compression, considerable vacuolation was found. Vessels were dilated and in the vacuolated areas there were scattered microglial nuclei.

COMMENT.

The disease process was dramatically rapid, so that death occurred three and one half months after the first symptom appeared. Despite the limited investigations carried out, the rib myeloma demonstrated the "multiple"

nature of the condition and death was a combination of the primary disease and its neural complication. This case typifies the very malignant course pursued by patients in which these conditions occur together. Treatment would probably have had little influence upon the course of the disease. The myeloma had grown from the laminae and the body was not involved.

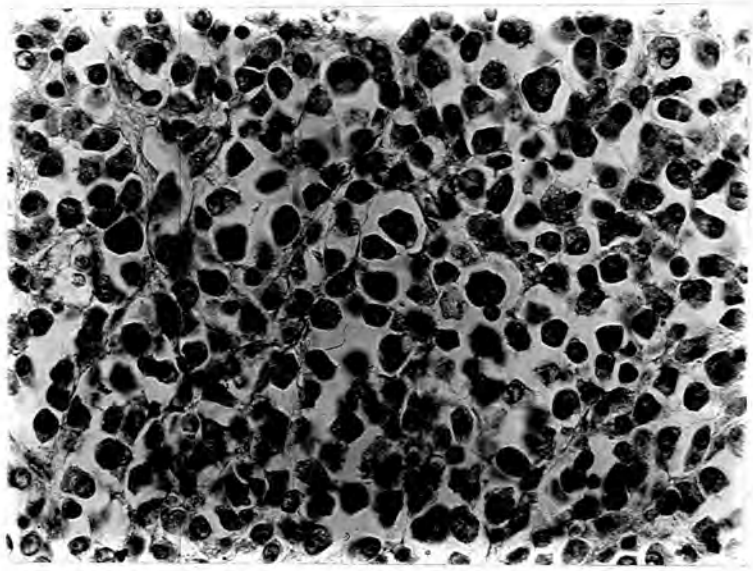

Fig.23. CASE TEN. Spinal plasma cell myeloma. There are a few mitotic figures in the plasma cells (x450).

CASE ELEVEN.

Male, 40. 9 months of neck and arm pain. 10 weeks increasing leg weakness. Spastic paraplegia with T4 sensory level. Partial manometric block. Bony erosion C7. Operation: extradural plasma cell myeloma at C7, and C7 laminae invaded. Known survival, one year. Ultimate fate unknown.

R.S., a stoker aged 40, was admitted to the National Hospital, Queen Square on 7 June, 1939, under the care of Dr. C.M. Hinds Howell.

HISTORY.

His past and family histories were not relevant.

Nine months before admission, he began to suffer from pain at the back of the neck that extended down both arms and into the upper part of the chest. This had persisted unaltered until a month prior to admission when it ceased. But ten weeks before coming to hospital weakness of the legs became apparent and, over a period of four weeks, they became severely paralysed. Hesitancy of micturition, present at the onset of the leg symptoms, slowly improved. He had no other complaints.

EXAMINATION.

The cranial nerves were normal and no abnormalities could be detected in the arms. In the legs, however, power was considerably decreased bilaterally, the proximal musculature being the more severely affected. Tone was slightly increased distally. Reflexes in the lower limbs were increased and plantar responses were extensor. All sensory modalities were impaired below a level at T4. The other systems were normal.

INVESTIGATIONS.

X-rays. Cervical spine: The laminae and spinous processes of C7 were seen to be eroded.

Right femur: Normal.

Cerebrospinal fluid. Partial manometric block. Cells, 1 lymphocyte. Protein, 30 mgm. per cent.

OPERATION. 7 July 1939 (Mr. H. Jackson).

The seventh cervical spinous process and the laminae were found to be replaced by tumour which was eroding the sixth lamina also. Firm, whitish tumour tissue was found in the extradural space extending down as far as T1, at least. Some of it was removed.

HISTOLOGY. (Dr. J.N. Cumings).

The tumour was considered to be a plasmocytoma.

There were many plasma cells, but no mitoses were seen. (Fig. 24).

The patient was discharged from hospital on 26 August, 1939. He had survived about one year at this time. Unfortunately, he could not be traced, so that his ultimate fate is unknown.

COMMENT.

Investigations were limited and follow-up impossible so that the designation of "solitary" myeloma cannot be safely applied. As in Case Ten, the tumour seemed to be arising from the laminae of the vertebra and X-ray findings at a later stage may have approximated to those in Figure 49 (Case Twenty One). The presence of a T4 sensory level, despite the cervical localization of the myeloma, could be very confusing if there was no radiological evidence of bone disease. It was interesting to note that the pain receded as the paraplegia advanced. The response to operation, both immediate and late, could not, unfortunately, be discovered.

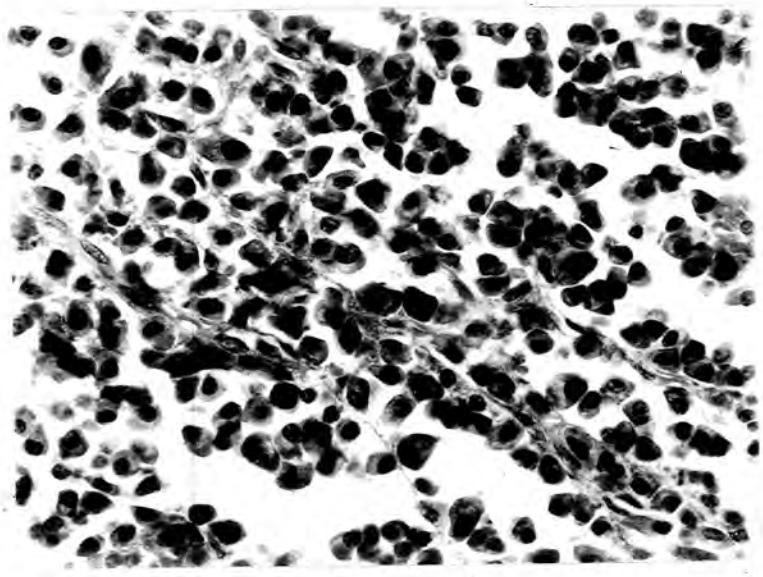

Fig.24. CASE ELEVEN. Spinal myeloma. The commonest element is the plasma cell (x450). There are no mitoses.

CASE TWELVE.

Male, 54. 6 months of pain, and 4 months of signs in the distribution of T2 to T4. Paraplegia of sudden onset. E.S.R. and serum globulin increased. Extradural plasma cell myeloma growing from T5 found at laminectomy. Death after generalization of disease. Survival, 7 months. Autopsy.

E.S. (Hospital No. 8881), a man aged 54, was admitted to the National Hospital, Queen Square on 12 March 1948 as an emergency, and was under the care of Mr. Harvey Jackson.

HISTORY.

Neither his family nor his past histories were relevant.

Six months before admission, he complained of a burning pain in the region of the right scapula, which then spread round the chest and down the right arm. It was aggravated by movement, coughing and sneezing. In addition he felt generally unwell and was depressed. Four months before, he was found to have hyperalgesia in the territory of the right T2 to T4 roots, and there was local tenderness over the spines of T3 and T5. Investigations at this time revealed no X-ray changes of the thoracic spine, the C.S.F. was normal and the

urine contained a trace of albumin. The diagnosis at this time was "radiculitis of unknown cause" and he was kept under close observation.

Three months later (and one month prior to admission) the pain and the signs were unchanged but his general condition had deteriorated. The E.S.R. was 90 mm. in the first hour and the serum globulin was increased. The thoracic spine was still normal radiologically and despite an adequate search a primary malignancy could not be found. A week later, however, there was a partial Horner's syndrome on the right and some weakness and wasting of the small muscles of the right hand were detected.

Events now moved rapidly and two days before admission he developed sphincteric paralysis and over a period of thirty six hours, he became almost completely paraplegic. The C.S.F. now contained 100 mgms. per cent of protein and there was a partial manometric block.

EXAMINATION.

His general condition was poor and he was suffering considerable pain. There was a right-sided Horner's syndrome and an almost complete paraplegia (right leg weaker than left). The sensory level was at T4 on the right and T6 on the left. He had severe tenderness and stiffness of the upper thoracic spine. The other systems

were normal.

INVESTIGATIONS.

X-rays. Thoracic spine: No abnormality could be detected.

Blood. Picture: Haemoglobin, 73 per cent. White cells, 7,000 per c.mm. (differential count normal). No plasma cells seen.

E.S.R.: 75 mm. in first hour.

Serum proteins: Total, 5.95. Albumin, 2.17. Globulin, 3.78 g. per 100 ml.

Urinalysis. No Bence Jones protein found.

OPERATION. 13 March 1948. (Mr. Harvey Jackson).

In the region of T1 to T4, purplish-grey extradural tissue was discovered and it seemed to be encircling the dural tube. It was only partially removed.

HISTOLOGY. (Dr. W. Blackwood).

The tissue was made up of typical plasma cells with lymphocytic infiltration. There were some features of malignancy. (Fig. 25).

PROGRESS.

Little change occurred in the patient's neurological signs following the operation. One month later, he fractured the left ninth rib when he lay on a urine bottle. His general condition deteriorated and he suffered a

great deal from generalised aching and local bone pains. He died on 21 April 1948, five weeks after the operation and about seven months after the first symptom.

POST MORTEM. (Dr. J.G. Greenfield).

On the right side of the bodies of T1 and T2 there was a pad of tumour tissue 2.0 in. long which was continuous via a intervertebral foramen with a smaller collection on the right side of the spinal canal, at the site of operation. In the spinal cord, the chief lesion was at T3, and was the result of compression by the extradural mass.

Myelomas were found in the left ninth rib and left femur.

COMMENT.

This is a typical case of myelomatosis presenting with an upper thoracic root irritation syndrome, which for six months was the patient's only complaint. The sudden cord compression must have been due to interference with the cord's blood supply by the extradural tumour, rather than bony collapse which is the more usual cause. The decompressing operation did not influence the course of the disease.

Although pain was his first symptom, it is possible that the generalized disease was present from the onset

and may have even antedated it. The high E.S.R. and abnormal serum proteins gave evidence of a widespread process.

The spine was normal radiologically, but histological examination of the bone was not carried out. Likewise the dura was not examined microscopically. In the absence of adequate pathological data it can only be suggested that, as in Case Seventeen (p.), the myeloma was of epidural origin. This case also closely simulates Case Fourteen. However it differs from them both in that clear evidence of multiple myelomatosis was present and eventually the disease killed him. It is important to note that the clinical pictures were very similar.

In the absence of bony disease, the extravertebral myeloma tissue was presumably due to extension from the spinal canal. That the tumour had originated outside of the canal and then invaded it cannot be denied and it would accord admirably with the progression of the clinical events.

CASE THIRTEEN.

Male, 49. 3½ months of left buttock pain and severe back pain for 5-6 weeks. Cauda equina picture due to extradural plasma cell myeloma originating from body of L.3. No evidence of myeloma elsewhere (limited investigations). Laminectomy and deep X-ray with no improvement. Alive. Survival, 2½ years.

H.R. (Hospital No. 27142), a maintenance fitter aged 49, was admitted to the National Hospital, Queen Square, on 30 October 1950, under the care of Sir Charles Symonds.

HISTORY.

His family and past history revealed no relevant information.

Three and a half months before admission, he noticed an aching in the left buttock which occasionally spread down the front of the thigh and was aggravated by coughing, sneezing and movements. Five to six weeks before, he was seized with severe low back pain which persisted. "Recently" he found that both his legs felt "numb" and he occasionally experienced a sensation like a tight band round the waist. There was no leg weakness and no sphincter dysfunction.

formation was taking place (Fig. 29). His general condition was good. Six months later, although there had been no radiological change, he was still complaining of severe backache.

COMMENT.

Again, a search for other evidence of myeloma was not carried out. At the moment, however, the spinal compression is the only significant clinical feature although symptomless manifestations have not been excluded. The X-rays (Figs. 26, and 27), demonstrate well one type of localised osteolysis and the subsequent events in the affected bone. Initially, tumour tissue rather than diseased bone was responsible for the cauda equina compression. Following operation and radiation therapy, he has survived 2 years'

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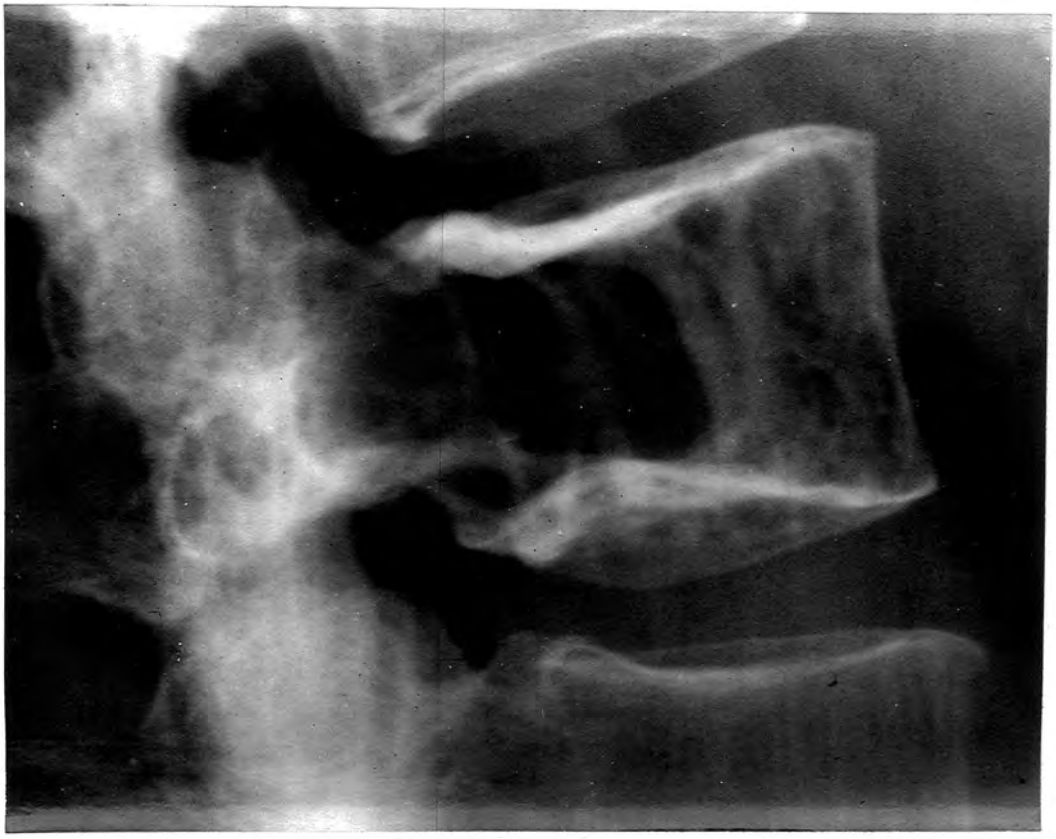

Fig.26. CASE THIRTEEN. X-ray of lumbar spine, lateral view. Myeloma of L.3 body and laminae. The "soap-bubble" type with no surrounding bony reaction.

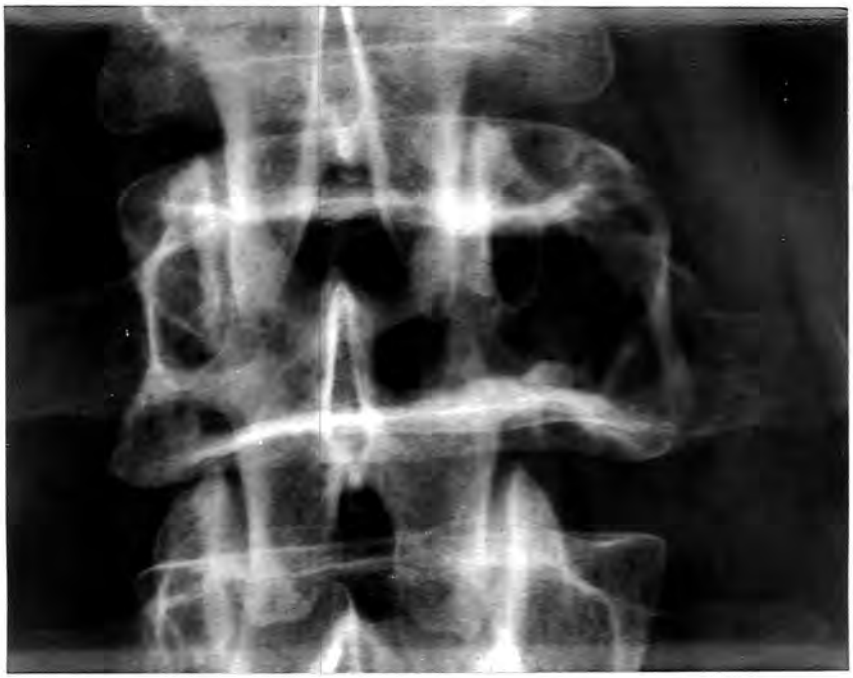

Fig.27. CASE THIRTEEN. X-ray of lumbar spine, A.P. view, showing myeloma of L.3.

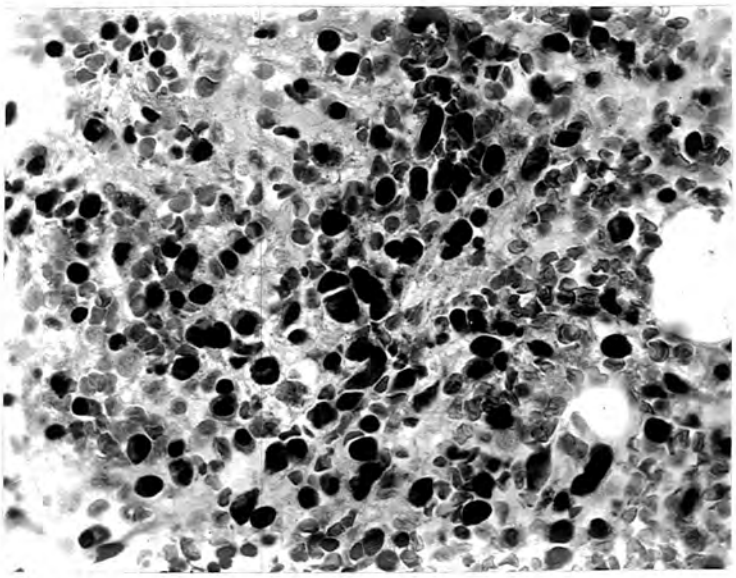

Fig.28. CASE THIRTEEN. Spinal myeloma. As well as plasma cells, there are a few eosinophilic leucocytes (x450).

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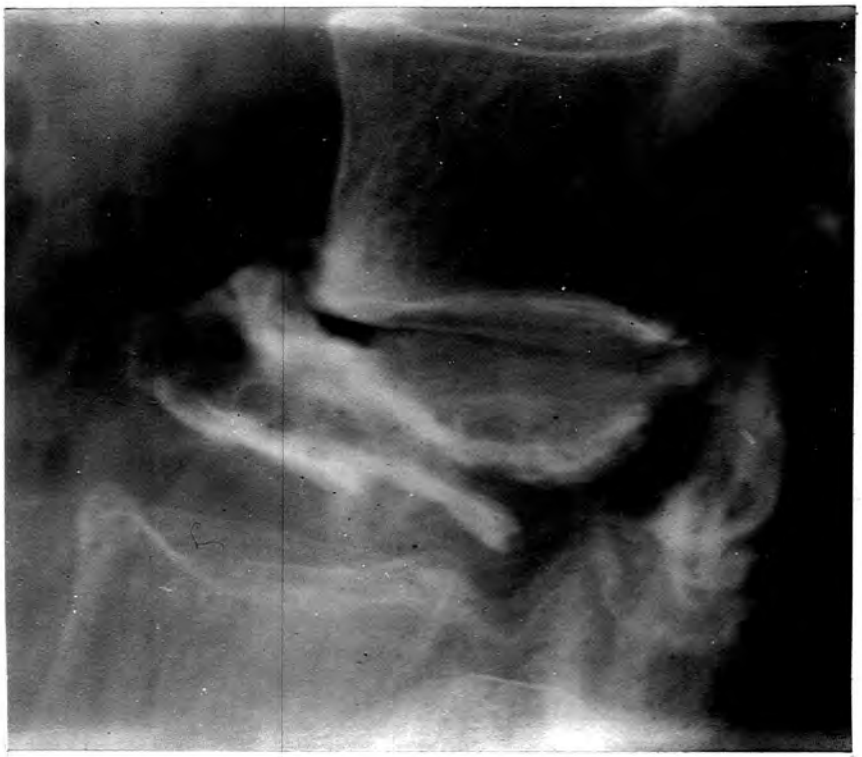

Fig.29. CASE THIRTEEN. X-ray of lumbar spine, lateral view, taken 1½ years after those of Figs.26 and 27. The body of L.3 has now collapsed and is severely compressed. The adjacent vertebrae are healthy.

CASE FOURTEEN.

Male, 30. 3 attacks in 1 year of low back pain and leg numbness, the last are being progressive. Paraplegia with myelographic block at T9. Spine radiologically normal. Extradural plasma cell myeloma removed and radiation therapy given. Rapid return to normal. 2 rib tumours of undetermined nature. Alive. Survival, 2¾ years.

L.A. (Hospital No. 33389), a West Indian barrister aged 30, was admitted to the National Hospital, Queen Square on 6 September 1951, under the care of Dr. Denis Williams.

HISTORY.

His family history was not relevant. He had in the past seven years suffered repeated attacks of low backache but had never had sciatica.

One year before admission, he had an attack but on this occasion the pain radiated to the anterior abdominal wall on both sides and moving and coughing made it worse. In addition the left leg felt "numb". These symptoms subsided but five months before admission became severe again. Again there was amelioration until six weeks prior to coming into hospital when the pain recurred and three weeks later the legs felt "numb".

Gradually the sensory changes progressed and at the same time weakness of the legs became apparent. The sphincters were not involved.

EXAMINATION.

His general condition was excellent. There was an almost complete spastic paraplegia with weakness of the lower abdominal muscles. A sensory level could be readily detected at T.9 and all modalities were affected. The spine was normal as were the other organs.

INVESTIGATIONS.

X-rays. Thoracic spine: Careful study revealed no abnormality (Fig. 30).

Ribs: There were cystic areas in the posterior end of the left fifth rib and the medial part of the left twelfth rib. Their nature could not be determined and they were not definitely diagnosed as myelomas.

Skull, pelvis, long bones and clavicles were normal.

Cerebrospinal Fluid. Partial manometric block. Cells, 1. Protein, 520 mgm. per cent. Lange, 0000112110. W.R., negative.

Blood. Picture: Haemoglobin, 80 per cent. Red cells, 3.98 million per c.mm. White cells, 5,400 per c.mm.

those in the ribs were unchanged.

COMMENT.

The spinal bones were normal in this case and the continued absence of vertebral lesions over a period of almost three years suggests that the myeloma was independent of bone. At operation, the dura did not seem to be involved. The fact that the tumour was posteriorly placed in the spinal canal (Fig. 31) suggests that it may have risen from the laminae as in Case Eleven. As far as could be determined, however, they were radiologically normal and histological examination revealed normal bone.

It seems therefore that the myeloma in this case was of the primary epidural type (e.g. Case Twelve). It is important to note that clinically this type could not be distinguished from the more commonly occurring spinal myelomas.

In the presence of the rib tumours, the spinal myeloma cannot be considered to be solitary, despite the fact that radiologically they do not appear to be typical myelomas. The prognosis which otherwise would have been good must be guarded because of these lesions.

The previous history of backache confused the clinical picture, and the onset of symptoms referable

to the myeloma could not be determined accurately. A prolapsed disc was demonstrated by myelography and no doubt this produced some of the back pain.

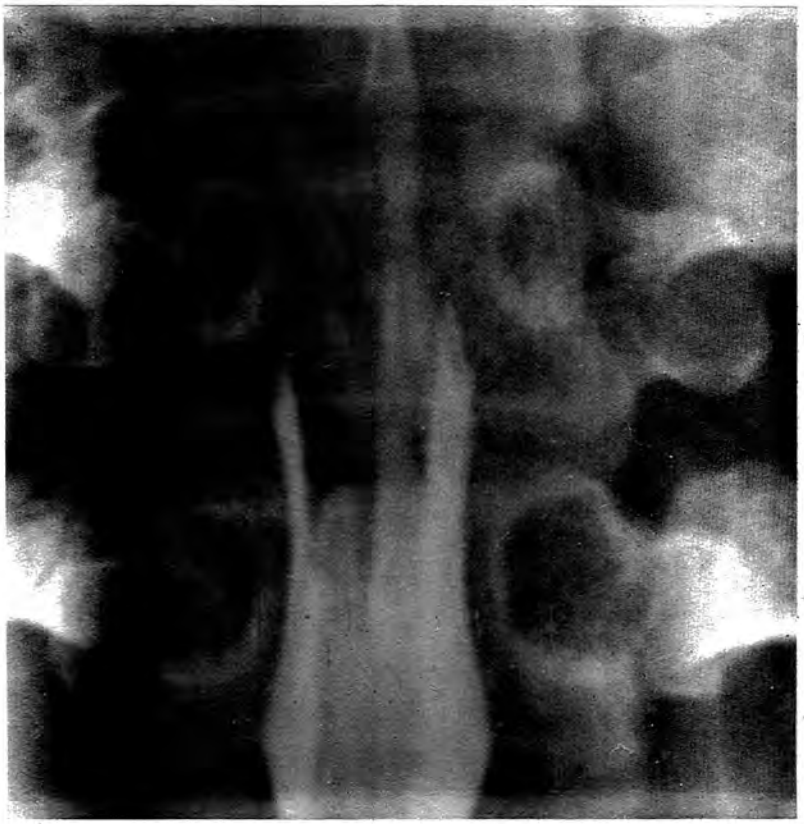

Fig.30. CASE FOURTEEN. Myelogram, axial view, showing hold-up of the opaque medium at the lower border of T.9. This and other vertebrae were radiologically normal.

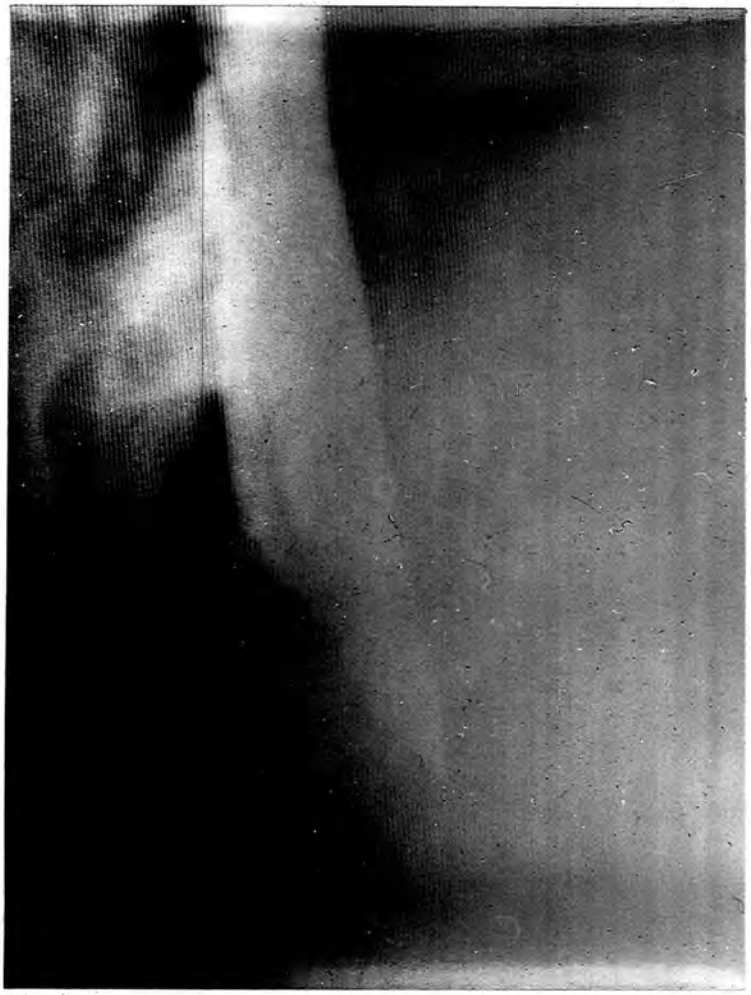

Fig.31. CASE FOURTEEN. Myelogram, lateral view. The hold-up is demonstrated again and the obstructing lesion is posteriorly placed.

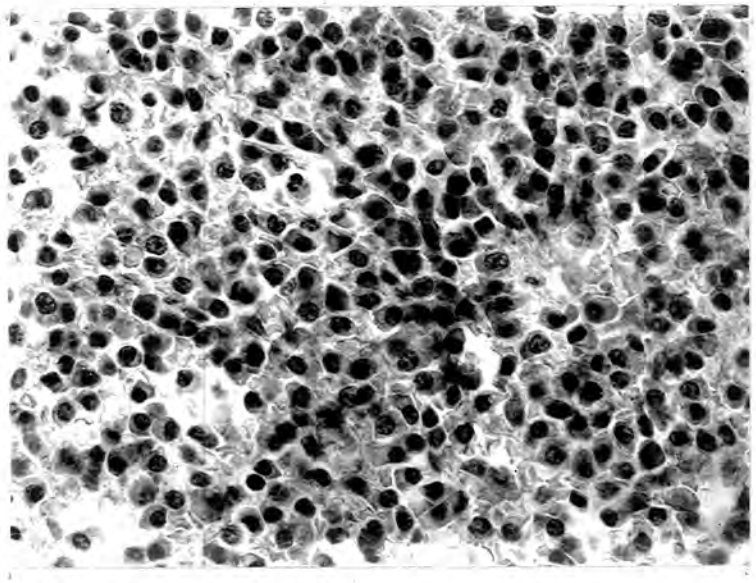

Fig.32. CASE FOURTEEN. Spinal myeloma, made up of many plasma cells and some lymphocytes (x450).

8

CASE FIFTEEN.

Female, 53. Known diabetic. Back pain for one year, leg weakness for 3 months and complete paraplegia and urinary retention for 24 hours, due to collapse of T.5 and compression of cord by extradural plasma cell myeloma. No evidence of myeloma elsewhere (limited investigations). Cord decompressed. Radiation therapy. Good recovery, but dissemination occurred. Alive. Survival, 2¾ years.

D.B. (Hospital No. 36600), a housewife aged 53, was admitted to the National Hospital, Queen Square, on 9 February 1952, under the care of Sir Charles Symonds.

HISTORY.

Her family history gave no relevant information. She had suffered from diabetes mellitus for some years but it was adequately controlled by diet and insulin.

One year before admission, she experienced pain in the right shoulder which spread down the back and at first was intermittent. Later a girdle-like pain appeared, which interfered with breathing. Three months previously, difficulty with walking had begun and this seemed to be due to thigh weakness. It was followed by a numbness over the outer surfaces of the thighs. These symptoms

were steadily progressive and the impairment of sensation ascended to the level of the breasts. The day before admission there was a sudden onset of paresthesiae in the legs and she very rapidly became completely paraplegic with retention of urine. There was no increase of pain at this time.

EXAMINATION.

She looked ill and had recently lost weight. The spine of T.5 was tender. There was a complete, flaccid paraplegia with absent tendon reflexes and extensor plantar responses. The abdominal reflexes were absent. At. T.4 on the right and T.5 on the left, a crisp sensory level was found and all modalities as well as sweating were impaired below it. There was complete retention of urine and constipation.

The other systems and the rest of the skeleton were normal.

INVESTIGATIONS.

X-rays. Thoracic spine: There was mottling of the bony texture of T.5 with slight compression and considerable excavation posteriorly. (Fig. 33).

Skull, chest pelvis and long bones, were normal.

Urinalysis. The urine was loaded with sugar and acetone.

X-rays of the thoracic spine (Fig. 36) showed that the collapsed vertebra (T.5) was sclerosing and bony fusion with the adjacent vertebrae was taking place. The ribs, however, contained many small myelomatous foci.

COMMENT.

This patient has survived 2¾ years with a T.5 myeloma as the only manifestation of a disease that has now become more generalised. But even so, her general condition is excellent and the disease would seem to be only slowly progressive. The onset of paraplegia was very rapid but, unlike the events in Case Twelve where this also occurred, recovery was considerable. The reason for this deterioration is not entirely clear for, as can be seen in Fig. 33, collapse of the vertebral body was slight when there was clinical evidence of a complete cord lesion. Presumably the myeloma within the spinal canal was compressing the cord and a sudden vascular lesion in the latter would account for the events. For some reason it was reversible in this case. The progressive changes within a vertebra attacked by a myeloma are well shown in Figs. 33, 35 and 36.

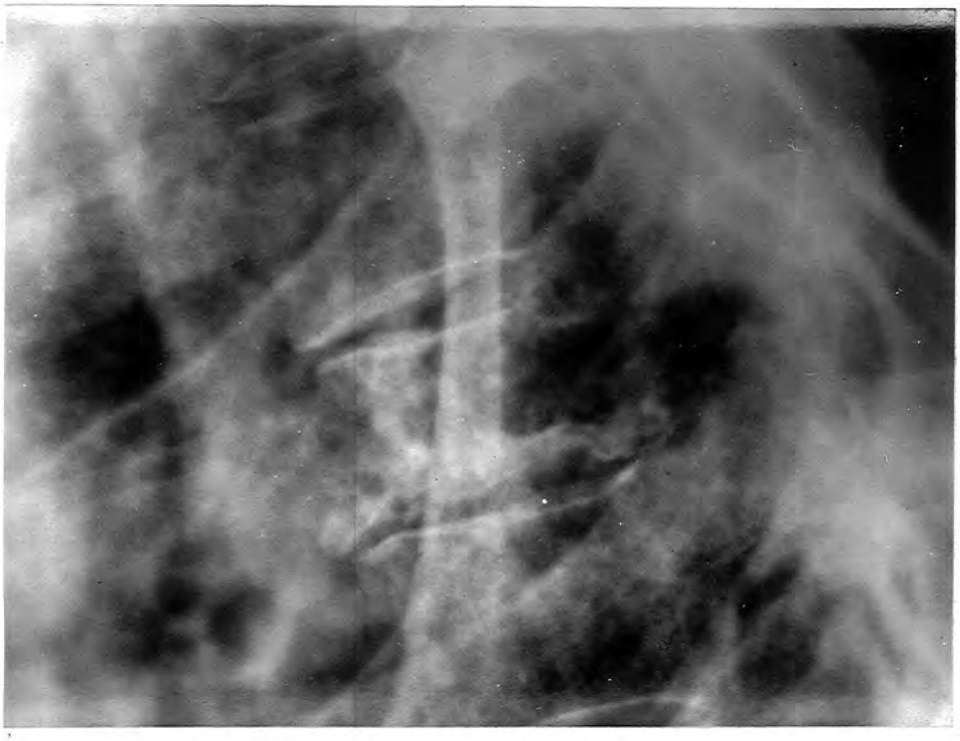

Fig.33. CASE FIFTEEN. X-ray thoracic spine, lateral view. Partial collapse of T.5 with excavation of posterior part of the body.

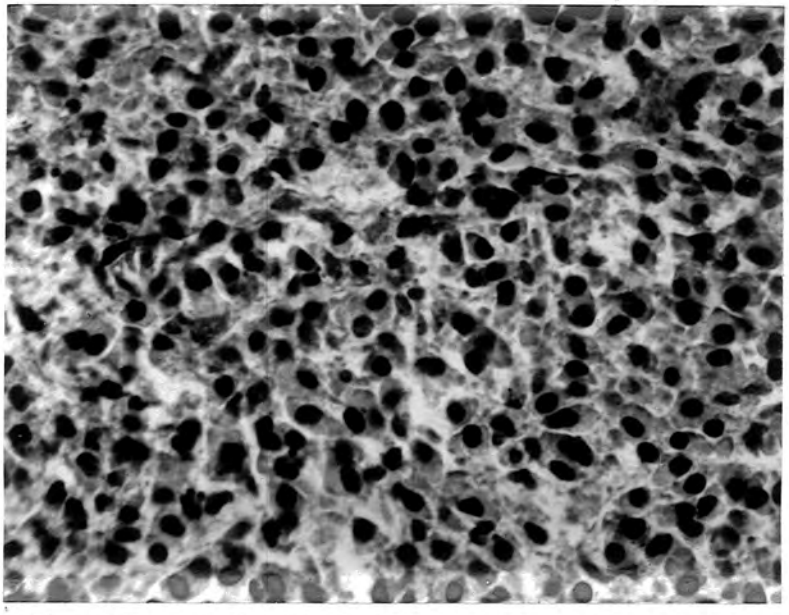

Fig.34. CASE FIFTEEN. Plasma cell myeloma of T.5 (x450).

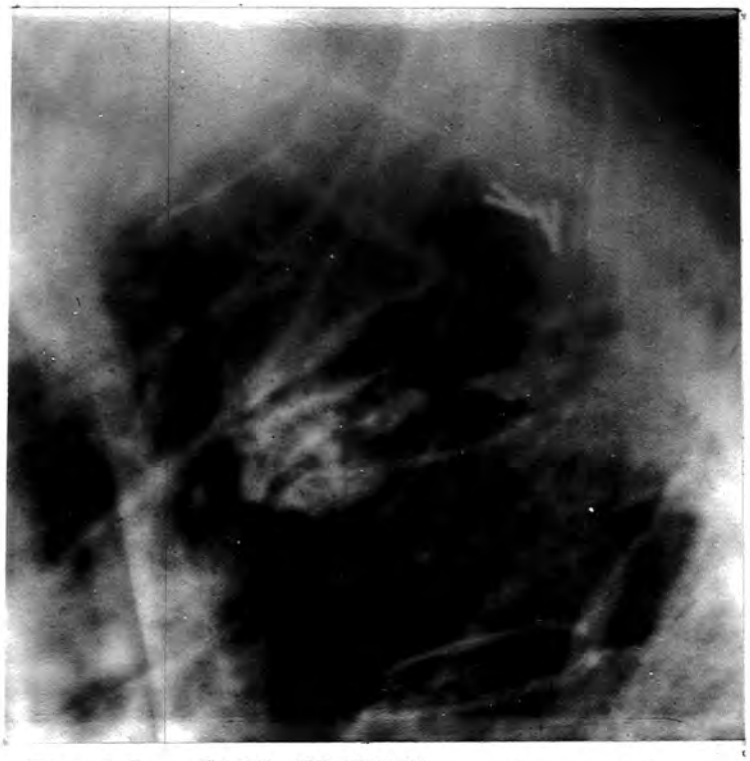

Fig.35. CASE FIFTEEN. X-ray of thoracic spine, lateral view. One month after operation. T.5 has now collapsed. Silver clips can be seen in the spinal canal.

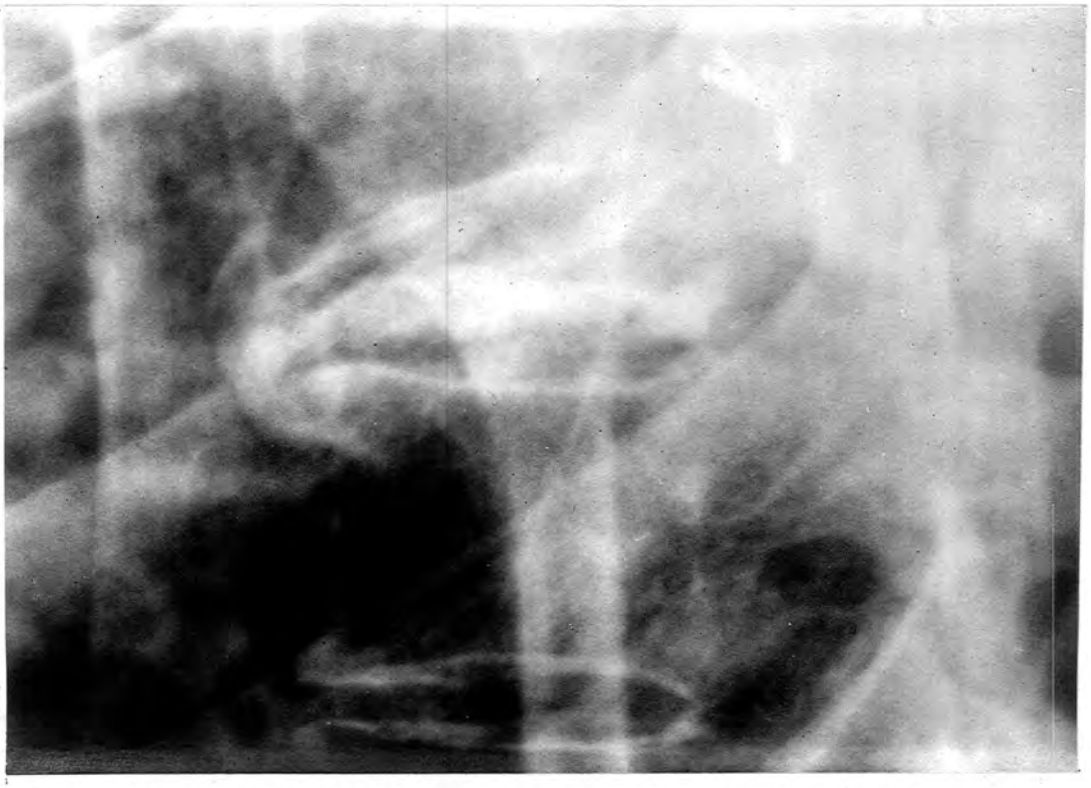

Fig.36. CASE FIFTEEN. X-ray of thoracic spine, lateral view. One year and 9 months after operation (and X-rays of Fig.33). The body of T.5 is completely collapsed and sclerosed. Bony union with adjacent vertebrae is taking place.

CASE SIXTEEN.

Female, 61. 6 months of upper dorsal pain becoming root-like in character. 5 weeks of motor and sensory changes in right leg and 1 week in left leg. Partial Brown-Séquard Syndrome. T3 diseased. Complete manometric and myelographic block. Partial removal of left-sided extradural plasma cell myeloma. Post-operative deterioration. No other lesions (limited investigations). Alive. Survival 2 years and 2 months.

K. S-T., (Hospital No. 34945), a lady's companion aged 61, was admitted to the National Hospital, Queen Square, on 22 November 1951, under the care of Dr. J. St. C. Elkington.

HISTORY.

Her past and family histories contributed no relevant information.

6 months before admission, she first experienced upper dorsal back pain which was made worse by movement, coughing and straining. Soon it began to radiate round the chest mainly on the left side but occasionally on the right side too. For five weeks, she had noticed a "numb" feeling over the right leg and

CASE SEVENTEEN

Female, 62. One year of increasing upper back ache and 5 months of progressive paraplegia with sphincter involvement. Complete motor and sensory paraplegia (level T4). No x-ray bony changes. No evidence of myelomatosis. Myelographic block T2. Extradural plasma cell myeloma (T2, 3 and 4) mostly removed. Radiation therapy. Complete recovery with 13 years survival. ? Primary epidural myeloma.

B.W., (Hospital No. 18720), a housewife aged 62, was admitted to the Radcliffe Infirmary, Oxford on 7 October 1941, under the care of the late Sir Hugh Cairns.

HISTORY.

Her past and family histories contained no relevant information.

One year before admission, she first experienced back pain in the region of the scapulae which persisted and gradually became more severe. Five months before, weakness of the left and then the right leg was noticed and this, like the pain, slowly increased until two weeks prior to admission she could hardly move the legs at all. In addition, there seemed to be no feeling in them and involuntary spasms of the muscles would occur. Meanwhile

the back pain had acquired a girdle-like quality, extending anteriorly more markedly on the right side. She had also suffered from constipation and some urgency of urination.

EXAMINATION.

She was moderately obese but her general condition was good. The nervous system above the waist was normal but below it, there was a virtually complete spastic paraplegia. The abdominal reflexes were all absent, tendon jerks in the legs were equally hyperactive and both plantar responses were extensor. There was a well-marked sensory level at T3 with severe involvement of all modalities below it except for a small degree of sacral sparing bilaterally. She had adequate control over the act of micturition.

The other systems were normal.

INVESTIGATIONS.

X-rays. Thoracic Spine: There was some marginal spondylosis but no localised disease of the vertebral bodies.

Chest: Normal.

Pelvis: Some decalcification only.

Cerebrospinal Fluid. Partial manometric block. Cells, one lymphocyte. Protein, 600 mgm. per cent with

however, was normal. Most of the mass was removed but a small fringe had to be left.

HISTOLOGY. (Professor D.S. Russell).

The tumour was considered to be a plasma cell type of myeloma. (Fig. 41).

PROGRESS.

The post-operative period was remarkable only for the rapid return in leg function that began three days after operation. She was given a course of radiation therapy to the thoracic spine and on discharge two months after admission, she could walk and had complete control of her sphincters. Sensation in the lower extremities was not yet normal.

Four years after the operation, she could walk more than three miles a day and apart from occasional urinary frequency and urgency, she had no complaints. It is now twelve years since the operation and thirteen years since the onset of her illness, but she has had no further symptoms referable to the spinal cord, or indeed to myelomatosis. She considers that her present health is very good.

COMMENT.

This is a remarkable case in that the patient is still alive, thirteen years after the spinal myeloma first

produced symptoms. One is tempted to suggest that it is an example of a true solitary myeloma for there is no evidence of multiple lesions many years after the first lesion was successfully dealt with. It is certainly strong evidence in favour of Christopherson and Miller's (1950) belief in this entity. The tumour was in the epidural space and extending out of it, but the adjacent bone was normal. Thus the case must be grouped with Cases Twelve and Fourteen as being true, extra-osseous epidural plasma cell myelomas. It has been suggested (Vol. 1. p. 117) that this tumour was arising from elements within the epidural space rather than from dura or nearby bone. In these respects, it is therefore a unique case.

It is to be noted that the clinical picture cannot be differentiated from the more usual type of case. The prognosis, however, if all the neoplastic tissue can be removed by operation and radiation therapy, might be expected to be better if at the time that therapy is instituted, there is no evidence of a generalised myelomatous process.

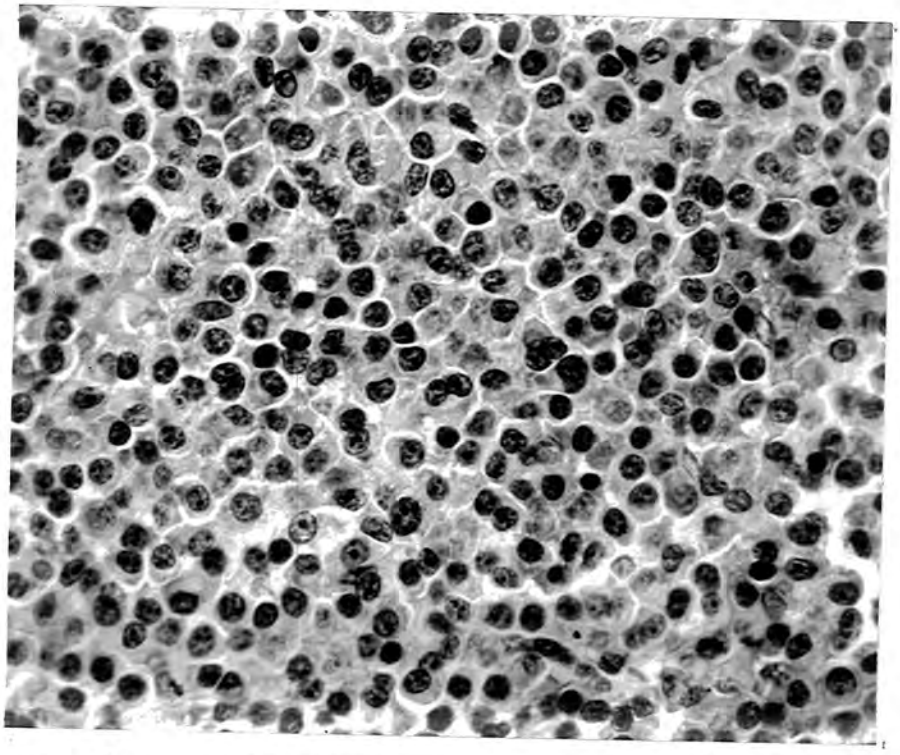

Fig.41. CASE SEVENTEEN. Epidural spinal myeloma. There are many typical plasma cells. (x580).

CASE EIGHTEEN

Male, 32. Transient abdominal pain and 2½ months of progressive motor and sensory paraplegia. Erosion of T8 lamina with myelographic and manometric block. Removal of extra-dural "? non-specific granuloma" with complete recovery. 16 months later, the clinical picture returned with collapse of T8. Removal of recurrent tissue, shown to be a plasma cell myeloma. D.X.R. treatment. Complete recovery. Alive. Survival, 5 years.

First Admission

A.W., (Hospital No. 86238/48), a boot and shoe maker aged 32, was admitted to the Radcliffe Infirmary on 17 April 1948, under the care of the late Sir Hugh Cairns.

HISTORY.

His past and family histories gave no relevant information.

Four months before admission he had experienced a dull, deep-seated lower abdominal pain that persisted for a month and then disappeared. A few weeks later (two and a half months before admission), the right leg began to drag and there was a "pins and needles"

sensation in the foot. Both these symptoms were progressive and soon the left leg was similarly affected. Recently he had been aware of a band-like sensation around the waist.

EXAMINATION.

His general condition was good and the abnormalities of the nervous system were restricted to the lower extremities. There was a moderately severe spastic paraplegia with hyper-reflexia and extensor plantar responses. A sensory level was detected at T8 and all modalities were impaired below it. No deformity of the spine was present.

INVESTIGATIONS.

X-rays. Thoracic spine: There was erosion of the pedicles of T8 but the right one was principally involved. (Fig. 42).

Chest: Normal.

Cerebrospinal Fluid. Complete manometric block. Cells, three lymphocytes and two polymorphonuclears. Protein, 140 mgm. per cent. Lange, not done.

Blood. Picture: Normal.

E.S.R.: 14 mm. in first hour (Westergren).

Myelogram. There was a complete block extending from T7 to T9. Figure forty-three shows the lower end of the obstruction.

FIRST OPERATION. 20 April 1948. (Mr. J.B. Pennybacker)

Grey tumour tissue was invading the bodies and laminae of T7, T8 and T9. For an area 8.0 cm. in length, the dural sac was surrounded by this tissue, which was also extending through the intervertebral foramina. As much as possible was removed but a small amount had to be left.

HISTOLOGY.

The microscopical appearances of the tissue were indefinite and the consensus of opinion was that it represented a non-specific granuloma.

PROGRESS.

He made a rapid recovery and when discharged three weeks after admission, he had regained considerable leg power. He returned to his work and was virtually normal until sixteen months later.

Second Admission

At this time (2 August 1949), he was re-admitted, having suffered severe back-ache for one month. It had begun while straining and, as before, leg weakness rapidly followed but, in addition, there was acute retention of urine.

EXAMINATION.

Again, only his legs were abnormal and on this occasion the weakness was more severe and the sensory impairment denser. He had an indwelling catheter.

The spine was normal.

INVESTIGATIONS.

X-rays. Thoracic spine: The body of T8 had now collapsed. (Fig. 45).

Cerebrospinal fluid: Partial manometric block. Protein, 420 mgm. per cent.

Blood. Pictura: Haemoglobin, 14.8 gm. White cells, 18,000 per c.mm.

Urea: 60 mgm. per 100 ml.

Urinalysis. Infected urine. Bence Jones protein not discovered.

Myelogram. A complete, transverse block at the lower border of T8 could be demonstrated. (Fig. 45).

SECOND OPERATION. 5 August 1949. (Mr. W.S. Lewin).

The grey extradural tissue was encountered again, compressing the cord, especially on the left side. The cord was also being compressed by the collapsed vertebra. As much of the tumour that was accessible was removed.

HISTOLOGY. (Dr. F.D. Bosanquet).

As well as many plasma cells, there were frequent giant cells and large deposits of amyloid substance. (Fig. 44). Professor R.A. Willis had no doubt that the case was one of plasma cell myelomatosis.

PROGRESS.

Again, he made a rapid post-operative recovery and

was given deep x-ray therapy to the thoracic spine. Improvement continued and he was able to return once more to his work. Further x-rays showed consolidation of the collapsed vertebra. In September 1953, he was found to be healthy and active. There were no remnants of his spinal cord lesion and no new symptoms had appeared.

He has thus survived five years since the first symptom.

COMMENT.

The interest here is the light that is shed upon the management of these cases. First of all, only a decompression of the spinal cord was carried out and within sixteen months a recurrence had occurred. When, however, decompression plus radiation therapy was employed survival has been more than four years and at the moment seems unlimited. This patient's history is very similar to that of Case Eight in this respect. A combination of surgery and radiotherapy in these patients is thus emphasised.

Initially, the only radiological change in the spine was laminal erosion, although the process advanced to vertebral collapse eventually.

The presence of amyloid substance within the tumour

caused some difficulties with the histological diagnosis. McMahon (1951) had a similar case.

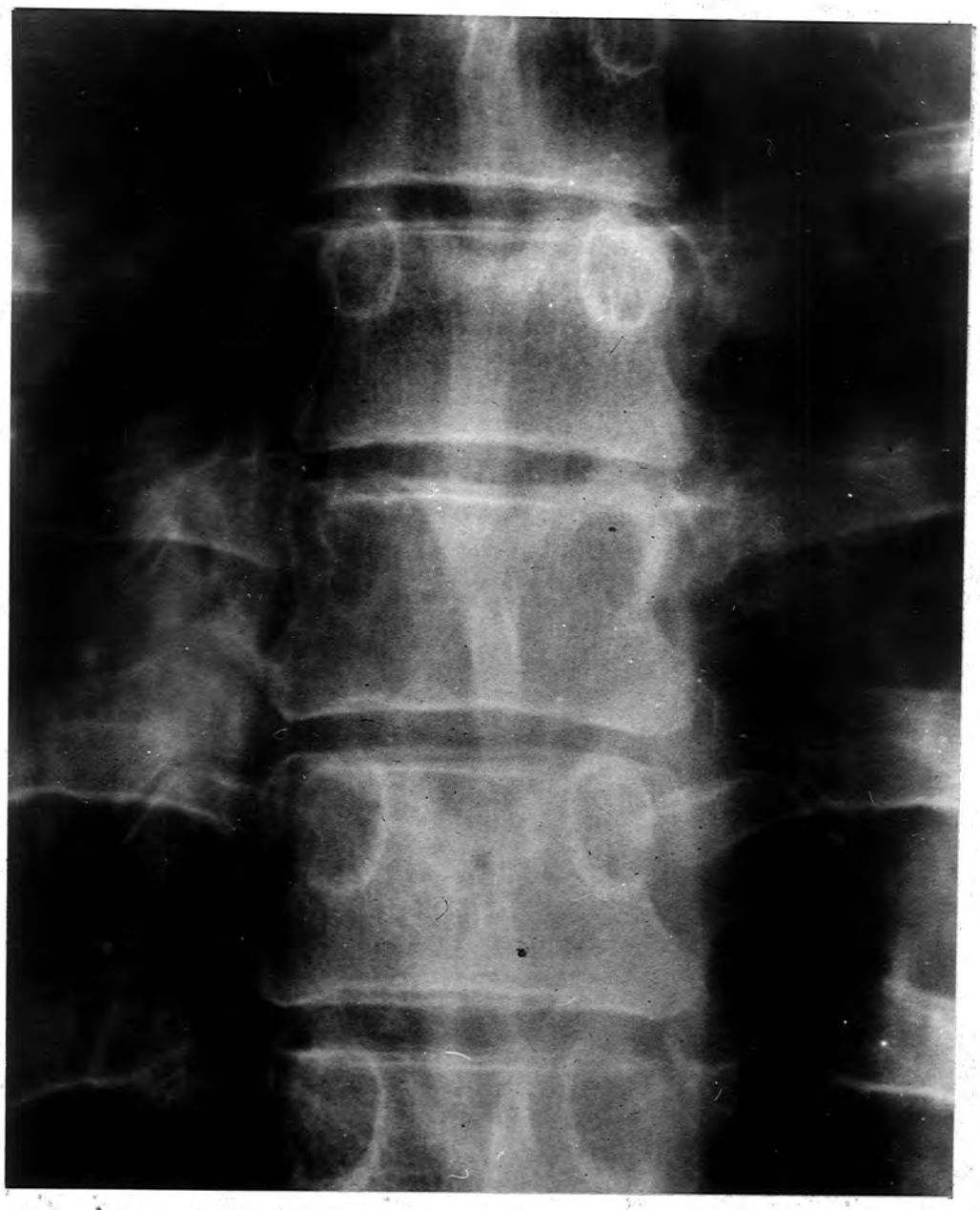

Fig.42. CASE EIGHTEEN. X-ray of thoracic spine, axial view. The pedicles of T.8 are eroded, the right more than the left.

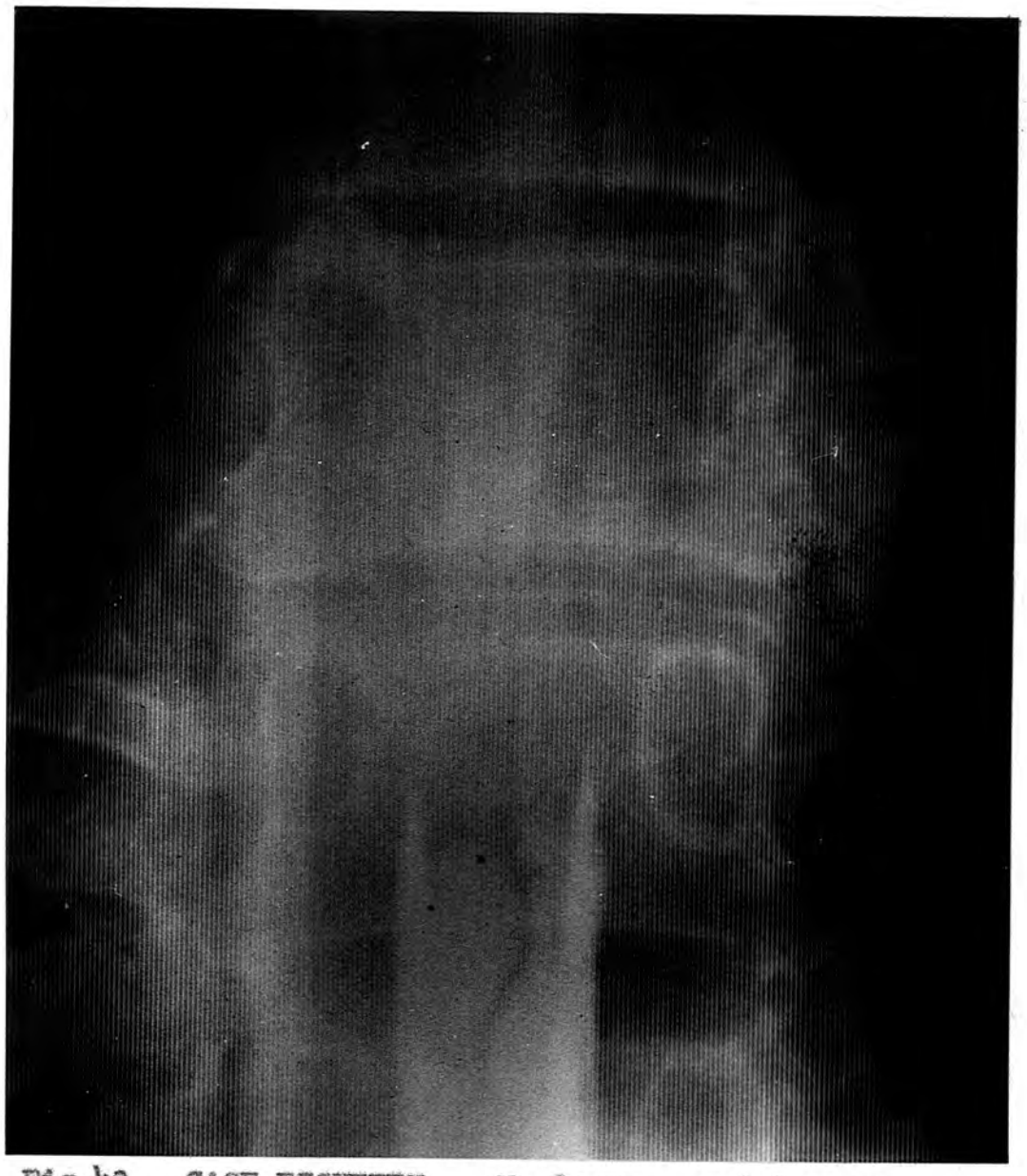

Fig.43. CASE EIGHTEEN. Myelogram, axial view.
There is a complete hold-up opposite the body of T.9.
The erosion of the pedicles of T.8 is again seen.

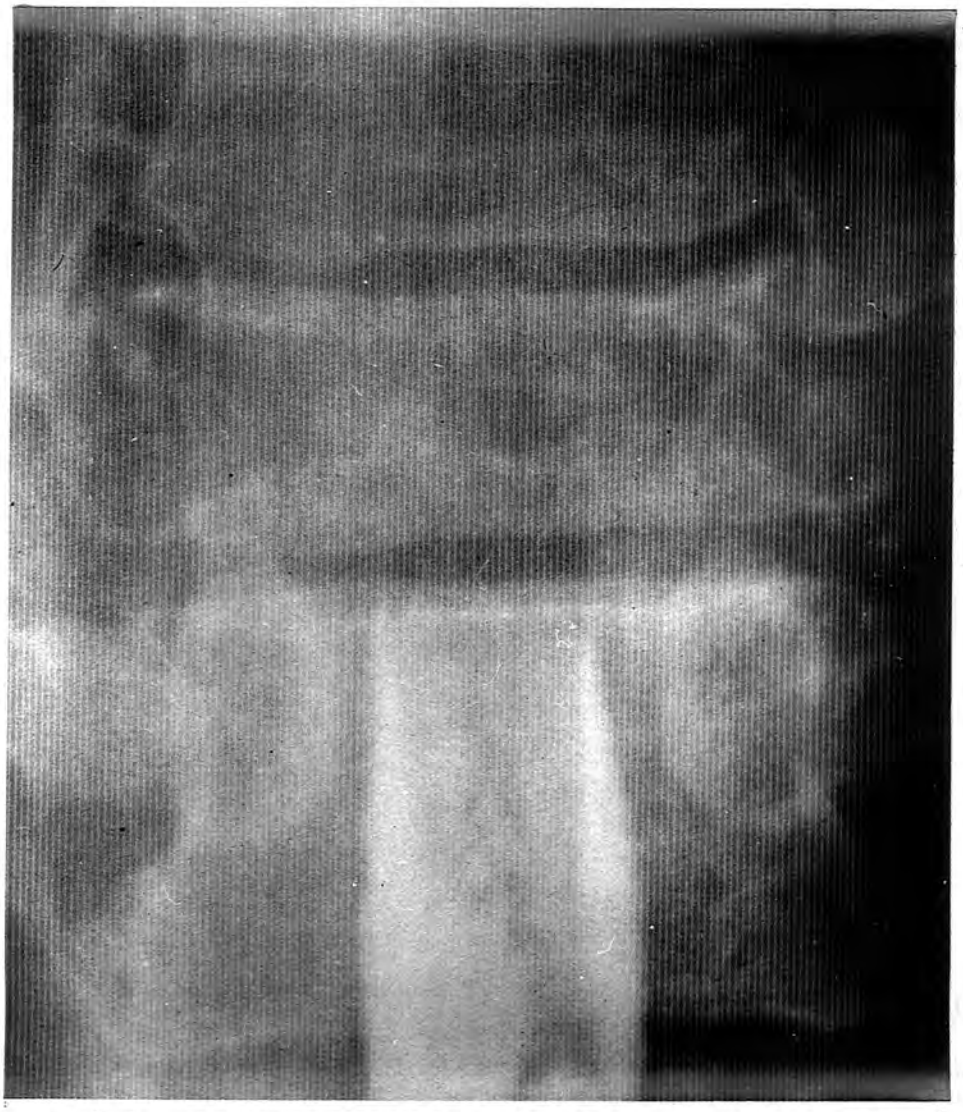

Fig.45. CASE EIGHTEEN. Myelogram, axial view, showing complete hold-up at lower border of T.8 which is now collapsed.

CASE NINETEEN 12

Female, 53. 9 months of post-traumatic perineal pain and sudden Brown-Séquard Syndrome 3 months before admission. Cord lesion at T2. Bones riddled with osteolytic foci; no vertebral collapse. Myelomatosis proven. Radiation therapy and stilbamidine only. Death almost 2 years after onset of disease. No autopsy.

G.S., (Hospital No. 108557), a housewife aged 53, was admitted to the Radcliffe Infirmary, Oxford on 8 July 1949 and discharged on 2 August 1949. She was under the care of the late Sir Hugh Cairns.

HISTORY.

Her past and family histories did not yield any contributory information.

Nine months before admission, she fell on her right side and thereafter experienced perineal pain that occurred in brief bouts. Three months before, over the period of one day, the right leg had become numb, and this rapidly spread to involve the right side of the trunk. The next day she noticed a weakness of the legs, the left more than the right, and the right arm became weak too. This state of affairs persisted with the addition of retention of urine and faecal

incontinence, for one week.

EXAMINATION.

She was pale and lethargic. On the right, a Horner's syndrome was present. There was a Brown-Séquard syndrome, in as much as the left leg was completely paralysed and joint position sense was impaired in it, and on the right, pain and temperature appreciation were diminished up to a level at T2. There was also slight weakness of the right thigh and all the reflexes were pathologically increased and both plantar responses were extensor in type. Vibration sense was absent in the legs.

Suprapubic bladder drainage was necessary.

INVESTIGATIONS.

X-rays. Spine: There were diffuse osteolytic areas scattered throughout but maximal in the lower cervical and upper thoracic regions. There were, however, no collapsed vertebral bodies.

Pelvis, ribs and skull: Similar riddling with myelomatosis.

Cerebrospinal Fluid. No block. Cells, 2 leucocytes per c.mm. Protein, 35 mgm. per cent. Lange, normal. W.R., negative.

Blood. Picture: Haemoglobin, 36 per cent.

E.S.R.: 146 mm. in one hour (Westergren).

Urea: 64 mgm. per cent.

Calcium: 14.5 mgm. per cent.

Serum Proteins: Total, 10.2. Albumin, 2.3. Globulin, 7.9 g. per 100 ml.

Urinalysis. No Bence Jones protein found.

Bone marrow biopsy (sternum). A relative increase of plasma cells was found.

PROGRESS.

It was thought that her condition was too desparate to warrant surgical intervention and she was therefore treated with deep x-ray irradiation to the cervico-thoracic spine. In addition she was given a course of Stilbamidine.

She returned to her home where the course of her disease was steadily progressive and spinal cord compression became complete. She died on 7 October 1950, nearly two years after the first symptom appeared. There was no autopsy.

COMMENT.

This is the type of case that has caused considerable confusion in the literature and has been referred to already (p. 99). The patient manifests adequate signs of a focal cord lesion and yet despite the diffuse involvement of the spinal bones there is no vertebral collapse and for various reasons, spinal cord compression may

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CASE TWENTY

Female, 58. 6 weeks of rapidly progressive motor and sensory paraplegia with urinary retention for 1 week. Sensory level at T2 with complete paralysis below. Thoracic spine x-rays normal. Manometric and myelographic block (lower limit) at T9. Operation, and death 2 days later. Survival, 7 weeks. Autopsy. Extradural plasma cell myeloma T2 - T9 with severe cord compression.

E.B., (Hospital No. 141793), a housewife aged 58, was admitted to the Radcliffe Infirmary, Oxford on 22 May 1951 under the care of the late Sir Hugh Cairns. She died four days later.

HISTORY.

No relevant information was found in either her past or family history.

Six weeks before admission, she had experienced the sudden onset of severe and continuous pain behind the upper sternum, extending deeply to the back where it was maximal in the region of the right scapula. One week before, the legs had become weak and urinary retention manifested itself. For five days, the legs had been completely paralysed and sensation was absent below the waist.

EXAMINATION.

She was obese and quite helpless. Abnormalities of the nervous system were confined to the lower extremities, where there was a complete, flaccid, motor paralysis. All the reflexes in the legs were absent, as were the abdominals. A sensory level to all modalities was present at T4 but sensation did not become normal until T2 was reached; there was also a lack of sweating below the latter boundary. Respirations were difficult and it seemed that only the diaphragm was working.

The other systems were normal.

INVESTIGATIONS.

X-rays. Thoracic spine: There were no bony abnormalities detected, although it is to be admitted that the region of T2 was not studied closely.

Chest: Normal.

Cerebrospinal Fluid. Complete manometric block. Cells, none. Protein, 600 mgm. per cent.

Blood. Picture: Haemoglobin, 65 per cent. White cells, 8,000 per c.mm.

Urinalysis. B. coli infection.

Myelogram. The radio-opaque material was introduced into the lumbar sac and a complete subarachnoid block could be demonstrated opposite T9. (Fig. 46).

OPERATION. 24 May 1951 (Mr. O.V. Jooma)

The cord from T2 to T9 was encircled by greyish-white, tumour tissue which was compressing it severely. Only a biopsy was taken, because the patient's condition was not good.

HISTOLOGY.

The piece of tissue examined did not have many of the characteristics of a plasma cell myeloma but taken in conjunction with the later findings there was no doubt concerning the diagnosis. (Fig. 47).

PROGRESS.

Owing to her obesity and respiratory embarrassment, she deteriorated rapidly after the operation and died two days later, on 26 May 1951. The events had occurred so rapidly in this case, that there had been no opportunity of extending the investigations to search for other evidence of myelomatosis.

AUTOPSY. (Dr. F.D. Bosanquet)

There was excessive and generalised deposition of subcutaneous fat. The lungs were bulky, oedematous and congested; a bronchopneumonia was found in the dependent parts. The heart cavities were generally dilated. The other systems and tissues were normal, but the bone marrow was not examined microscopically.

Nervous System. The brain was normal. At the

because of the patient's helpless and desparate state. The histological samples, however, showed that the bone was involved and the possibilities are that the myeloma grew from it, despite the lack of radiological evidence, or invaded the bone secondarily. If the latter was the case, an extra-osseous source must be sought. It is clear that the myeloma did not grow from the dura mater - or at least not from the portions that were examined - and the remaining type of neoplasm would be of the primary epidural variety. On the whole, it seems more likely that a type of bony lesion was responsible and it had probably grown from the laminae, as has been seen before (Case eleven, to quote only one example).

Whatever its aetiology, this myeloma grew very rapidly and compressed the cord over a distance of nine segments. The total survival (seven weeks) is one of the shortest on record. Although full investigations were not carried out, it seems likely that other evidence of myelomatosis was present and contributed to the fulminating clinical course. No biochemical or fresh bone marrow studies were made.

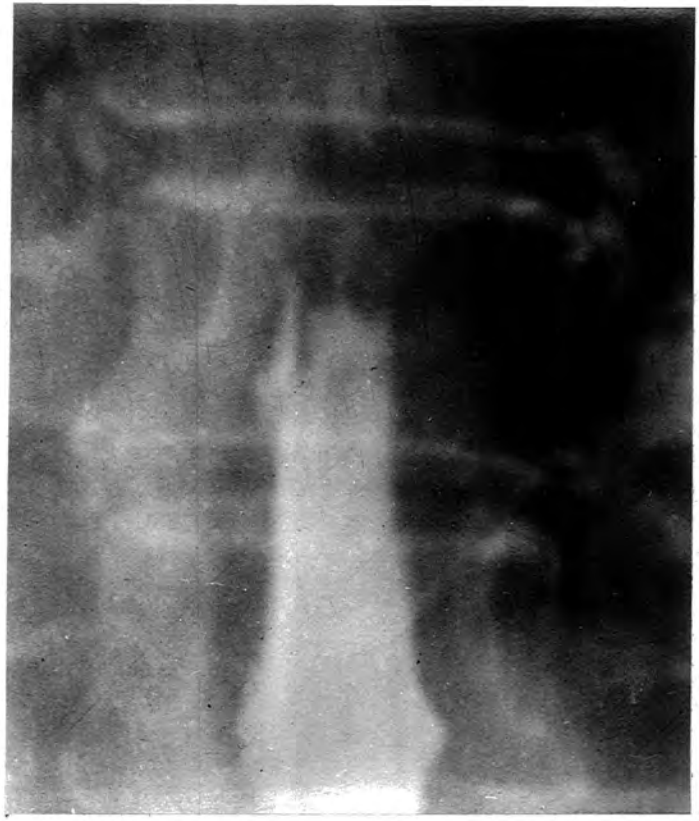

Fig.46. CASE TWENTY. Myelogram, axial view. There is a complete hold-up opposite the body of T.9. The vertebrae are healthy.

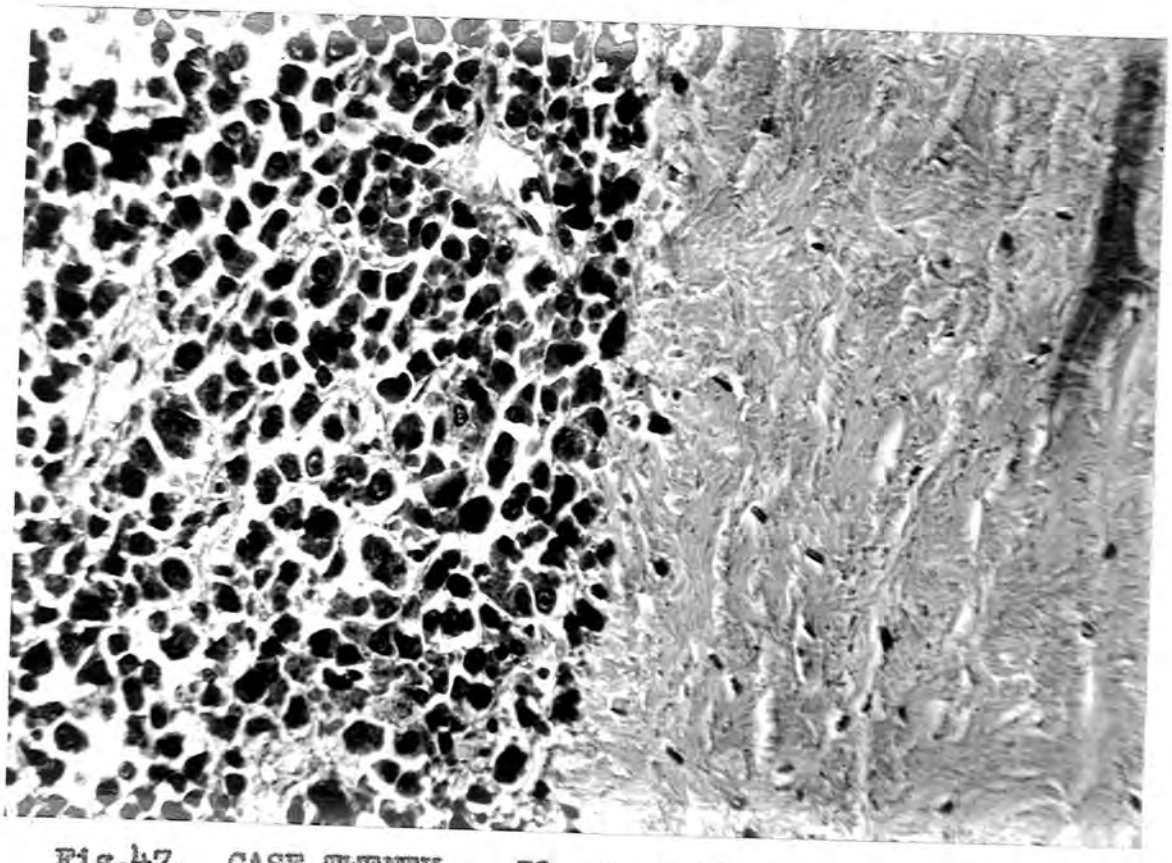

Fig.47. CASE TWENTY. Plasma cell myeloma. The tissue on the right is the spinal dura mater which is thickened (see Fig.48), and the boundary between it and the tumour tissue is a very sharp one. There is no infiltration of the dura (x420).

14

CASE TWENTY-ONE.

Male, 57. Traumatic compression fracture L.1 6 years ago with no sequelae. 2 years of low back and leg pain. 4 months of increasing leg weakness due to cauda compression. L.1 collapsed and eroded: extra-vertebral extension. Manometric and myelographic block. Partial removal of plasma cell myeloma from spinal canal. Recovery began after D.X.R. (palliative dose). Evidence of widespread disease. Good recovery. Alive. Survival, 4 years.

C.S. (Hospital No. 138084), a male railway checker aged 57, was admitted to the Radcliffe Infirmary, Oxford on 1 March 1951, under the care of the late Sir Hugh Cairns.

HISTORY.

In the past, (six years before admission) he had fallen at work and suffered severe backache. Subsequent X-rays showed a compression fracture of L.1. There were no neurological signs at this time and he made a complete recovery, being symptom-free until the onset of the present illness.

His family history was not relevant.

Two years before admission, he first experienced a sharp, aching pain in the right sacro-iliac region, later

spreading to the left. For four months this pain had been radiating down the backs of both legs and had the characteristics of root pain. Also, four months before, he found that his legs were becoming weak (left more than right) and this gradually became more severe. His sphincters were functioning normally.

EXAMINATION.

A well developed healthy-looking man. All was normal except his back and legs. In the former, movements were limited by pain and at L.1 there was a small subcutaneous swelling which was painful to touch. The left leg showed generalized wasting and both legs were severely weak. The tendon reflexes were either absent or hypoactive and the plantar responses were both flexor. In the right L.1 and L.2 dermatomes, hypo-aesthesia and hypo-algesia were found, but all other modalities were normal.

Other systems were normal.

INVESTIGATIONS.

X-rays. Lumbar spine: The body of L.1 was collapsed and there was extensive erosion of it, especially on the right side. To the right, was a soft tissue mass (5.0 cm. in diameter) with shell-like peripheral calcification. The lamina and transverse process on this side were extensively destroyed. (Fig. 49 and 50).

Cerebrospinal fluid. Partial block. Fluid faintly

yellow. Cells, 3 polymorphs and 2 lymphocytes per c.mm. Protein, more than 1000 mgm. per cent. Lange, 4444332211. W.R., negative.

Blood. Picture: Haemoglobin, 93 per cent. Red cells, 4.95 million per c.mm. White cells, 8,500 per c.mm.

E.S.R: normal.

Calcium: 9.4 mgm. per cent.

Myelogram. There was a complete obstruction opposite the upper border of L.2 (Fig. 50).

OPERATION. 6 March, 1951 (Mr. J.B. Pennybacker).

The subcutaneous swelling was found to be the outcrop of a tumour that had invaded and largely replaced the spinous process and laminae of L.1 and part of T.12 also. The extravertebral extension visible on X-ray (Fig. 50) was found and it was seen to be infiltrating muscle. In the spinal canal, purplish-grey tumour material was extending in a caudal and cephalad direction, investing the dural tube like a collar and pressing upon the cord. Despite troublesome bleeding, most of the accessible tumour was removed. It came away easily from the dura and the piece taken out measured 9.5 cm. long by 2 cm. thick.

HISTOLOGY. (Dr. F.D. Bosanquet).

Typical plasma cells without mitoses were seen invading muscle. It was diagnosed as a plasma cell

myeloma. (Fig. 51).

PROGRESS.

There was little or no change in his physical state post-operatively except for diminution of the root pain. He was nursed in a plaster bed.

A few months later, he had a course of deep X-ray treatment to the lumbar spine. As an X-ray of skull had now revealed multiple osteolytic lesions, only a palliative dose was given. Further investigations at this time revealed:- normal bone marrow (sternum and iliac crest), normal plasma proteins and no Bence Jones proteinuria.

Following the radiation therapy, recovery began to take place and when seen three months after the operation, he was able to walk short distances unaided and had no pain. He was wearing a spinal support. One year after this, improvement was continuing and he had returned to work. He was last seen in January, 1953 when he reported further progress and his activities were normal. No abnormal physical signs could be detected. He has thus survived two years post-operatively and four years in all.

COMMENT.

It is of exceptional interest to note that four years before the onset of his present illness, he had suffered a compression fracture of L.1. The nature of the acident was such that there could be no question of the fracture

being pathological: that is, there was an adequate degree of trauma. Thus it seems unlikely that this episode was the first manifestation of myelomatosis, especially as he was symptom free for four years following it. It is perhaps most likely that the myeloma grew in the area of traumatised tissue, as also occurred in the patient of Flax (1941). The true sequence of events, however, will never be known.

The other point of note concerning this case is that only a palliative dose of X-ray irradiation was given because evidence of generalized myelomatosis was present (multiple skull lesions). Despite this, he made a gratifying recovery, which lends support to the belief that even in the face of the widespread disease which is however of a slowly progressive nature as in the present case, adequate and active therapy should be undertaken. Admittedly, the overall prognosis is not good but the patient is at least spared the pain and distress of a spinal myeloma compressing the cord.

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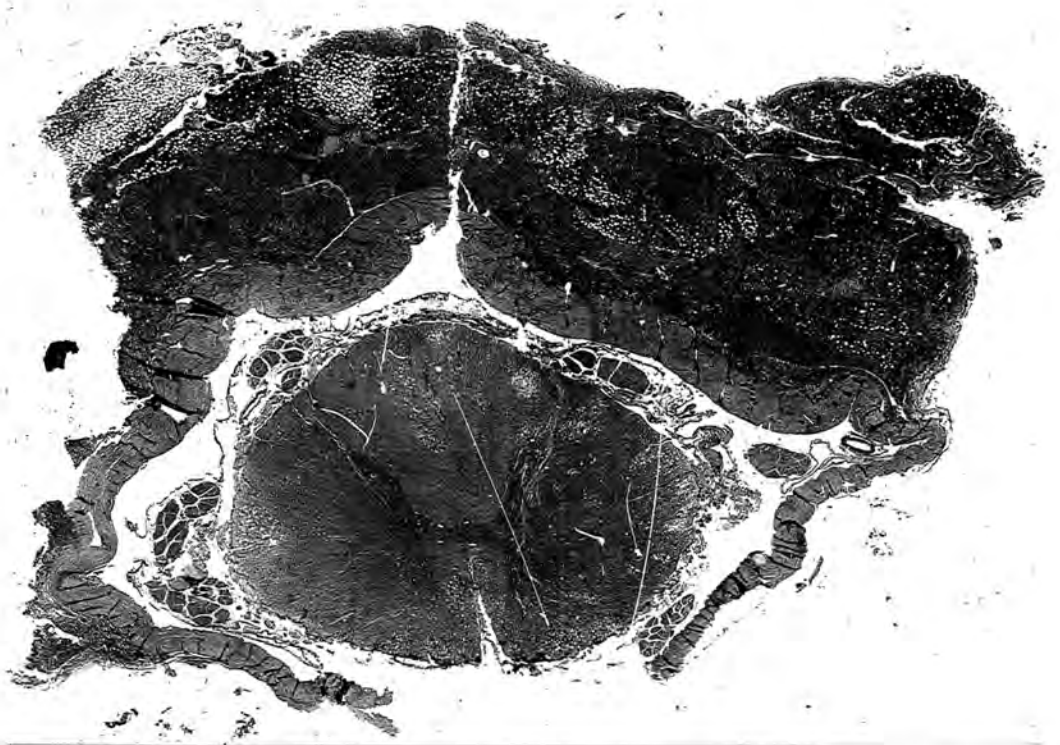

Fig.48. CASE TWENTY. Transverse section of the spinal cord and surrounding tissue, at the mid-thoracic level. There is considerable disorganisation of the cord due to pressure, the dura is thickened and there is a layer of myelomatous tissue posteriorly. (x9).

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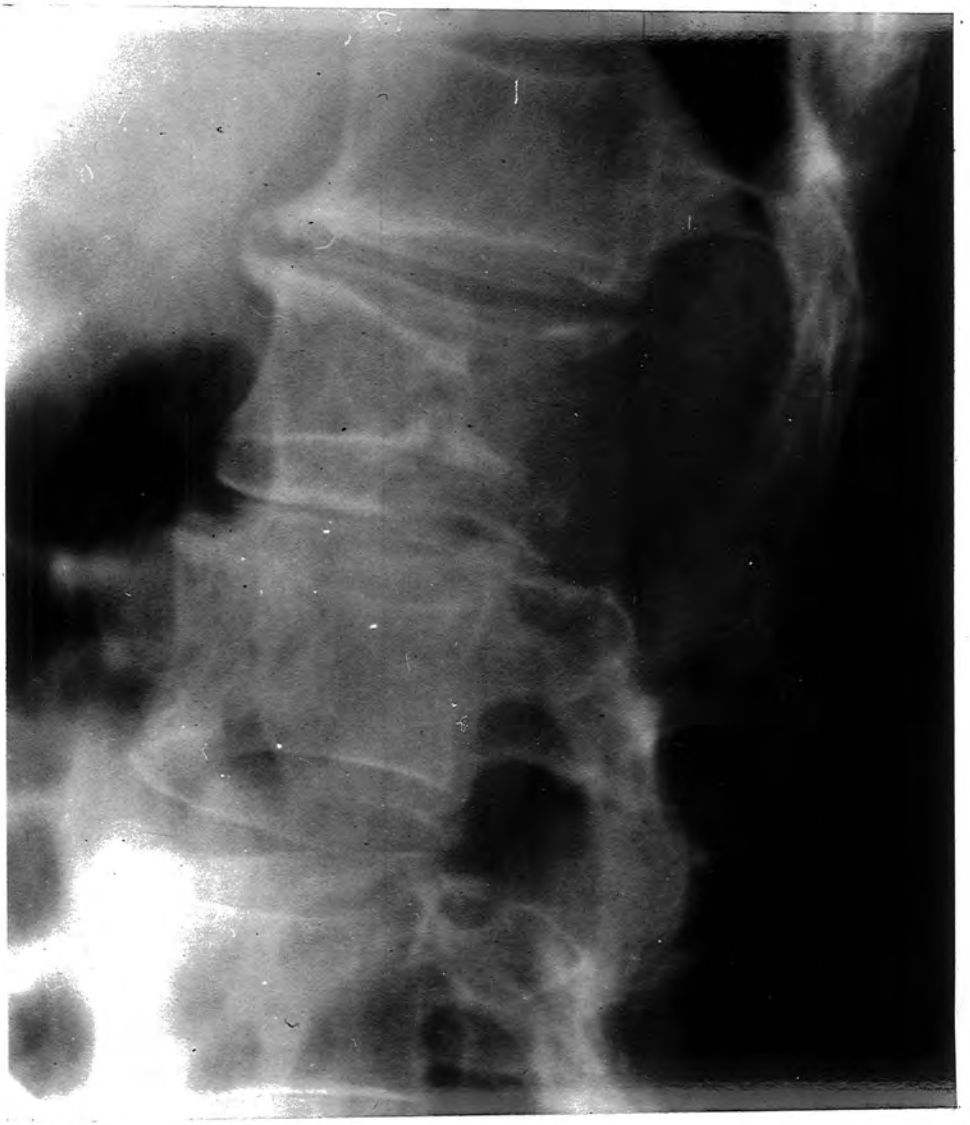

Fig.49. CASE TWENTY-ONE. X-ray of lumbar spine, lateral view. The body of L.1 is compressed and there is erosion of its posterior part. The laminae are destroyed.

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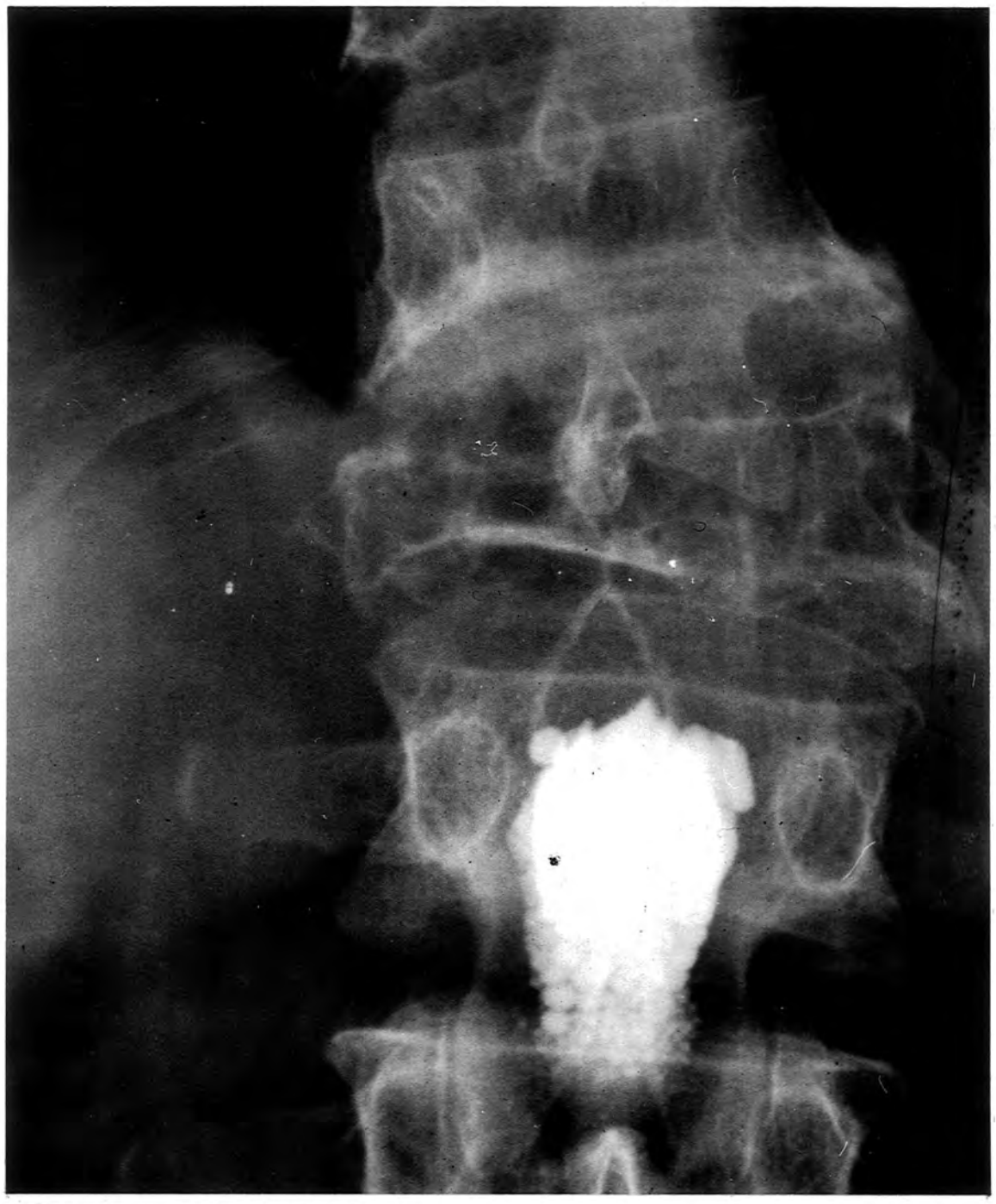

Fig.50. CASE TWENTY-ONE. Myelogram. There is a block at the upper border of L.2. The diseased L.1 vertebra can be seen, as well as the paravertebral soft-tissue shadow on the right.

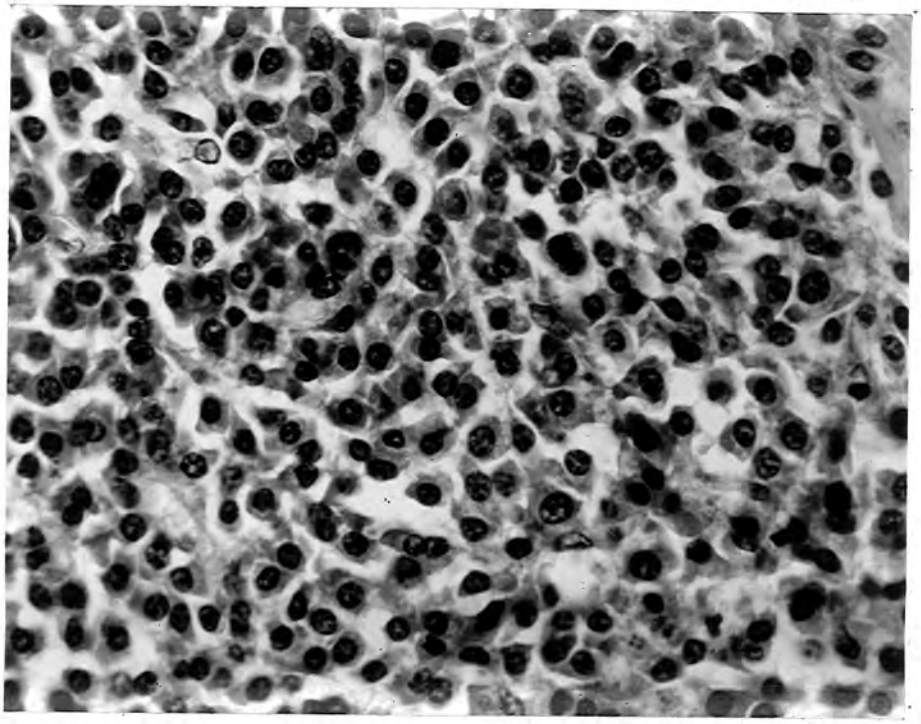

Fig.51. CASE TWENTY-ONE. Spinal myeloma made up of very numerous plasma cells. No mitoses. (x580).

15.

CASE TWENTY-TWO.

Female, 66. Known diabetic. Backache following pneumonia 4 months previously. Sudden onset of cord compression 1 month before admission, due to collapse of T8. Complete motor and sensory paraplegia. Operation. Death 4 days later. Total survival 5½ months. Autopsy. Complete disappearance of T8 with spinal canal encroachment and cord compression by plasma cell myeloma. Microscopic deposit of plasma cells in right lung.

F.H. (Hospital No. 154978), a housewife aged 66, was admitted to the Radcliffe Infirmary, Oxford on 5 March 1952, under the care of the late Sir Hugh Cairns, and died there 2 weeks later.

HISTORY.

She was known to have had diabetes mellitus for at least a year. Five months before admission, she had suffered pneumonia with cellulitis of the anterior chest wall and a staphylococcus aureus organism was cultured from this region. After this, she began to lose weight and four months before admission, she first complained of backache with girdle-like extension. She was confined to her bed and one month prior to admission, while being lifted, she felt something "give" in her back and found that the legs were weak and numb; there was no

accompanying increase of pain. Over the next 10 days, the leg weakness became much worse and the sphincters were now affected. She was suffering no back pain, however. X-rays showed a collapse of T8 vertebral body (Fig. 52) and on account of this and a continued pyrexia, a diagnosis of tuberculous spinal disease was made and she was sent for surgical treatment.

EXAMINATION.

She was pale and "toxic"-looking and there was a severe flaccid paraplegia with a sharp sensory level at T8. The spinous processes of T8 and T9 formed a prominent, angular kyphosis. There was overflow urinary incontinence with cystitis. The blood pressure was 105/40 and examination of the cardiovascular system revealed auricular fibrillation.

INVESTIGATIONS.

X-rays. Thoracic spine: There had been further collapse of the body of T8 (Fig. 53). The compression of this bone had been so complete that it was difficult to visualise it in the lateral view (Fig. 53). The bodies above and below (T7 and T9) had closed down upon it and were themselves somewhat wedge-shaped but otherwise normal.

Cerebrospinal Fluid. A faintly turbid fluid. Cells, 2 polymorphonuclears and 4 lymphocytes per c.mm.

Protein, 65 mgm. per cent.

Blood. Picture: Haemoglobin 11.8 g. White cells, 27,000 with a polymorphonuclear leucocytosis.

PROGRESS.

An attempt was made to regulate the diabetes more carefully and to improve her general condition. When this had been partially accomplished, operation was proceded with.

OPERATION. 15 March 1952. (Mr. J.B. Pennybacker).

The lamina of T8 was found to be invaded by tumour tissue and a purplish-grey circumscribed mass was partially encircling the cord and compressing it at this level. Much of the tumour was removed; it was not unduly vascular.

HISTOLOGY. (Dr. F.D. Bosanquet).

The histological characteristics were those of a plasma cell myeloma. (Fig. 54).

PROGRESS.

She tolerated this procedure well, but soon declined and died of a combination of heart failure, diabetic coma and urinary infection on 19 March, 1952, four days after the operation. Her illness had lasted five and one half months.

AUTOPSY. (Dr. F.D. Bosanquet).

The whole of the vertebral body of T8 had disappeared

The incorrect diagnosis of tuberculous spine is one of the frequent mistakes made when dealing with spinal myelomas. The initial therapy, however, decompression of the spinal cord, is much the same in each condition.

Autopsy and X-ray revealed how complete the destruction of a vertebral body attacked by a myeloma can be. Its collapse accounts for the sudden access of limb dysfunction and the association with the mildest of trauma should be noted.

Apart from the lung lesion, no other evidence of myelomatosis could be found but as with other cases in this series, investigations were not exhaustive either during life or at post mortem. As noted above, it is impossible to be certain about the plasma cell deposit in the lung. On the whole it seems unlikely that it was a part of the generalized disease.

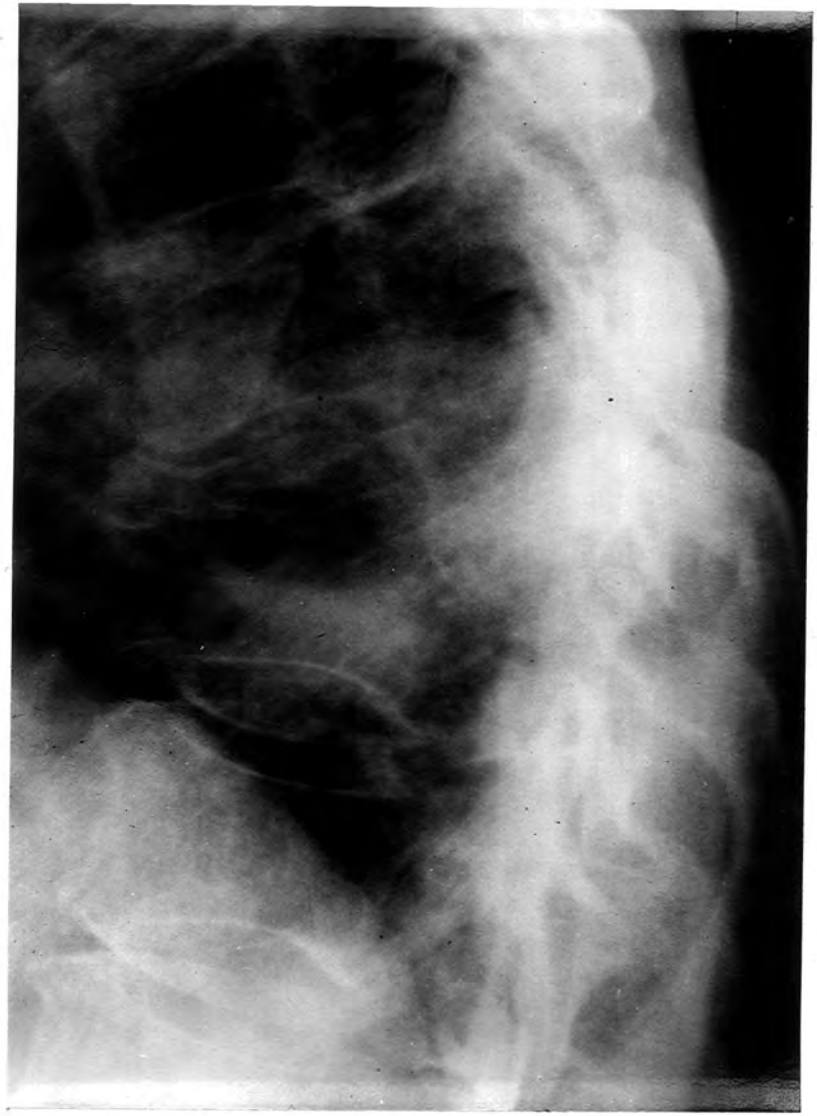

Fig.52. CASE TWENTY-TWO. X-ray of thoracic spine, lateral view. The body of T.8 has collapsed and is severely compressed.

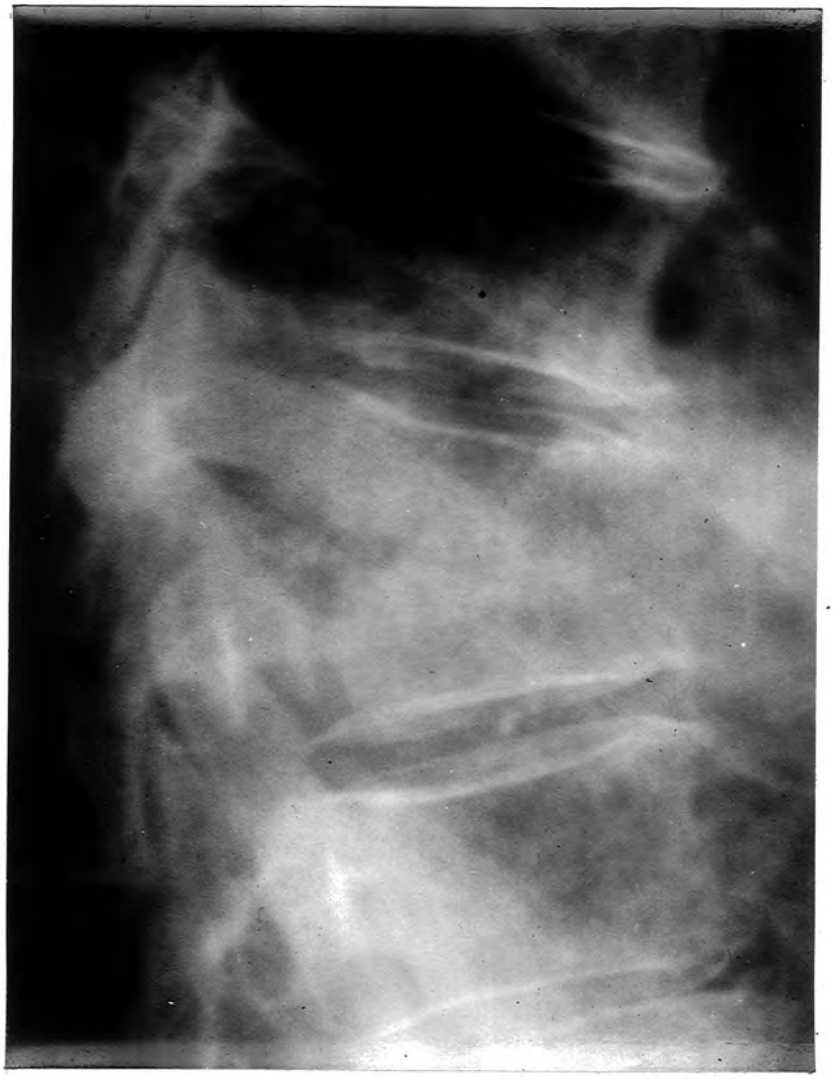

Fig.53. CASE TWENTY-TWO. X-ray of thoracic spine, lateral view, 3 weeks later. The body of T.8 has now almost disappeared.

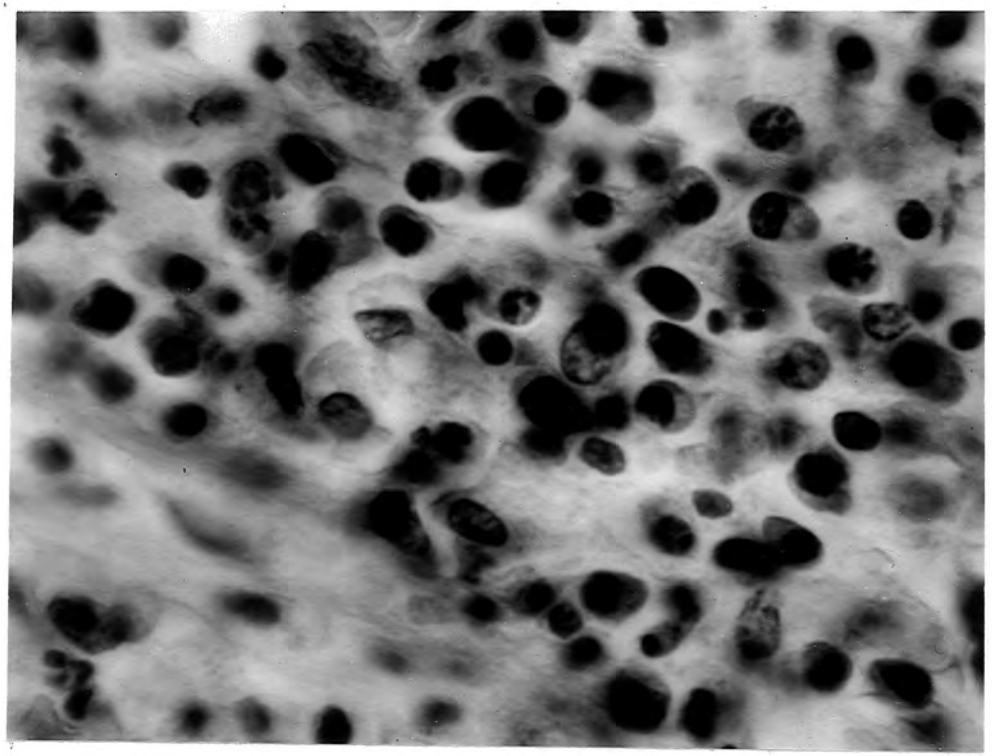

Fig.54. CASE TWENTY-TWO. Spinal myeloma. Plasma cells are numerous. (x1230).

16

CASE TWENTY-THREE.

Male, 50. 15 years of back ache, more severe for 3 months. One month of increasing weakness with urinary retention for 24 hours. Collapsed L3 body. Laminectomy with partial removal of plasma cell myeloma invading bone and canal. Radiation therapy and survival 8 years, with multiple myelomatosis during last two. No autopsy.

J.S. (Hospital No. 97761), a Polish dentist, aged 50, was admitted to Hammersmith Hospital on 25 March, 1949.

Seven years previously, in 1943, he had been admitted elsewhere with a fifteen year history of intermittent back ache. A much more severe pain with radiation to the groins had been present for only three months. For ten weeks, he had noticed progressive leg weakness which had become much more severe twenty-four hours before admission and was accompanied by urinary retention. He had the signs of a compressing lesion of the cauda equina and X-ray showed collapse of the body of L3 a finding that had not been present one month before. There was a complete manometric block. On 24 December, 1943, a laminectomy was carried out and grey tumour tissue was found to be surrounding, but not entering, the

dural tube at the level of L3. The laminae of the affected vertebra and nearby muscle were infiltrated. Some of the tissue within the spinal canal was removed and histological examination revealed a plasma cell myeloma (Fig. 55).

Post-operatively, return of power in his legs was rapid but bladder function took longer to recover. He was treated with deep X-ray irradiation both locally to the spinal lesion and generally, and he seemed to make a complete recovery.

Five years later, however (two years before admission to Hammersmith Hospital), he began again complaining of intermittent back ache. On examination a lesion in the body of T8 was discovered and, in addition, there was now adequate evidence of generalisation of the disease. The body of L3 had recalcified and was stable (Fig. 56). He was treated with further irradiation and stilbamidine but in spite of this he slowly deteriorated. At one time, he complained of paresthesiae on the right side of his face. An X-ray of skull (Fig. 57) was thought to indicate a sphenoidal bone myeloma and it was considered that this was producing the facial paresthesiae. Later, however, it became evident that it was due to a toxic effect of stilbamidine. He died on 4 January, 1951, eight years

after the spinal operation and onset of the disease. An autopsy was not carried out.

COMMENT.

This patient illustrates very well the type of case where the disease multiple myelomatosis begins as a "solitary" focus in the spine and then years later the widespread disease appears and kills the patient (Dalgaard and Dalgaard, 1952). Even if he had been followed for three or four years, his case may still have been put forward as an example of a solitary myeloma. Lengthy follow-up is therefore paramount in the diagnosis of a true solitary lesion. It should be noted that there was no recurrence of the spinal tumour and that death was due to the generalised disease itself.

The time relationships are difficult to establish in this case because of the back ache that had existed for many years. Rather than suggest that the disease process began when this symptom first appeared, it would be better to assume that up till three months before admission, when the back pain changed in character, the causative lesion was coincidental and perhaps a prolapsed intervertebral disc as was proved to be so in Case Fourteen.

The end results of stabilization of the once-diseased

vertebral body are clearly showed in Fig. 56.

It was suggested that X-rays of the skull revealed a myeloma of the sphenoid bone (Fig. 57) and that it was responsible for the trigeminal nerve symptoms. These latter, however, were the toxic effects of stilbamidine therapy and if a basal myeloma was indeed present (and this could not be verified, as an autopsy was not carried out) it was symptomless. Owing to the considerable uncertainty, this doubtful myeloma has not been mentioned elsewhere.

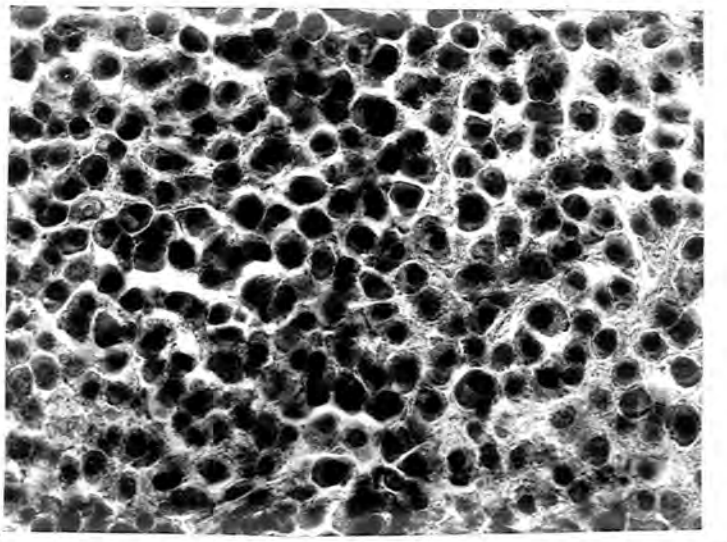

Fig.55. CASE TWENTY-THREE. Spinal myeloma. The most prominent element is the plasma cell and there is very little intercellular tissue. (x450).

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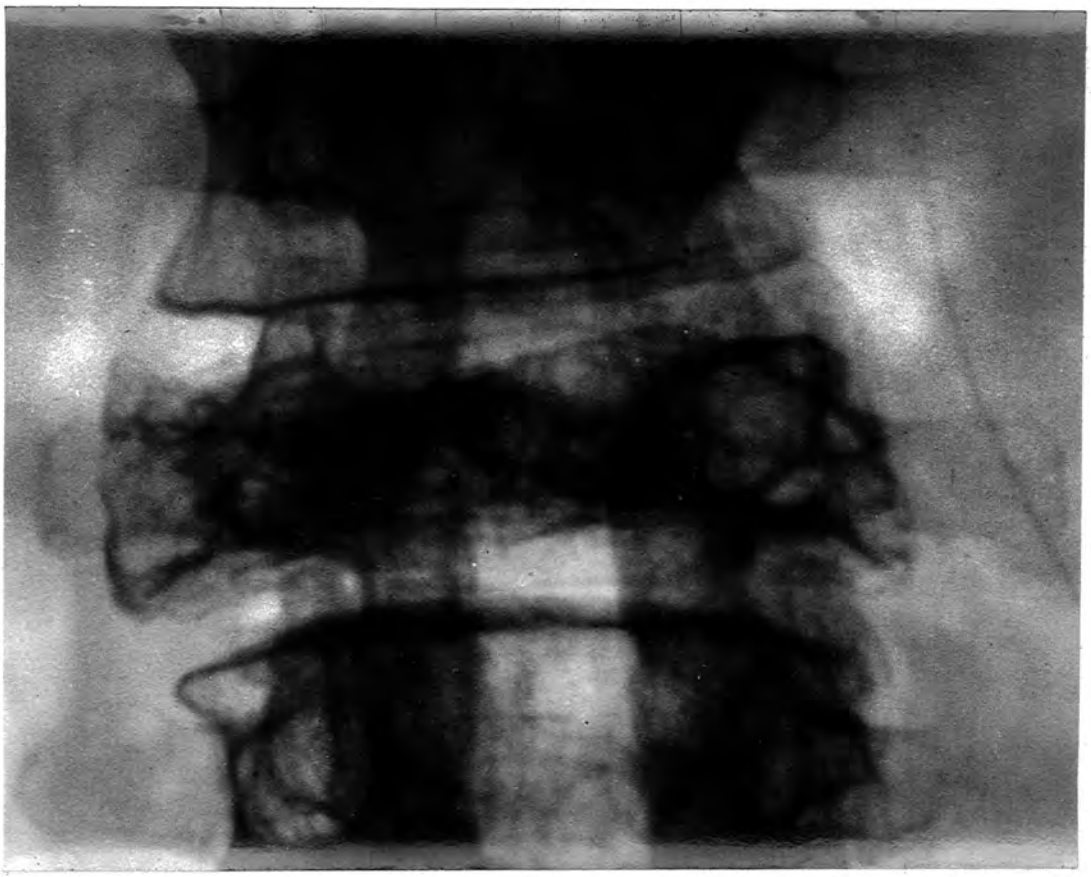

Fig.56. CASE TWENTY-THREE. X-ray of lumbar spine, lateral view, taken 6 years after first symptom. L.3 is collapsed and sclerosed; local recurrence had not taken place.

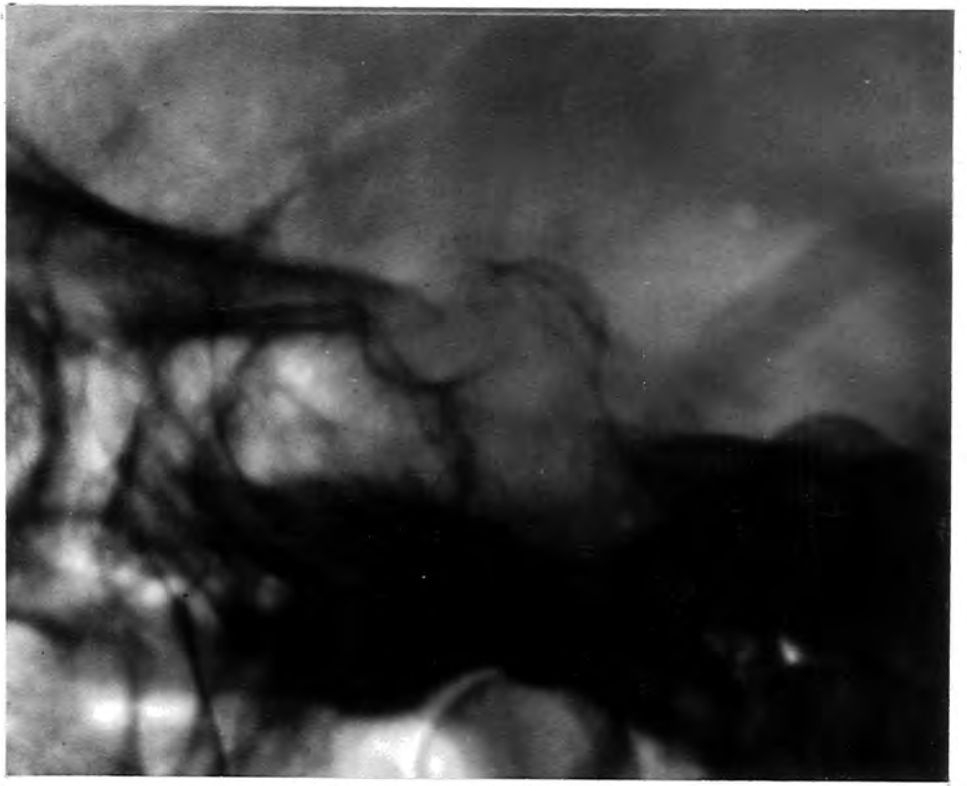

Fig.57. CASE TWENTY-THREE. X-ray of skull, lateral view, showing the sella turcica. The posterior clinoid processes and the dorsum sellae are enlarged and it was considered that there was a myeloma in this region.

Case Number [illegible]

Male. 54. 1½ years of back pain and ½ months of bladder dysfunction. Marked dorsal kyphosis with distortion of L1 and L2. Decreased leg reflexes with bilateral extensor responses. Incontinence of urine. Abnormal Lange. Generalised disease. No response to therapy. Death. Survival, 2 years. No autopsy.

F.N., (Hospital No. 84973), a linesman aged 54, was admitted to Hammersmith Hospital on 3 March 1948, under the care of Dr. W.M. Brigden.

HISTORY.

His past and family histories were not relevant.

One and a half years previously he had noticed low back pain which spread occasionally up to the shoulders but never into the legs. For four months, he had experienced difficulty in controlling his bladder and had frequently wet himself. From this time onwards he was bedridden and needed an indwelling catheter. Investigations at another hospital had shown a normal genito-urinary system but there was a wedge-shaped deformity of the bodies of L1 and L2, as well as a high serum calcium, an infected urine and anaemia.

EXAMINATION.

He was pale and wasted. There was a marked dorsal kyphosis (Fig. 58), so that the costal margins were almost in contact with the iliac crests. In the legs, there was a generalised mild weakness with diminished tendon reflexes and bilateral extensor plantars. The abdominal reflexes were absent. Sensation was intact. He was equipped with an indwelling catheter.

INVESTIGATIONS.

X-rays. All the bones were so severely demineralised that radiological visualisation of them was difficult. However, myelomas were found in the skull and some long bones. The bodies of L1 and L2 were distorted.

Cerebrospinal Fluid. Pressure 115 mm. with normal manometrics. Cells, one. Protein 35 mgm. per cent. 2354321000.

Blood. Picture: Haemoglobin varied from 52 to 70 per cent. Red cells varied from 1.8 to 3.2 millions per c.mm.

E.S.R.: At first it was 75 and later 120 mm. in one hour (Westergren).

Serum Proteins: Total, 9.1. Albumin, 3.5. Globulin 6.6 g. per 100 ml.

Serum Calcium: 13.4 mgm. per cent.

Serum Phosphatase: 3.1 mgm. per cent.

Urinalysis. Repeated testing failed to reveal Bence Jones proteinuria.

PROGRESS.

He was given blood transfusions, stilbamidine and urethane but the drugs had to be discontinued because of toxic effects. Urinary retention continued and the urine remained infected; the responsible organisms were resistant to all forms of therapy.

His legs became weaker but there was always some movement possible. Three months after admission, he was transferred to another hospital and then to his home where he soon died. His fatal illness had lasted almost two years. An autopsy was not carried out.

COMMENT.

This patient is an example of the diffuse demineralisation of bones that is occasionally described in myelomatosis (Weissenbach and Lièvre, 1938). The truncal distortion produced (Fig. 58) is the same as that produced by senile osteoporosis (Dent, Milne, Roussak and Steiner, 1953); it resembled that seen in the patients of Seegelken (1898), Weber (1903) and Geschickter and Copeland (1928, Case 1). The distortion of L1 and L2 were probably due to this diffuse osseous involvement rather than a focal myeloma.

However, encroachment upon the spinal canal had taken place and a compressing lesion at this level would account for the mixture of cord and cauda equina picture, that is a conus medullaris syndrome. The compression could not have been severe, as judged by the physical findings and the normal cerebrospinal fluid, protein and manometrics. The characteristic first zone Lange, however, indicated an abnormality of globulin.

This patient followed the usual course seen with multiple myelomatosis and the spinal compression was a less important aspect of his illness.

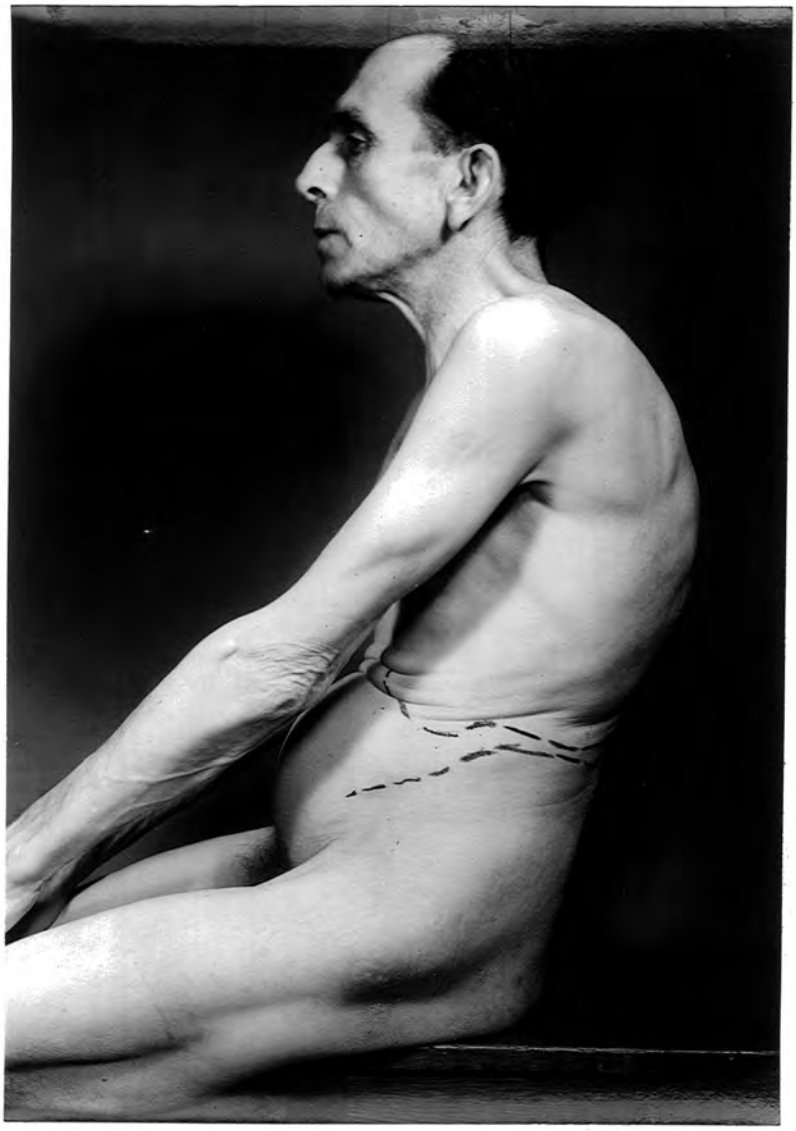

Fig.58. CASE TWENTY-FOUR. Lateral view of patient showing dorsal kyphosis. The costal margins and iliac crests are marked.

CASE TWENTY-FIVE

Male, 65. Left T8 herpes zoster occurring one year after onset of disease and one year before death. T7, 8, 9 and 10 vertebral bodies collapsed. No root pain. Autopsy confirmed spinal lesions: no examination of nervous system.

W.F., (Hospital No. 120090), a singing teacher, was admitted to the Hammersmith Hospital on three occasions. The first was in 1950 when the diagnosis of multiple myelomatosis was substantiated, the second was on 13 April 1951 and his final admission on 12 September 1951. He died on 22 October 1951 at the age of sixty-five having survived exactly two years. He was under the care of Dr. Russell Fraser.

Eight weeks before his first admission, one year after the onset of the disease, and one year before death, he had suffered from herpes zoster on the left side of his lower chest. By the time that he was examined, only the scars of this eruption remained and they were in the territory of the left T8 root. There was a dorsal scoliosis and the lower thoracic spinous processes were prominent, forming a localised gibbus. They were all tender. X-rays revealed collapse of the

bodies of T7, 8, 9 and 10 as well as L1 and L3. There was ample evidence of the primary disease and he was treated with pentamine.

The herpetic eruption did not reappear and his progress was steadily downhill. He suffered pains in many parts of the body including his back but there were never any root pains related to the lower left thoracic region.

Autopsy confirmed the diagnosis and the collapsed vertebral bodies as shown radiologically were found. The spinal roots and ganglia were not examined.

CASE TWENTY-SIX.

Male, 66. One year of generalised paraesthesiae with pain and coldness of fingers and toes. Severe back pain 7 months and leg weakness for 4 months. Picture of polyneuritis (with ? peripheral vascular occlusive disease). X-rays, C.S.F. and myelogram normal. Hyperglobulinemia with E.S.R. 140. Bence Jones proteinuria. Abnormal pyruvate metabolism. Death. Survival, c. 15 months. No autopsy.

R.C., (Hospital No. 75045/1947), an agricultural agent aged 66, was admitted to the Radcliffe Infirmary, Oxford on 21 July 1947 under the care of the late Sir Hugh Cairns.

HISTORY.

Eighteen months previously, he had suffered from "arthritis" of the left hip which was dispelled by treatment.

His family history contained no relevant information.

One year before admission, he noticed the gradual onset of "pins and needles" all over the trunk and limbs. The toes and fingers were painful and his hands and feet would be frequently cold, despite the summer weather. The paresthesiae, at first intermittent, soon became

constant and more severe. For seven months, there had been a pain across the shoulder blades, which a month later began to radiate to the front of the chest. The pain spread to involve most of the spine and had some of the characteristics of root irritation. For four months, he had found that walking was becoming difficult on account of leg weakness, as well as the back pain.

He had lost a considerable amount of weight recently but had no other complaints.

EXAMINATION.

His general condition was good. The grip bilaterally was poor (due mainly, he said, to pain) weakness of both legs, more marked proximally and affecting the left leg slightly more. All the arm tendon reflexes were greatly diminished and those in the legs were absent; plantars were equivocal. There was a glove and stocking type of sensory impairment and varying patches of hyperalgesia. The modalities other than pain and touch were normal.

Diffuse tenderness of the spine could be demonstrated and movements were limited because of pain. The muscles of his legs were also tender. The peripheral arteries were thickened but pulsating. The left ring finger, however, was a bluish colour and was tender and cold to touch. Blood pressure = 170/100.

a course of thiamine and nicotinic acid, the abnormality was decreased although not removed.

Myelogram. It was thought that a spinal compressing lesion could not be ruled out entirely on the results of these investigations and a myelogram was therefore carried out. No abnormality could be demonstrated.

PROGRESS.

Despite the biochemical improvement, there was little change clinically. The pain persisted and at times he was irrational and noisy and had to be sedated with paraldehyde.

He was discharged on 22 August 1947, one month after admission and returned to his home where he died some months later. Unfortunately, an autopsy was not carried out.

COMMENT.

This case is an acceptable example of a very rare condition, myelomatous neuropathy. The clinical picture and the investigations are all in keeping with the presence of a neuropathy and myelomatosis was proven beyond doubt. Spinal compression was excluded by myelography. A defect of peripheral nerve metabolism was indicated by the abnormal pyruvate tolerance curve (Fig. 59).

It is held that amyloidosis may in some cases of myelomatosis account for the presence of a neuropathy. The only points in favour of it in the present case, are the features suggestive of peripheral vascular occlusive disease and the normal x-rays of bones despite the widespread nature of the disease.

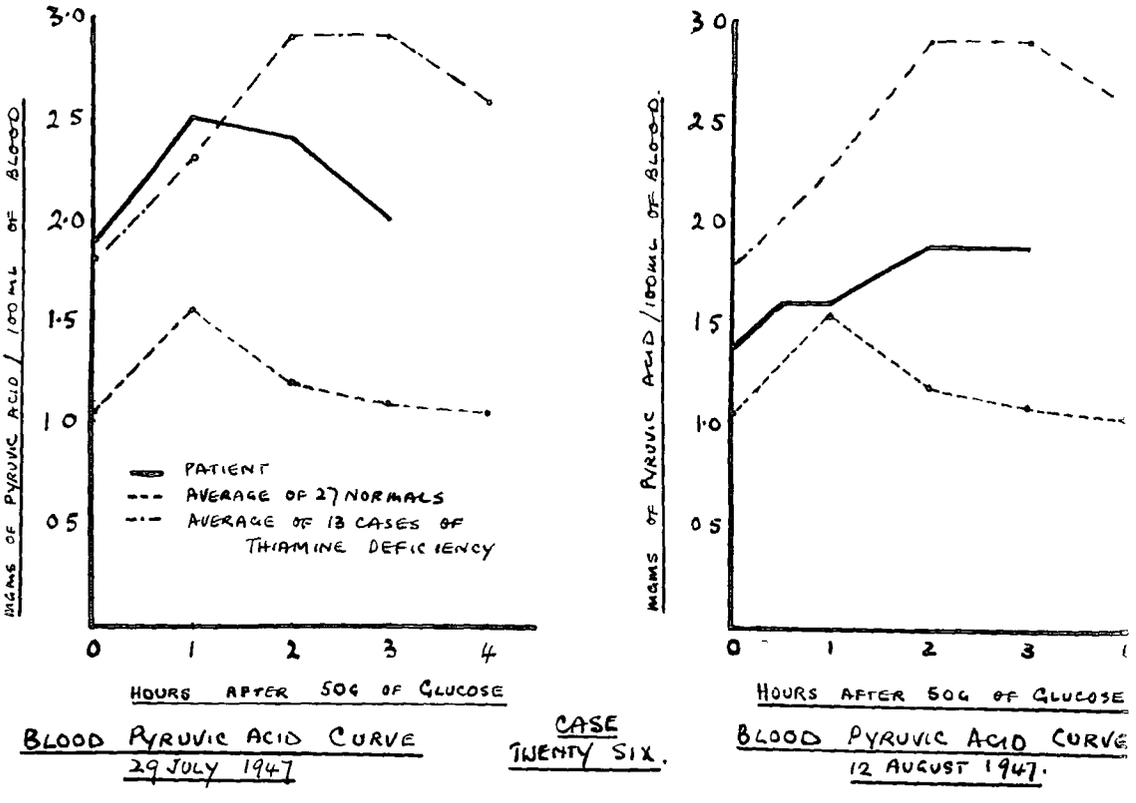

Fig.59. CASE TWENTY-SIX. Blood pyruvic acid curves, before and after the administration of thiamine and nicotinic acid.

APPENDIX II

CASES OF MULTIPLE MYELOMATOSIS WITH SPINAL CORD OR CAUDA EQUINA COMPRESSION SELECTED FROM THE LITERATURE

A. Cases with adequate clinical and pathological data (141 cases).

Rustizky (1873)
Stokvis (Kühne, 1883, etc.)
Hammer (1894)
Seegelken (1897
Bozzolo (1898)
Winkler (1900)
Wright (1900) } same case.
Wright (1900) }
Thomas (1901) }
Thomas (1902) } same case.
Christian (1907, Case 1) }
Bender (1902)
Jellinek (1904)
Moffat (1905)
Devic and Beriel (1906)
Permin (1907, Cases 1 and 3)
Christian (1907, Case 3)
Warstat (1913)
Glynn (1914)
Bomhard (1914)
Schütz (1914)
Kaess (1915)
Wallgren (1920, Cases 4, 5 and 7)
Martin and Colrat (1920)
Wells (1921)
Kohlmann (1921, Case 1)
Turner (1921)
Hansen (1922, Case 7)
Osgood (1923)
Walthard (1924)
Guggenheimer (1924, Cases 1 and 2)
Gaube (1925)
Grosz (1925, Case 16)
Laesecke (1927)
Pines and Pirogowa (1928, Case 1)

Hallermann (1929, Case 4)
M.G.H. Case Record No.16482 (1930)
Bryan and Levitin (1931)
Zäh (1932)
Busser and Lichtenburger (1933) } same case.
Busser and Hugueny (1939, Case 15) }
Scott, Stanton and Oliver (1933, Cases 1 and 4)
Bell (1933, Case 39)
Klemme (1933, Cases 1,2,3,4 and 5)
Jacox and Kahn (1933, Cases 1 and 2)
Ellermann and Schrøder (1933)
Peyton (1934, Cases 1 and 2)
Denker and Brock (1934, Cases 2,3 and 4)
Esperson (1934)
Carlson (1936, Case 3)
M.G.H. Case Record No.22122 (1936)
Cutler, Cantril and Buschke (1936, Case 19)
Hilton (1936)
Rosselet and Decker (1936a and b)
Walker and Bloom (1937, Case 3 and 5)
Busser and Bugaut (1937) } same case.
Busser and Hugueny (1939, Case 17) }
Wright (1937) } same case.
Campbell (1951) }
Davison and Balser (1937, Cases 1,2,3,4 and 9)
Mills and Pritchard (1937, Case 3)
Váradi (1937, Case 3)
Jarre (1938, Case 37704)
Leclerc (1938, Case L)
M.G.H. Case Record No.24192 (1938)
Ghormley and Pollock (1939, Case 6)
Petrides (1939)
Browder and de Veer (1939, Case 6)
Gordon (1939)
Schuppli (1939)
Batts (1939, Cases G.H., M.W. and U.K.)
M.G.H. Case Record No.26072 (1940)
Paul and Pohle (1940, Cases 2,3 and 4)
Kamman (1941)
Abel (1941)
Willis (1941)
Flynn and Sailer (1941)
Donhauser and de Rouville (1941, Case 3)
Tavernier and Leclerc (1941, Case 1)
Brunner (1943, Case J.L.)
Moeschlin (1943, Case 4)

Ley and de Vinals (1943)
Mody (1943, Case 2)
Ectors (1943)
Verda (1944, Case 1)
Shenkin, Horn and Grant (1945, Cases 10 to 16 inclusive)
Bernard, Paget, Bera, Henninot and Samain (1946, Cases 1 and 2). Dereux (1946) - same as Case 2.
Kirschbaum (1947)
Sparling, Adams and Parker (1947, Cases 18 and 19)
Gilbert-Reyfus, Mamou and Attal (1947)
Lumb and Prossor (1948, Cases 6 and 13)
Snyder and Wilhelm (1948)
Baker and Casterline (1948)
Coasacesco (1948)
Lawrence and Rosenthal (1949, Case 1)
Raven and Willis (1949)
Codounis (1949a, Case 4) } same case.
Codounis (1949b, Case 4) }
Rundles and Reeves (1950, Cases 12 and 21)
Christopherson and Miller (1950, Case 3)
Bichel (1950, Case 9)
Stratemeyer (1950)
Spota, Tagliabue and Ginesta (1951)
Albert (1951, Case 1 and 2)
Limarzi (1951, Case 1)
McMahon (1951, Case 6)
Layani, Aschkenasy and Nadel (1952)
Dalgaard and Dalgaard (1952, Case 2)
Ford (1952, Case 12819-u. 8625)
Greenwald, Bronfin and Auerbach (1953, Case 1)
Snapper, Turner and Moscovitz (1953, p.33)
Rogers (1953, Cases 1,2,3 and 4)

B. <u>Cases deficient in either clinical or pathological details (24 cases).</u>

Buchstab and Schaposchnikow (1899)
Venturi (1901)
Menne (1906, Case 2)
Klemperer (1919)

Citron (1921)
Ghon and Jaksch-Wartenhorst (1925)
Abriskof and Wulff (1927)
Simmons (1931)
Simmonds (1931)
Grögler (1932)
Davison and Balser (1937, Case 8)
Flax (1941)
Adson (1941, Second case)
Beck (1942)
Martinez-Gomez (1946)
Lichtenstein and Jaffe (1947, Fig.3c)
Castleden (1948)
Degenhardt and Sheehan (1949, Case 11)
Lawrence and Wasserman (1950)
Harrington and Moloney (1950, Cases 3 and 5)
Madonick and Solomon (1953, Cases 19,20 and 21)

C. Cases only mentioned (12 cases).

King (1911)
Coley (1931, Cases 5 and 8)
Hellner (1938, Abb.224, p.128)
Ghormley and Pollock (1939, Case 1)
Adson (1941, second case)
Lichtenstein and Jaffe (1947, 2 cases)
Chase (1948)
Hanisch (1950)
Harrington and Moloney (1950, Case 10)
Bichel (1950, Case 6)

The following authors have published case reports of patients with spinal compression complicating myelomatosis which have not been included in the above collection:-

Geschickter and Copeland (1928, Case 2)
Morin et al. (1953, Case 4)
Otenasek (1953, Case 6)
Snapper (1949, p.257)
Svien et al. (1953), seven cases.

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To affect completeness, an attempt has been made to trace all duplicate articles, published by authors in different journals. Likewise, where several authors have recorded one case, each report is included.

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Authors that have been referred to in the text or tables are collected together. Those appearing in Appendix II but not elsewhere are not included. The numbers refer to pages which are invariably in Volume One unless otherwise stated.

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