TRIGEMINAL NEUROFIBROMA

REVIEW AND FOLLOW-UP REPORT OF A CASE IN A BANTU MIMICKING DISSEMINATED SCLEROSIS

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In an article entitled 'Does disseminated sclerosis occur in the Bantu?' one of us (R.L.) and others, in 1956, described a neurological illness consistent with disseminated sclerosis, but because the patient was of pure Bantu extraction (Zulu father and Sotho mother), we stated[1] 'one accepts this diagnosis with reservation and awaits further developments'. The patient has died and we now have a full clinical and necropsy follow-up.

SUMMARY OF THE PREVIOUS REPORT

First Admission

The patient, M.M., a female aged 26 years, was admitted to Baragwanath Hospital in July 1955. One month previously she had become ataxic and developed diplopia on looking to the right. She also became dizzy on turning her head to the same side. Her left hand had become clumsy. Examination revealed nystagmus with a coarse component to the left, a diminished left corneal reflex, hypotonic left limbs, well-developed left cerebellar signs and mild right cerebellar signs. Lumbar puncture showed a pressure of 150 mm. H_2O and protein, 118 mg. per 100 ml.; the other constituents were essentially normal. Skull X-rays and a vertebral angiogram were normal. Five weeks after admission she ceased complaining of diplopia and dizziness and the cerebellar signs diminished.

Two-and-a-half months later the cerebellar signs returned and were now accompanied by excessive salivation, dysphagia and slurring of speech. The salivation and dysphagia disappeared after a week, but the speech defect worsened. Next, a bilateral spastic pyramidal weakness developed in the legs, particularly the left leg. Over the next month this improved and was replaced by a left spastic hemiparesis. An air encephalogram done at this stage showed good filling and no abnormality of the 4th ventricle and aqueduct of the midbrain. An audiogram and caloric tests were also normal. A transient enlargement of the left pupil was noted. She again improved and was discharged from hospital towards the end of January 1956.

Second Admission

In April 1956 the patient was readmitted with slurring of speech and nystagmus; corneal reflexes were normal; and there were bilateral spastic signs and bilateral cerebellar signs, particularly on the left. She became bedridden. Joint sense in the right big toe was lost, but returned within two weeks. Inequality of the pupils reappeared for a few days. She was discharged in May 1956 able to walk on crutches. At this stage her case record was published.[1] At home she continued to improve for some months and was able to move around and do her housework.

FOLLOW-UP

Third Admission

In early February 1957 the patient began to deteriorate again and on 18 April 1957 she was readmitted to hospital with the following complaints:

One month before admission she developed a cough and had difficulty in clearing her throat. There was progressive worsening of her speech, dribbling from the left angle of her mouth and conjunctivitis of her left eye. There were no headaches, tinnitus, or vomiting.

On examination of the central nervous system, many signs were elicited, including severe bilateral papilloedema, a left external rectus palsy, a loss of the corneal reflex on both sides, and a left lower motor neurone type of facial weakness, and her palate elevated sluggishly in the midline. Hearing was still normal and there was no gag reflex. She was severely dysarthric and had difficulty in swallowing sputum, but the cough reflex was still present. She was unable to shrug her left shoulder and her tongue deviated to the left. There was a severe spastic left hemiparesis and mild spastic weakness of the right leg with bilateral extensor plantar reflexes. Coordination was normal on the right, but could not be tested on the left. Joint sense was again impaired in the small joints of the right foot, but elsewhere this modality was intact. Exteroceptive sensation was normal throughout. General examination revealed a bronchitis, but nothing else of note.

On 19 April 1957 a ventriculogram was done and comparison with the earlier plates showed that the 4th ventricle was displaced backwards and to the right by a space-occupying lesion in the posterior fossa and that the whole ventricular system was dilated (Fig. 1). She refused operation and steadily deteriorated. The dysarthria became worse and on 24 April 1957 a complete left hemiparesis was present. Total left trigeminal anaesthesia was detected and the symptoms became stationary until 13 February 1958, 10 months later, when her cough reflex became depressed. She developed bronchopneumonia and died on 28 February 1958.

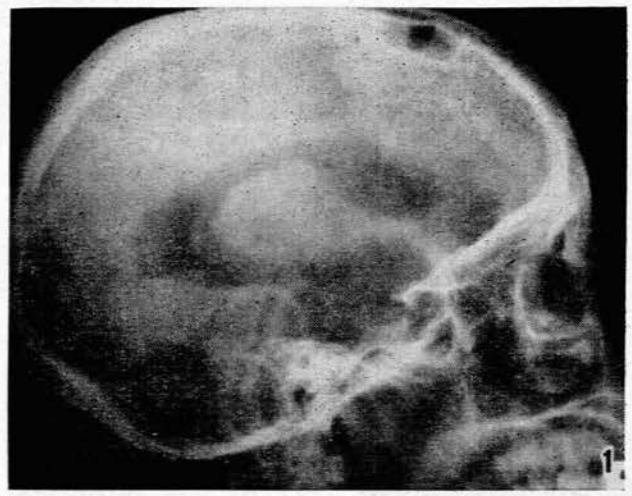

Fig. 1. Ventriculogram showing posterior displacement of the 4th ventricle and generalized dilatation of the ventricular system (4th ventricle slightly retouched).

NECROPSY

This was performed 86½ hours postmortem, but the body had been refrigerated.

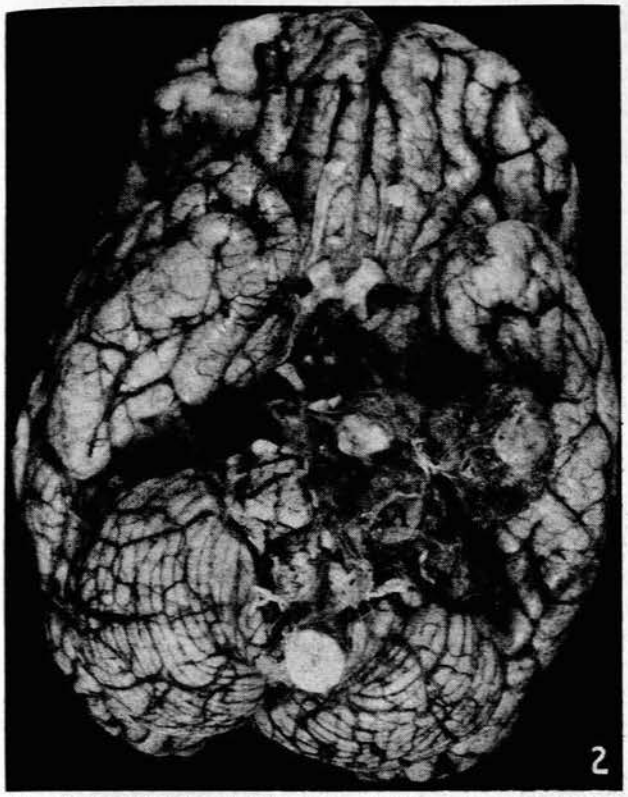

Fig. 2. The left abducent nerve curves over the letter 'A'. Note the flattening of the left uncus and distortion and displacement of structures in the region of the hypothalamus.

Central Nervous System

A large, firm tumour, shaped like an asymmetrical dumb-bell, lay partly in the posterior fossa and partly in the middle fossa on the left side (Fig. 2). The overall size of the tumour was 5·3×4·8×5·0 cm., and the colour was greenish-brown with a few opaque yellowish-white patches. The larger, medial portion in the posterior fossa was covered by leptomeninges and indented both the brainstem and the left cerebellar hemisphere. This portion of the tumour appeared to have arisen from and destroyed the trunk of the trigeminal nerve, and a thin, white strand arching over the base near the midline was identified as the left abducent nerve. The basilar artery was not displaced laterally and traversed the most medial edge of the tumour without appreciable elevation.

The smaller lateral protrusion of the tumour lay in the floor of the left middle fossa extradurally in the region of the trigeminal impression, and fitted into a shallow depression formed by erosion of the left side of the floor of the sella turcica, the left posterior clinoid process, and the superior wall of the carotid canal. Loose adhesions bound the exposed petrous part of the internal carotid artery to the tumour. The bony floor of the depression was opaque-white, with a finely worm-eaten appearance, a change present in the surrounding bone for some distance. The free edge of the tentorium cerebelli passed over the constriction at the junction between the two parts of the tumour.

The third ventricle was distended, and ruptured during the removal of the brain with the escape of a large volume of cerebrospinal fluid.

The structures in the region of the hypothalamus, including the optic chiasm and left optic tract, were a little distorted and displaced towards the right side (Fig. 2). Also the left uncus showed striking evidence of tentorial herniation, being flattened and grooved, with a maximum width from the groove to the medial edge of 11 mm. Anteriorly the groove extended round the temporal pole, following the curve of the lesser wing of the sphenoid bone. The corresponding measurement for the right uncus was 2 mm. The cerebellar tonsils were grooved to a degree suggestive of some herniation through the foramen magnum. The cerebral hemispheres showed slight flattening of gyri and obliteration of sulci, and a cerebral fungus 1·5 cm. in diameter bulged through the right frontal burr-hole. The brain and tumour together weighed 1,175 G.

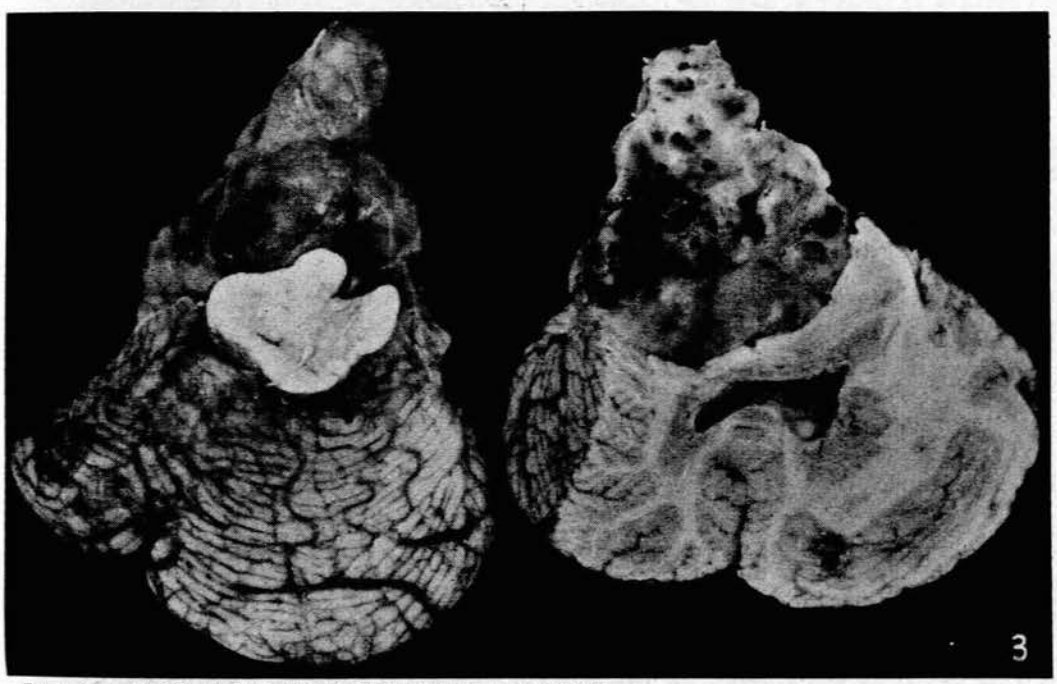

Fig. 3. Left: distortion and narrowing of the aqueduct of the midbrain.
Right: haemorrhage in the tumour. Between the distorted and elevated floor of the 4th ventricle and the tumour is compressed pontine substance.

On section the tumour was solid and presented a mottled appearance, with dark haemorrhagic areas, greyish gelatinous areas, brown and yellowish-brown streaks caused by blood pigment, and a few small areas of cystic change. At the level of the upper border of the tumour the aqueduct of the midbrain was distorted and narrowed (Fig. 3), and at the level of the centre of the tumour the outline of the 4th ventricle was flattened by elevation of the floor. Here gross distortion of the pons was evident. Between

the two levels mentioned, an elongated depressed area of altered consistency was found in the pons lying to the right of the midline, except for the anterior extremity, which appeared to lie in the line of the raphe pontis (Fig. 4). The tumour shelled out from the brainstem and cerebellum with

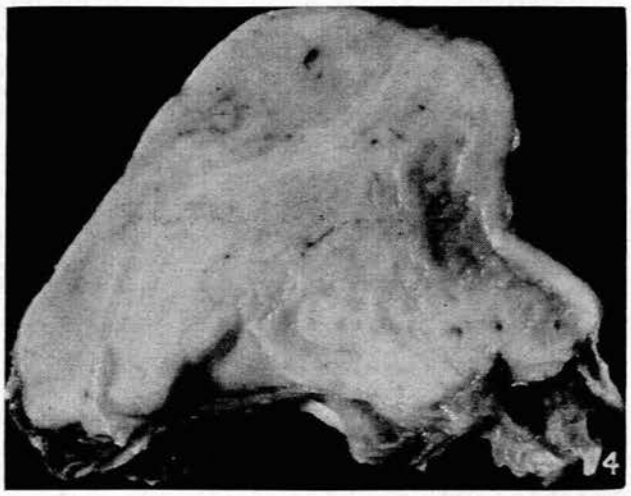

Fig. 4. Pons: the vague curved dark line is the upper end of the 4th ventricle, obliterated at this level. The concavity on the left is tumour bed. Just medial to the notch in the right border is the depressed area of altered consistency.

ease, confirming the fact of indentation only and exposing the facial and auditory nerves lying in the deep hollow remaining (Fig. 5). The lateral and third ventricles were slightly dilated, and a cavum septum pellucidum was present.

The spinal cord appeared healthy at first, but after fixation an area of pallor became obvious in the lateral column corresponding to the affected pyramidal tract (see below). The dural venous sinuses and middle ears were healthy.

Histology

The tumour. Characteristic features of a solitary neurofibroma (schwannoma) are present. Although the appearances vary from field to field on account of extensive secondary

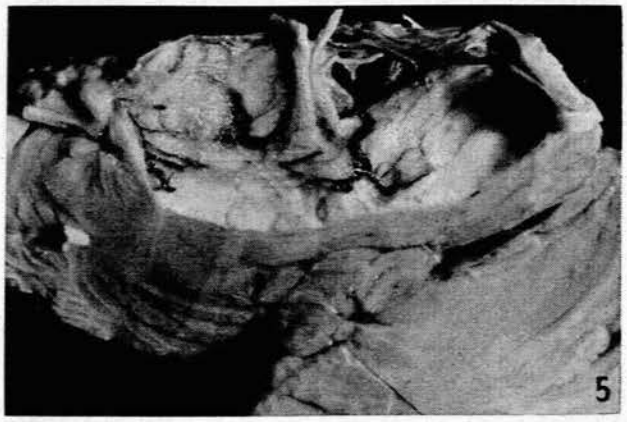

Fig. 5. The tumour bed in the cerebellum and pons with facial and auditory nerves.

changes, the predominant pattern is one of interlacing bundles of compact spindle-shaped cells having elongated, rather vesicular nuclei with fine, evenly distributed chromatin and inconspicuous nucleoli (Fig. 6). There is a slight tendency to palisading, especially in the lateral part of the tumour. Between

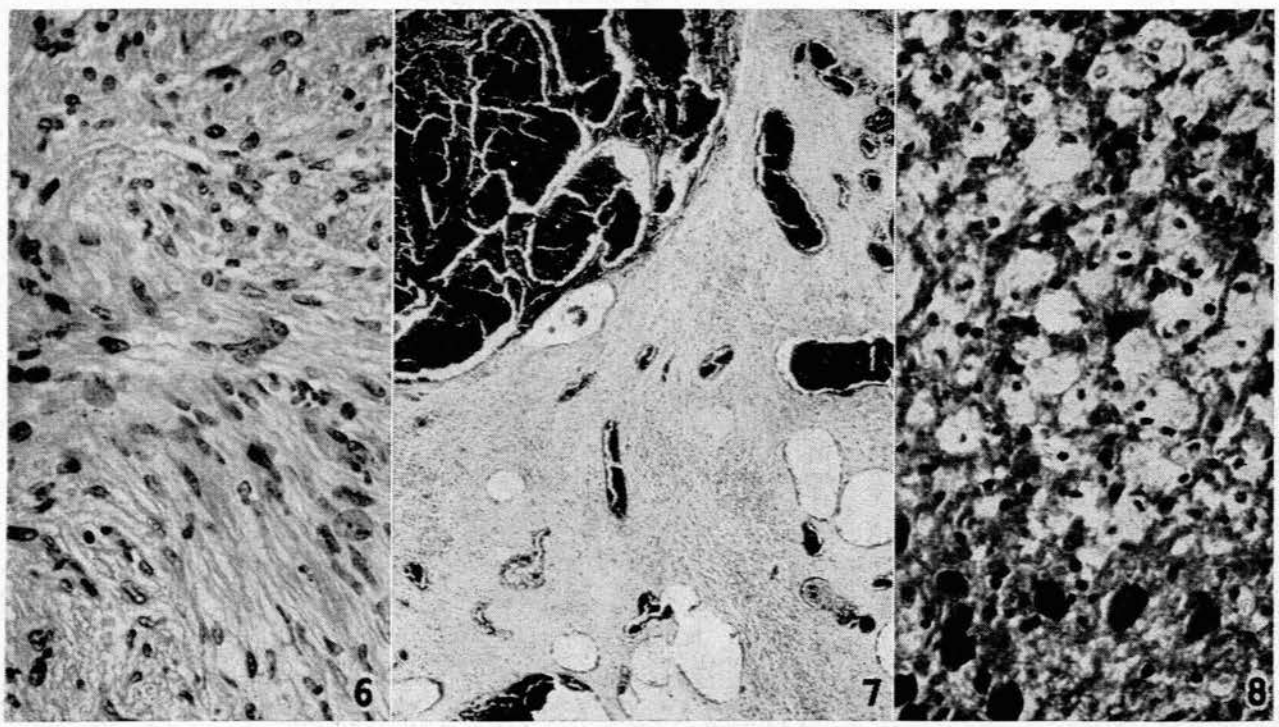

Fig. 6. General appearance of the tumour. A suggestion of palisading of tumour cells is present in the lower half (haematoxylin and eosin × 300).
Fig. 7. Thin-walled vessels in the tumour. The large quadrantic dark mass consists of a collection of vessels lying in an area of haemorrhage (Masson × 30).
Fig. 8. Compound granular corpuscles localized to descending corticospinal and corticopontine fibres (haematoxylin and eosin × 300).

the cells in some parts and particularly in relation to vessels near cystic areas, there are collagen fibres staining pink with van Gieson's stain. Other secondary changes include recent and old haemorrhage, thrombosis and foam-cell aggregation. In several areas collections of large, thin-walled vessels are a striking feature (Fig. 7). At the surface of the lateral protrusion of the tumour are several ganglion cells, and degenerate ganglion cells are recognizable deeper in the substance. The tumour appears to be completely benign.

Pons. On the left side, beneath the concavity of the tumour bed, the tissue is necrotic and has disappeared in places, forming microscopic cysts, and there is little indication of cellular reaction, recent or old. Fragments of myelin sheaths stain up in Luxol Fast Blue preparations, and only scattered compound granular corpuscles, occasional hypertrophied astrocytes and a few glial fibres can be found. On the right side of the pons towards the tegmentum, at a slightly different level from that shown in the photographs, are large areas of compound granular corpuscles, sharply localized to degenerating corticospinal and corticopontine fibres, and separated by relatively healthy transverse pontocerebellar fibres (Fig. 8). In Bielschowsky preparations axons are present, though reduced in number in these areas.

Medulla. Descending degeneration of the pyramidal tract appears as pallor of the *right* medullary pyramid in a Luxol Fast Blue preparation (Fig. 9) and abundant neutral fat is demonstrable here in a frozen section stained with Oil Red O. An area of slight myelin loss is also visible in the restiform body of the opposite side (Fig. 9), affecting the spinal tract of the trigeminal nerve, but no degeneration to neutral fat is demonstrable.

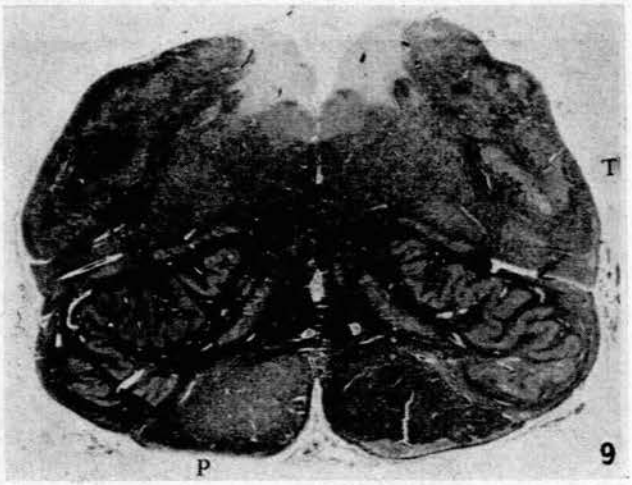

Fig. 9. Medulla: letters 'P' and 'T' indicate myelin pallor in pyramid and area of spinal tract of trigeminal respectively (Luxol Fast Blue).

Spinal cord. In the cervical, thoracic and lumbar areas of the cord, pyramidal-tract degeneration can be traced downwards as pallor of myelin and degeneration to neutral fat in the *left* lateral column (Fig. 10).

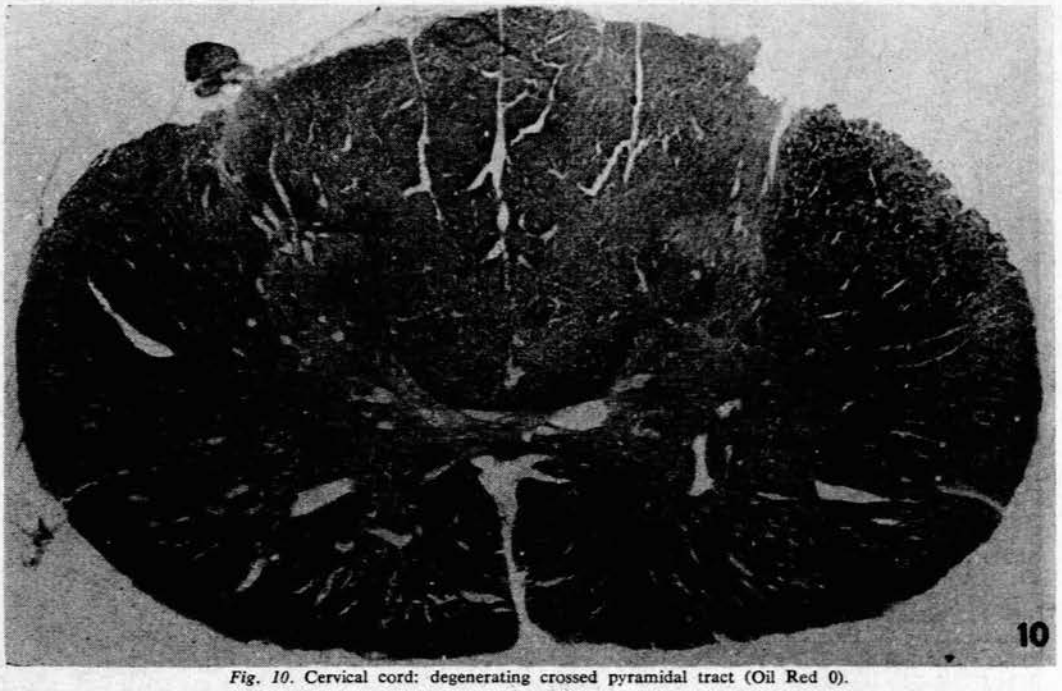

Fig. 10. Cervical cord: degenerating crossed pyramidal tract (Oil Red 0).

Left abducent nerve. There is fairly severe swelling and vacuolation of myelin sheaths (Fig. 11) with either loss of axons or irregular beading and slight vacuolation (Fig. 12).

Right trigeminal nerve. At the site of attachment to the pons and just within the substance of the pons, the myelin sheaths are vacuolated and swollen, and swollen axons have become visible in ordinary preparations. A Bielschowsky preparation reveals coarse swelling and fragmentation of these structures (Figs. 13 and 14).

The optic chiasm and left optic nerve. The chiasm was sectioned in a horizontal plane. There are a few melanoblasts and lymphocytes in the leptomeninges and a few melanophores and lymphocytes in a perivascular position in the substance of the chiasm. On the left side of the chiasm at the commencement of the optic tract, corpora amylacea are moderately abundant and there are widened perivascular spaces with vacuolation of the ground substance, apparently mainly due to severe swelling of oligodendroglia, whose nuclei are sometimes seen in the vacuoles so produced. In myelin preparations these vacuoles appear to be situated mainly between sheaths. However, slight loss of myelin is evident in this area laterally and axons are reduced in number, and are fine and fragmented when compared with the corresponding area on the right side. These slight but definite changes are more clearly seen in the left optic nerve some distance proximal to the chiasm (Fig. 15). Other areas showing vacuolation only are at the decussation and on the right side of the chiasm at the beginning of the tract.

Cerebellar cortex. In the right hemisphere and affecting mainly the molecular layer of the cortex of several adjacent folia is a small area of dense gliosis together with a proliferation of small vessels having fibrous walls (Fig. 16). The Purkinje cells and some granular cells have been replaced by the gliosis. There are a few haemosiderin-filled phagocytes and lymphocytes on the surface. The appearances suggest an old vascular lesion.

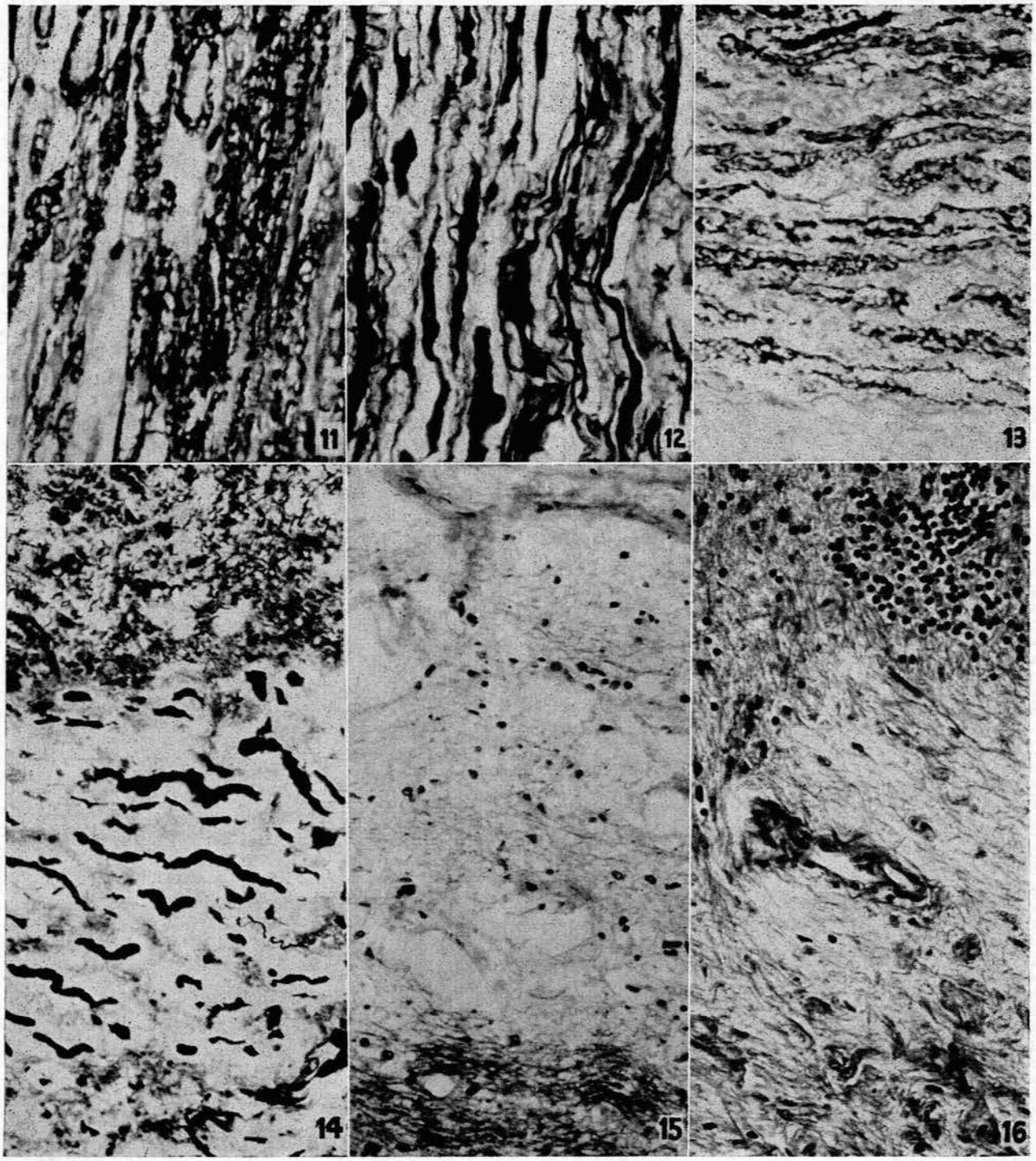

Fig. 11. Left abducent nerve: swelling and vacuolation of myelin sheaths (Luxol Fast Blue × 480).

Fig. 12. Same as Fig. 11. Beading and slight vacuolation of axons. There is some non-specific staining of endoneurial collagen (Bielschowsky × 480).

Fig. 13. Right trigeminal root: irregular swelling of myelin sheaths (Luxol Fast Blue × 300).

Fig. 14. Same as Fig. 13. Coarse swelling and fragmentation of axons (Bielschowsky × 300).

Fig. 15. Left optic nerve: between the leptomeningeal sheath (top) and well-stained myelin (below) is a zone of myelin loss (Luxol Fast Blue × 240).

Fig. 16. Cerebellum: area of gliosis containing small vessels with fibrous walls. Note surviving cells of granular layer of cortex — top right (haematoxylin and eosin × 300).

The rest of the central nervous system. No significant changes are present in numerous blocks taken from the cortex, white matter, basal ganglia and cord. The only other nerves examined were the left vagus in the thorax and part of the left sacral plexus.

Other Systems

The body was extremely emaciated, weighing 55 lb.; however, the length was only 4 ft. 10 in. An interesting incidental finding was the state of the body fat. Subcutaneous and breast fat was inconspicuous, retroperitoneal fat was invisible, and there was little or no omental fat. Histologically, adipose tissue from all the above regions and elsewhere is *atrophic*, consisting of shrunken, sometimes crenated, adult-type fat cells, well separated from one another either by a loose granular ground substance or collagen strands. This appearance resembles that seen in skin biopsies in undernourished Germans in Wuppertal,[2] and is unlike foetal fat. Skin from the anterior aspect of the chest and abdomen is also atrophic.

The lungs (right 275 G., left 280 G.) show a bilateral *inhalation bronchopneumonia*. The liver (595 G.) and heart (130 G.) show the features of *brown atrophy*. In a single section from the pituitary (0·6 G.), 18 separate *cysts* are visible; these are mostly intermedial in position, and two, including one measuring 1·7 mm. in diameter, are situated in the pars anterior. Several *nests of squamous epithelial cells* are present in the pars tuberalis. A small, encapsulated, *cortical nodule* lies external to the capsule of the left adrenal (5·6 G.; right gland 5·2 G.). The thyroid (9·8 G.) and spleen (30 G.) are *atrophic*. One kidney (both together 210 G.) contains a small focus of *healed chronic pyelonephritis*. The bladder shows a mild *chronic cystitis* and the cervix a mild *chronic cervicitis*. The endometrium is inactive, and apart from one or two haemorrhagic cysts seen macroscopically, there are very few graafian follicles in the ovaries. Bone from the sella turcica shows slightly *attenuated trabeculae* only. No significant pathological changes, apart from atrophy and sometimes disappearance of adipose tissue, are seen in sections from the other organs.

DISCUSSION

Trigeminal Nerve Signs

Obviously the signs on the left side were due to destruction of the trigeminal nerve and ganglion. Pallor indicative of myelin loss was present in the region of the spinal tract of the trigeminal, although breakdown products of myelin were not demonstrated. Bergman[3] showed that when the sensory root of the trigeminal nerve degenerated at its entrance to the pons, the spinal tract of the trigeminal likewise degenerated. St. Clair and Safanie[4] observed partial degeneration of the spinal tract as far caudally as the lower pontine level in their case of trigeminal neurofibroma in a Dobermann Pinscher dog. In our case the degeneration was seen in the medulla

TABLE I. SUMMARY OF CRANIAL NERVE AND X-RAY SIGNS IN SOME RECENTLY REPORTED CASES OF TRIGEMINAL NEUROFIBROMA

	1956 Shaldon[5]	*1957 St. Clair and Safanie*[4]	*1957 Olive and Svien*[6]	*1959 Axmann and Danes*[10]	*1959 Krayenbühl*[8]	*1960 Schisano and Olivecrona*[7]	*1961 Arnould* et al.[15]
No. of patients	3	1 (dog)	13	1	4	15 (+5 in addendum)	2
Site of tumour:							
Middle fossa			6	+	4	13 ganglion, 5 root, 1 both (1 not operated on)	1
Posterior fossa	2	+	4				
Both fossae	1		3		1		1
Trigeminal nerve signs:							
Motor	3	+	8 } total 10, nil in 3		2	about half the cases	—
Sensory	3	+	9 }	+	4		2
Other cranial nerve signs:							
2nd nerve:							
optic pathways			4	+		5 (compression of the optic nerves)	
papilloedema	1		1		2	7	
3rd nerve	—		—	+	—	9	—
4th nerve	—		—	—	—		—
6th nerve	2		5	—	4		1
7th nerve	3		5	+	2	10	1
8th nerve	2		8	—	3	5 objective (10 subjective)	1*
9th nerve	—		—	—	—	**	1
10th nerve	—		3	—	—		—
11th nerve	—		—	—	—		—
12th nerve	—		2	—	—		—
X-ray changes:†							
Erosion of petrous tip	1/3	ND	8/12	+	4	12/15	2
Abnormal air studies	3	ND	2/3	+	ND	12/13	1/2*
Abnormal angiogram	ND	ND	2/2	ND	2/2	9/10	1/1

Numbers represent the patients in the various series in whom the particular findings were made.
* Had second operation for acoustic tumour (see text).
** No details of personal cases; stated that these nerves were affected in a quarter of the cases in the literature.
† Numerators of fractions in this section = no. of positives; denominators of fractions = total number investigated.
ND = not done.

(Fig. 9). There is no other reference to degeneration of the spinal tract in the cases reported by the authors quoted below or in the review of the literature to be mentioned.

The contralateral trigeminal-nerve involvement which developed towards the end of the illness would seem to be related to degeneration in the right trigeminal root (Figs. 13 and 14). Having observed similar, but much less pronounced histological changes in this region in control cases, we cannot be certain that this is a definite lesion; and if so then we are at a loss to explain its pathogenesis unless displacement can be incriminated.

Diagnosis of trigeminal neurofibroma is difficult, and sensory or motor signs do not always dominate the clinical picture. Since 1955 a number of case reports and at least one review of the subject have been published in the English, French and German literature. Some of the authors referred to the difficulties of diagnosis. Thus Shaldon,[5] in discussing the differentiation of root tumours from acoustic neurofibromas, mentioned the finding of trigeminal sensory symptoms as an initial event in the history of 10% of acoustic tumours in one particular series. He stated that trigeminal paraesthesiae or numbness should appear early in the history of a trigeminal tumour, often as an initial event, and that sensory loss does not progress to the point of a stony-numb face. Facial pain is rare and weakness rather than paralysis of masticatory muscles is the rule. But Olive and Svien,[6] in a larger experience of 13 cases of trigeminal neurofibroma, encountered 3 in which there was no objective evidence of trigeminal-nerve involvement whatsoever (Table I). Also, sensory change was a presenting symptom in only 6 cases. Schisano and Olivecrona[7] likewise stated that diagnosis may be more difficult, or impossible, in a trigeminal tumour situated mainly in the posterior fossa. Trigeminal-nerve symptoms of one type or another were the initial symptoms in about half their 15 cases and in a little more than half the 46 cases that they found in the literature. In our own patient slight left trigeminal signs did appear early, but were not prominent, being overshadowed by other more manifest features. At a later stage in the illness right-sided trigeminal signs were also detected, and only towards the end did the disturbance on the left progress to a total anaesthesia.

Abducent Nerve Involvement

The left external rectus palsy resulted from unequivocal degenerative changes in the left abducent nerve following stretching by the tumour. Schisano and Olivecrona[7] did not separate the 3 types of ophthalmoplegia which together occurred in 9 of their cases (Table I). In their series, trochlear-nerve paralysis was the most serious, yet the experience of the other authors is different — not one of them found this nerve to be affected.

Facial and Auditory Nerve Involvement

A lower motor neurone type of facial-nerve paralysis was detected in our patient during her last admission to hospital, presumably caused by pressure from the tumour, and it is astonishing that the accompanying auditory nerve should have escaped (Fig. 5). Two of Krayenbühl's patients[8] had a middle-ear type of deafness assignable to compression of the eustachian tube following erosion of the apex of the petrous temporal bone. Krayenbühl regarded this type of middle-ear deafness, previously noted by Jefferson,[9] as characteristic of trigeminal neurofibroma.

Optic Pathway and Other Cranial Nerve Signs

Twice during the illness the left pupil enlarged and towards the end bilateral papilloedema appeared. It is very likely that displacement of the left oculomotor nerve by the adjacent tumour was responsible for the pupillary signs. Tentorial herniation may also have contributed (see below). While some changes were present in the chiasm there appeared to be an alteration in both myelin and axons in the posterior portion of the left optic nerve sampled. Early secondary optic atrophy complicating papilloedema may have been beginning, but another possibility was pressure and displacement by the tumour. Some degree of shift of these structures was obvious (Fig. 2). Again, because we have observed similar but less marked alterations in the optic nerve in control cases, we have some reservations about a genuine lesion even though the association with clinical abnormality is highly suggestive.

The glossopharyngeal, vagus, spinal accessory and hypoglossal nerves were also affected in our patient. A possible mechanism is discussed below.

Cerebellar Signs

Interpretation of the cerebellar signs is easier, and bilateral abnormalities were present. Firstly, there was indentation of the left cerebellar hemisphere, secondly, gross distortion and indentation of the left middle cerebellar peduncle and thirdly, an area of gliosis in the right hemisphere suggestive of an old vascular lesion. The pathogenesis of this vascular lesion is obscure unless, as in the right trigeminal root appearances, displacement can be incriminated.

Cerebellar signs are well recognized and they are said to occur when all or part of the tumour is situated infratentorially. In the case we describe the bulk of the tumour was infratentorial. Jefferson considered pressure on the peduncles to be more important than direct disturbance of the cerebellum.[9] Both of Shaldon's patients with cerebellar signs had tumours in the posterior fossa.[5] Nine of Olive and Svien's patients showed these signs, and in 7 all or the greater part of the tumour was in the posterior fossa, but in 2 it was mainly in the middle and only partly in the posterior fossa. Three of Krayenbühl's patients showed some or other cerebellar signs, and in the patient with the most pronounced signs the tumour was situated in both the posterior and middle fossae; in the other 2 patients with mild signs, middle-fossa tumours were found. Similarly, 9 of Schisano and Olivecrona's patients had nystagmus,[7] and in some of these the tumours almost certainly lay in the middle fossa, for they classified the situation of the tumours according to their origin either in the ganglion or in the root; 11 were of the former type and only 4 of the latter. Thus it seems that, although cerebellar signs in trigeminal neurofibroma occur typically when the growth lies in the posterior fossa, a middle-fossa tumour may sometimes be to blame.

Long-tract Signs

The ipsilateral pyramidal-tract disturbance could be related unquestionably to a destructive lesion in the right side of the pons. No doubt compression of the displaced right side of the pons against the free edge of the tentorium cerebelli (Kernohan's notch) was responsible. In

fact, a depression in the right lateral border of the pons was visible (Fig. 4). Degeneration of pyramidal fibres was present and can be traced down to the contralateral medullary pyramid and as far distally as the lumbar cord.

Although at the pontine level there was evidence of a destructive lesion as well as deformity on the left side, no signs of descending-tract degeneration were visible. It is reasonable to suppose that pressure on the left side of the pons interfered with function and that the destruction there was too recent for descending degeneration to have appeared at the time of death. The relative absence of local reaction supports this supposition.

Two of Shaldon's 3 patients showed contralateral pyramidal signs,[5] and in one the tumour had embedded itself so deeply in the middle cerebral peduncle that the 4th ventricle was opened at operation. In the same patient there was also a complete loss of pain and temperature sensibility down the contralateral half of the body, including the face. Olive and Svien's case 13 showed an ipsilateral hemiparesis,[6] for which they postulated a Kernohan's notch mechanism. This patient also showed a diminution of 2-point tactile discrimination in the ipsilateral hand and a contralateral extensor plantar reflex. Three of their other patients complained of paraesthesiae in the hand, one ipsilateral (following radium therapy) and 2 contralateral, but there were no objective sensory disturbances; Krayenbühl's case 1 had a contralateral motor weakness of the hand.[8] Seven of Schisano and Olivecrona's patients[7] had exaggerated tendon reflexes or slight hemiparesis, and in 4 bilateral weak or absent abdominal reflexes were detected. No details were given about the relation to the side of the tumour. Axmann and Danes' patient[10] had bilateral pyramidal signs.

From the above, it can be seen that long-tract signs are not uncommon in trigeminal neurofibroma, a fact recognized by Shaldon,[5] and the pyramidal signs at least appear to be due to compression of the brain stem by the tumour locally or against the opposite free edge of the tentorium cerebelli. The degree to which distortion and compression of the brain stem can occur without destructive changes is illustrated by the case of the Dobermann Pinscher dog of St. Clair and Safanie.[4] In their Figs. 2 and 5 the outlines of the midbrain and pons resemble those of our case, but they stated that as far as the motor system was concerned, the various motor tracts in the brainstem appeared normal. This is the only case among these quoted in which the long tracts were studied pathologically.

Another probable case, not included in Table I, is that of an 8-year-old fox terrier male reported by Palmer.[11] There were neurological signs, including atrophy of the temporal and masseter muscles on the left side. Necropsy revealed a fairly large tumour, from the line drawings a little less in diameter than the pons, involving the left trigeminal nerve and invading the cranial cavity with compression and displacement of the brainstem to the right. Damaged parts of the brain included the left trigeminal and vestibular nerves and the left spinal tract of the trigeminal. The left corticospinal tract was compressed. Palmer did not classify the tumour, but has since stated[12] that he believes schwannoma to be the most likely diagnosis.

X-ray Changes

These were thought to be of the greatest importance in diagnosis by some of the authors previously cited, but in our patient definite changes were only observed very late in the course of the illness.

(*a*) *Bony changes.* The most constant change is erosion of the apex of the petrous temporal bone.[13] Loew and Tönnis[14] went as far as to say that erosion of the apex of the petrous temporal bone is so characteristic that contrast X-rays are unnecessary. A meningioma is said to give less destruction of bone, and a large acoustic neurofibroma in this area has an enlarged internal auditory meatus. Erosion may extend to adjacent areas: to the sella turcica with destruction of the dorsum sellae and posterior clinoid processes, or to the clivus and sphenopetrosal fissure; the foramen lacerum, foramen ovale and foramen spinosum may be enlarged, while anteriorly the defect may be so extensive as to involve part of the greater wing of the sphenoid together with the superior orbital fissure and even the lesser wing of the sphenoid as in Axmann and Danes' case.[10]

(*b*) *Air studies.* These provided proof of the presence of a neoplasm in our patient, and others have found them useful in localizing the tumour or in estimating its size.[7,15]

(*c*) *Angiography.* In our patient a vertebral angiogram appeared normal and at necropsy the basilar artery was seen to be hardly displaced by the tumour. The basilar artery was displaced 1·5 cm. to the opposite side in one of Schisano and Olivecrona's patients,[7] and a lesser distance in one of the patients of Arnould *et al.*[15] Schisano and Olivecrona considered that a vertebral angiogram is hardly ever indicated. A carotid angiogram, however, may reveal vascular connections with the tumour, the dislocation of the carotid artery occurring with large tumours, and may help to exclude a carotid aneurysm or pituitary tumour.

Cerebrospinal Fluid

The alterations in the cerebrospinal fluid were, for the reasons stated in the previous article,[1] considered to be compatible with a diagnosis of disseminated sclerosis. In retrospect the alterations were most significant, and the tentative diagnosis of disseminated sclerosis was stretched too far to include a slightly increased pressure, a protein of up to 150 mg. per 100 ml., and a negative colloidal-gold reaction.

The cerebrospinal-fluid chemistry in neurofibroma, whether of acoustic or trigeminal origin, is too well known to be repeated here. In all the cases of Krayenbühl,[8] Olive and Svien[6] and Shaldon,[5] where the fluid was examined, there was an increase in either protein concentration or pressure or both.

Psychiatric Disturbances

Our patient was euphoric. Axmann and Danes' patient underwent a change in character, becoming irritable and disliking company.[10] Case 13 of Olive and Svien[6] suffered from attacks of unprovoked laughter which improved postoperatively. Their case 7 had an abnormal electroencephalogram (grade 2 generalized dysrhythmia maximal in both temporal regions, but stronger on the tumour side) without mental change. One of the patients of Arnould *et al.*[15] suffered from 'considerable intellectual asthenia' without electro-encephalographic abnormalities. Case 2 of

Krayenbühl[8] had been in the University Psychiatric Clinic for treatment of paranoid hebephrenia before operation, and although his condition had improved after operation it is not clear if his mental state had changed. Of these patients, our own, case 13 of Olive and Svien,[6] and the patient of Axmann and Danes[10] showed bilateral pyramidal signs in addition to mood change. It is thus tempting to speculate on the possibility of a pseudobulbar-palsy mechanism operating in these patients, and in fact such a diagnosis was considered in their case 13 by Olive and Svien.

Waxing and Waning of Symptoms and Signs

Only one explanation (admittedly a rather unsatisfactory one) for the fluctuation of the symptoms and signs presents itself — namely, repeated haemorrhages into the tumour. There is evidence of recent and old haemorrhage in the tumour and also of displacement of nervous tissue, and the presumption is that haemorrhage caused expansion, and then some degree of contraction followed when secondary changes occurred in the blood, resulting in alternate pressure and release of pressure upon neighbouring structures. The tumour was so big that it is conceivable that any further encroachment on available space in the posterior fossa would have had damaging effects.

Haemorrhage into the tumour in case 3 of Olive and Svien[6] precipitated the symptoms; apart from this example, however, there is no apparent connection between symptoms and bleeding in any of the cases quoted. Schisano and Olivecrona[7] were of the opinion that these tumours are not very vascular. Russell and Rubinstein,[16] however, mentioned that even in the smaller tumours the included blood vessels may show focal sinusoidal dilatations. Collections of wide vascular channels were a feature of our tumour (Fig. 7).

Cysts and areas of xanthomatous change, usually the sequel to haemorrhage, are quite common. One of the tumours in Olive and Svien's series[6] contained 10 ml. of yellow fluid, and 20 ml. were aspirated from another, but it is uncertain if all this fluid was derived from an intraneoplastic cyst (case 7).

Other Pathological Features of Trigeminal Neurofibroma

The general pathology of trigeminal neurofibroma is similar to that of solitary neurofibromas occurring elsewhere and will not be discussed here. The histogenesis and problems of terminology have been considered by Russell and Rubinstein.[16] A few particulars of these tumours require comment, however. Trigeminal neurofibromas are very rare, forming about 0·2% of all primary intracranial tumours.[7] The ages of all the patients considered varied from 14 - 67 years and most were between 30 and 40. About half were males, although in the literature before 1956 there was a masculine predominance.[7]

In our patient the tumour was situated on the left side, as were 21 of those cited; 18 were on the right. Our tumour, measuring 5·3 × 4·8 × 5·0 cm., seems to have been larger than those in the cases mentioned. Thus, the largest of Olive and Svien's tumours measured about 6 × 4 × 4 cm.,[6] and the 'walnuts' and 'hazel nuts' of some of the other authors and the 'chicken egg' of one were probably smaller than our tumour. Schisano and Olivecrona[7] mentioned that some grew to a large size, without giving dimensions; theirs may have been larger than ours. From descriptions of some tumours and the fact of involvement of both fossae (Table I), it is apparent that dumb-bell shaped tumours are fairly common.

The appearances of extensive temporal-lobe herniation on the affected side in what is mainly an infratentorial tumour, appear to have resulted from elevation of the tentorium cerebelli on that side, i.e. a herniation *in reverse*. We visualize the raised tentorial edge having pressed against and into the under-surface of the brain until a state of affairs was reached where the difference in the levels of the two structures concerned was the same as if the uncus had been thrust downwards past a fixed tentorial edge. Hydrocephalus may have contributed to the herniation by producing a slightly larger hemisphere. Many of the cases previously mentioned had dilated ventricles on X-ray examination, most likely owing to obstruction of the aqueduct of the midbrain.

All the tumours considered were single examples of trigeminal neurofibroma, although some had one or more attached or separate protrusions. The second patient of Arnould *et al.*[15] later showed the seemingly unique development of an acoustic neurofibroma on the same side. At the time of the first operation the tumour was confined to the middle fossa. A year or so later an acoustic tumour was removed from the same side, when a separate, yellowish, attenuated trigeminal trunk was clearly seen above the tumour. Stigmata of von Recklinghausen's disease appear to have been lacking, but the possibility of a *forme fruste* cannot be discounted easily, even though bilateral acoustic tumours are usually accepted as the hidden form of that disease.

Disseminated Sclerosis

We do not yet know of a single case of disseminated sclerosis in a patient of pure Bantu descent. A Bantu population numbering about 2 million is served by the Neurological Department of Baragwanath Hospital.

SUMMARY

This is the clinical and pathological follow-up on a case reported in 1956 as having the typical clinical presentation of disseminated sclerosis.[1] A large neurofibroma of the trigeminal nerve found at necropsy to be compressing and distorting the brainstem and cerebellum could be related to the majority of the following, viz. pyramidal-tract degeneration, degeneration of the spinal tract of the trigeminal, degeneration of the abducent nerve, an old cerebellar vascular lesion, and probable lesions in the other trigeminal nerve, an optic nerve, and the optic chiasm. Repeated haemorrhage into the tumour may have caused the fluctuating course.

Since 1955 several series of case reports and a review have been published; some of these are analysed and compared with the present case. Long-tract signs are not uncommon in trigeminal neurofibroma and it is suggested that the mood disturbance or pathological laughter sometimes present may be a manifestation of an incipient pseudobulbar palsy due to brainstem compression.

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