THE CEREBELLAR ASTROCYTOMAS

A REPORT ON 25 CONSECUTIVE CASES

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Since 1931, when Harvey Cushing[1] in a masterly presentation of 76 cases of cerebellar astrocytoma showed that good results could be expected to follow an adequate surgical attack on these lesions, a large number of series have been reported. Although few surgeons, if any, have equalled the low mortality rate obtained by Cushing in the latter part of his series, it has now been frequently re-affirmed that these tumours can be surgically removed with the expectation of a low operative mortality and prolonged postoperative survival.

Even in the well-informed medical mind a posterior fossa tumour occurring in childhood tends to be regarded as synonymous with the highly malignant medulloblastoma, and to be almost invariably fatal. The object of this paper is to show that this is not so, and to describe the clinical features, the pathology, the treatment and the prognosis in 25 consecutive cases of cerebellar astrocytoma treated in the Neuro-Surgical Unit of the Johannesburg Hospital in the years 1944 - 1965.

All the cases, except one, were histologically verified, and the follow-up extends up to 20 years after operation. The earliest case in the series, although not histologically verified, was otherwise a classical cerebellar astrocytoma; we were unable to resist the temptation of including her.

Incidence. During the period covered by this report, 65 medulloblastomas and 20 ependymomas or ependymoblastomas of the posterior fossa were operated on; the astrocytomas thus formed 22·7% of the posterior fossa gliomas treated in this Unit. This figure is lower than that quoted by most other authors, e.g. Cushing 42·7%,[1] Ringertz and Nordenstam 49·4%.[4] Gol and McKissock[2] feel that about half the posterior fossa gliomas in children are cerebellar astrocytomas.

Age distribution. The average age in this series is 12 years and 8 months, which corresponds closely to that reported by other authors. The range, however, is wide, as the youngest patient was 6 months old and the oldest 64 years.

Sex distribution. Fifteen of the patients were male and 10 were female. There is thus a male preponderance which is greater than that reported in most other series. The numbers are, however, too small to draw firm conclusions.

Race distribution. Thirteen of the patients were of Afrikaans extraction, 9 English, 2 Greek and 1 Portuguese. There was a notable absence of Jewish patients when compared to our medulloblastoma series, in which 12·5% of the patients were Jewish.

SYMPTOMATOLOGY

Duration of symptoms. The duration of symptoms varied from a few days to 6 years, and averaged 7 months. One patient presented 9 years after tapping of the cyst and a Torkildsen's procedure had been performed in Greece at the age of 2 years.

Headache. Headache was the commonest complaint and was present in 22 patients; 3 of the patients were too young to allow assessment of this symptom. In only 10 was the headache suboccipital with or without generalized headache. In the remaining cases the site of the headache was not specified and the headache was not noted as being generalized.

Vomiting. This was a feature in 21 patients. It occurred predominantly early in the morning in 7. In 1 patient an appendicectomy had been performed in an attempt to cure this symptom.

Staggering. This occurred in 18 patients. In 2 the age of the patients precluded an assessment and in 5 cases no mention of this feature was made in the case histories.

Visual impairment. In only 4 patients was blurring of vision a complaint. Papilloedema was present in all of these, and associated retinal haemorrhages in 1. This is in marked contrast to Cushing's figures: Of his 76 cases reported in 1931, 40 had impaired vision and 22 were blind or nearly so. The disparity, in accordance with Cushing's prediction, is almost certainly due to earlier diagnosis in this series, which conforms to most other recent reports in this respect.

Dizziness. This was complained of by only 3 patients.

Fits and episodes of impaired consciousness. Fits, and/or episodes of impaired consciousness occurred in 3 patients. One patient was admitted unconscious with a

history of having had a generalized convulsion. Another had 9 attacks of impaired consciousness which were possibly due to fits, but may have been due to episodes of intracranial hypertension. The third patient had had one attack of unconsciousness which may have been associated with a generalized seizure.

Papilloedema. This was present in 22 patients. The ages of the patients without papilloedema were 6 months, 4 years and 22 years. The elasticity of the infant skull thus did not appear to influence this factor, nor did the duration of symptoms appear to do so. In 5 patients the papilloedema was associated with retinal haemorrhages, and in 1 patient there was associated consecutive optic atrophy. The low incidence of visual impairment in the presence of papilloedema has been remarked on; possibly the young age of many of the patients partly accounts for this low figure.

SIGNS OF CEREBELLAR DYSFUNCTION

(a) *Ataxia*

Ataxia was noted to be present in 17 patients. In 5 it was absent and in 3 it was not assessed; 2 of these having been too young for careful examination. This ataxia was present in 68% of cases, either in the upper limb or in the lower limb, or both. It is felt that if this sign is carefully looked for it will be found in an even higher percentage of cases.

(i) *Upper-limb ataxia.* This was noted in 16 patients, was absent in 6, and in 3 was not assessed for reasons already given. In 8 patients the ataxia was confined to one side. In 3 of these the tumour was confined to the ipsilateral cerebellar hemisphere, and in the remaining 5, both the ipsilateral hemisphere and the vermis were involved, as well as the opposite hemisphere in 1 of these. In the other 8 patients, the ataxia was bilateral. In 6 of these the ataxia was more marked on one side, and this indicated the side of maximum cerebellar involvement in all except one in whom the vermis alone was involved. Thus in no instance did a unilateral, or predominantly unilateral, ataxia lead to erroneous lateralization of the tumour.

(ii) *Lower-limb ataxia.* The presence of ataxia in the lower limbs was elicited in 12 patients as compared to 16 who had upper-limb ataxia. It was absent in 10 patients and in 3 was not assessed. There was thus 1 patient who had lower-limb ataxia without involvement of the upper limbs, and 6 in whom the opposite occurred.

In 3 patients with unilateral lower-limb ataxia, the ipsilateral cerebellar hemisphere was involved alone in 1, and together with the vermis in the other 2.

In 9 patients the ataxia was bilateral, being more marked on one side in 6. As in the upper limb, the more ataxic side indicated the side of maximal cerebellar involvement, except in the patient in whom the vermis alone was found to be affected.

(iii) *Truncal ataxia.* Although truncal ataxia was noted in only 3 patients, it is felt that this sign was not deliberately elicited in the vast majority.

(b) *Tonal Changes*

(i) *Hypotonia.* Hypotonia was present in 15 patients. It was generalized in 9, being predominantly unilateral in 1 of these. In 1 patient the arm and leg on one side only were involved. In 5 patients only the upper limbs were involved, in 2 unilaterally so. Unilateral, or predominantly unilateral, hypotonia was thus present in 4 patients. In 3 it was of lateralizing value; in 1 both hemispheres were involved. In no case was hypotonia elicited in the lower limbs when it was not also present in the upper limbs.

(ii) *Hypertonia.* In 3 patients increased tone was noted in the lower limbs. In 2 patients this was associated with a Babinski sign and increased tendon reflexes in the lower limbs.

(c) *Nystagmus*

This was elicited in 12 patients. In 7 it was present on deviation of the eyes to either side, and in 5 it was present on looking to one side. No relationship could be established between this and the side of the tumour.

Reflexes

In 10 of the 15 patients exhibiting hypotonia the tendon reflexes were also low; in the remaining 5 the tendon reflexes were normal. Thus in the presence of hypotonia the reflexes were normal or low in all cases.

A unilateral or bilateral Babinski sign was present in 5 patients and equivocal in 2. It is noteworthy that in 5 of these patients the reflexes in the lower limbs were normal or low, and in only 2 increased.

Position of Head

There was neck stiffness in 5 patients; in 3 of them the cerebellar tonsils were found to be herniated at operation. In 4 patients the head was tilted to one side. In 3 this was to the side opposite the lesion; in 1 the lesion involved both hemispheres and the vermis. In 2 of these patients there was also tonsillar herniation found at operation. In one the tonsil on the side opposite the tilt was herniated, and in the other both tonsils were herniated, but the one on the side opposite the tilt maximally so. Thus the head tends to be tilted to the side opposite both to the tumour and to the maximally herniated tonsil. This is perhaps analogous to the scoliosis accompanying a prolapsed intervertebral disc.

Cranial Nerve Palsies

The presence of a squint was noted in 4 patients, and proptosis in 1. Diplopia was present in 3 patients, and 4 had dysarthria. One patient had a depressed corneal reflex on the same side as the tumour.

There were 6 patients with abducens palsy; in 3 the palsy was bilateral. It had no lateralizing value.

Six patients exhibited an infranuclear facial palsy; in 4 it was on the same side as the tumour and in 2 on the opposite side. There was 1 patient with a supranuclear palsy on the same side as the lesion. Of the 7 cases of facial palsy 5 were thus on the same side as the lesion. A 7th nerve palsy thus appears to be of limited localizing value.

There was only one instance each of a vagal and hypoglossal palsy, both on the side opposite the lesion.

Apart from 6th and 7th nerve palsies, cranial-nerve involvement is thus rare. It is probably due to a non-specific pressure effect of the tumour, and particularly in

the case of abducens palsy to raised intracranial pressure, which is liable to lead to involvement of this cranial nerve, irrespective of the cause of the intracranial hypertension. Occasionally direct invasion of the brain stem may, of course, be responsible.

Thus, to summarize the main clinical features, these patients present with the classical triad of increased intracranial pressure, i.e. headache, vomiting and papilloedema, in almost every instance. They tend to stagger when walking, are ataxic—maximally so on the same side as the cerebellar involvement, with hypotonic limbs and low tendon reflexes. Cranial nerve palsies are not a common feature, but nystagmus is often present.

RADIOLOGICAL FEATURES

A. Straight X-rays

Only 20 out of the 25 were analysed.

(i) *Splaying of sutures.* This occurred in 12 cases (60%). It may be of interest to note that splayed sutures were found at ages as advanced as 16 years, 14 years and 13 years. The youngest patient with splayed sutures was 20 months. In 40% of the cases the sutures were not splayed and, as may be expected, this occurred either in the older age group or else in the very young, before closure of the fontanelles.

(ii) *'Silver beating'.* This was found in 6 cases (30%). Ages varied from 20 months to 16 years. In those cases with 'silver beating', the pre-operative history ranged from 1 month to 1 year. In all cases except 1, where 'silver beating' was seen, the sutures were also splayed.

(iii) *Abnormal clinoid processes.* In 8 out of 20, i.e. 40% of cases, there was either depression or attenuation of the anterior clinoids or attenuation of the posterior clinoids. One case with a 6-year pre-operative history also had an enlarged pituitary fossa, owing to increased intracranial pressure. The majority of these cases had a pre-operative history of longer than 1 year.

(iv) *Calcification in tumour.* Only 1 case showed well-marked calcification within the tumour.

(v) *Position of the pineal body.* In the few cases where the pineal was visualized no displacement was evident.

(vi) *Thinning of posterior fossa.* In 6 out of 20 cases, i.e. 30%, obvious thinning of bone over the posterior fossa was evident. In these cases the pre-operative history ranged from a few days to 1 year.

(vii) *Large head.* In 2 out of 20 cases, i.e. 10%, the head was grossly and obviously enlarged.

B. Ventriculography

Air ventriculography alone or air plus positive-contrast ventriculography, employing Myodil, was carried out in all but 1 case, and this showed enlarged lateral ventricles in all but 1 case. The ventricle-skull ratio varied from 18·1% to 71·9%, the average being 42·3%. The ventricle-skull ratio is the ratio of the maximum transverse distance across the anterior horns as seen on the A-P view, to the maximum transverse diameter of the skull from inner table to inner table. The normal should be 25 - 33%.

C. Displacement of Aqueduct and/or 4th Ventricle

In only 12 out of 19 cases (63%) did the air or contrast ventriculography show unequivocal evidence of shift or distortion of the aqueduct or 4th ventricle. In all these cases the aqueduct or 4th ventricle was shifted either way from the midline, forwards, forwards and upwards, or it was obstructed by the tumour.

In the remaining 37% of cases the aqueduct or 4th ventricle were either not visualized adequately (5 cases) or not shifted or distorted (2 cases).

MACROSCOPIC APPEARANCES OF THE TUMOUR

Six of the lesions were solid, 13 presented as a mural nubbin within a cyst, and 6 presented as a cyst surrounded by tumour; we did not encounter a macroscopically multicystic tumour. Nineteen of the 25 lesions were thus cystic, the volume of the cysts varying from a few ml. to 100 ml.

The prevalent theory on cyst formation is that of Cushing, namely that in a majority of cases the cyst is formed by transudation. He recognized that in a few it might be due to degeneration within the tumour. Others (e.g. Mabon *et al.*[3]) feel that transudation can only account for the cyst in a minority of cases and that most are formed by necrosis and liquefaction within the tumour. We are in agreement with Cushing. These tumours are of low-grade malignancy, and necrosis is not a prominent feature histologically. The walls of the cysts are smooth and glistening and do not show evidence of degeneration macroscopically; the contents are usually a clear amber fluid without debris.

HISTOLOGY

All 24 astrocytomas showed abundant glial fibre formation. They were graded as follows:

Grade I activity. 21 tumours (87·5%). Mabon *et al.*[3] classified 83% of their tumours as grade I, and Gol and McKissock 79%.[2]

Grade II activity. 3 tumours (12·5%). Mabon *et al.*'s[3] figures were 10% and Gol and McKissock's[2] 17%.

Considerable variation in the microscopic appearances was noted; nevertheless we were able to divide the tumours into two groups according to one or other of the following architectural patterns:

(*a*) Solid and highly characteristic microcystic areas conforming to the pattern commonly described and illustrated in the literature—19 tumours (79%) (Fig. 1), and

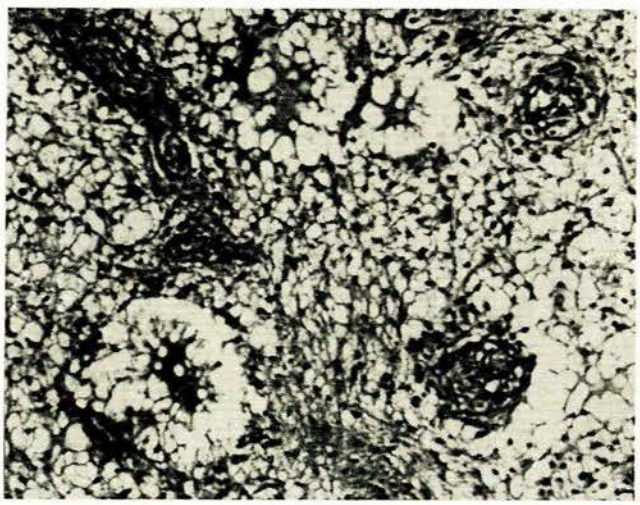

Fig. 1. Microcystic appearance of a typical low-grade cerebellar astrocytoma. (H & E)

(*b*) Less distinctive solid neoplastic tissue similar to that seen in diffuse cerebral astrocytomas—5 tumours (21%).

None of our tumours fulfilled the histological criteria necessary for a diagnosis of a 'juvenile' form of piloid astrocytoma and in those in which it was considered, we came to the conclusion that there were too few piloid cells of the type described by Russell and Rubinstein[5] and too many stellate cells.

Some of the secondary changes require comment. *Rosenthal fibres* (Fig. 2) were found in 11 tumours (46%), which is close to the 44% in Ringertz and Nordenstam's series. Because *hyalinized vessels* were so numerous as to be a dominant feature in 2 of our tumours, they were specifically searched for and found in a total of 12 (50%). Cushing[1] noted the tendency for the vessels to undergo hyaline change and remarked that in some tumours hyaline change could be very pronounced. Ringertz and Nordenstam[4] likewise noted that capillaries very often showed hyaline degeneration.

Hyperplasia of vascular endothelial cells in such slowly growing astrocytomas is an incongruous feature which has been remarked upon by others. Thus Russell and Rubinstein[5] noted vascular endothelial hyperplasia in 15% of tumours in their series and Ringertz and Nordenstam[4] commented on the formation of glomular-like clusters. Vascular endothelial

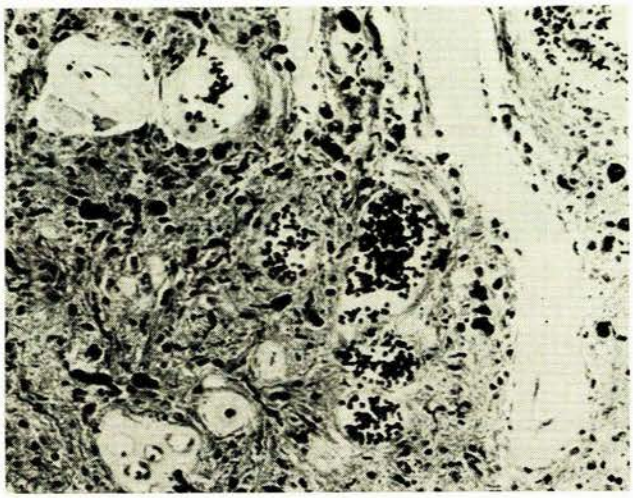

Fig. 2. Numerous thick-walled blood-vessels and abundant Rosenthal fibres in their fibrillary astrocytomatous stroma are shown.

hyperplasia was present in 11 of our tumours (46%). *Foci of calcification* were present in 7 tumours (29%) and in a few capillary walls were also calcified. Surprisingly, the tumour in which calcification was most abundant histologically, was not the one in which calcification was seen on radiological examination. *Foci of pleomorphism*, atypical cells, or nuclear grouping were seen in 8 tumours (33%). Ringertz and Nordenstam[4] mention clusters of 2 - 5 nuclei simulating the nuclear content of giant cells and Russell and Rubinstein,[5] multinucleation. The latter authors saw cellular atypia of one form or another in 15% of their tumours. *Invasion of the leptomeninges* had occurred in 3 tumours (12%), while Russell and Rubinstein[5] and Ringertz and Nordenstam[4] observed invasion in 55% and 36% of their series respectively. These authors state that the true percentage may be even higher because a number of observations were made on biopsy material only. The same holds true for our 12%. In any event, leptomeningeal invasion, whether localized or massive, seems to have little if any prognostic significance.

We were unable to settle the question of whether the wall of a large cyst containing a tumour nubbin was composed of glial tissue or neoplasm because of the fragmentary nature of some biopsy specimens. Gliosed cerebellar folia were however present in many of the specimens.

LOCATION

In only 1 case was the lesion confined to the vermis. In 14 others the vermis with either one or both cerebellar hemispheres was involved. In 10 cases the lesion was confined to a single hemisphere.

TONSILLAR HERNIATION

This was present in 15 cases. It is noteworthy that in 5 of the 7 cases with a positive or equivocal Babinski sign, tonsillar herniation was not present, so that medullary or spinal compression at the foramen magnum cannot be the important factor in producing this sensitive index of cortico-spinal derangement.

TYPE OF OPERATION AND RELATION TO SURVIVAL

Eighteen of the patients had a total macroscopic removal —one patient after a third operative procedure. Seven patients had a partial tumour removal performed as the surgeons felt that the patient's life would be jeopardized by an attempt at removal of a widely infiltrating growth.

Of the cases who had the tumour totally removed, there was 1 death within 24 hours of operation. In this case the lesion had infiltrated the pons and death was associated with hyperpyrexia and failure of the vital centres.

Of those who underwent sub-total removal, 1 death occurred within 1 month, from meningitis.

The operative mortality was thus 8%.

Of the 23 cases who survived the postoperative period, there has been, to our knowledge, only 1 death from tumour recurrence at $3\frac{3}{4}$ years after operation, in a patient who had undergone a sub-total removal of the tumour. At the time of presentation with recurrence, a ventriculo-atrial shunt was provided in preference to another direct approach to the tumour, because of the extreme degree of hydrocephalus and the poor general condition of the child.

At present, the longest interval following total removal is 20 years, and following sub-total removal 10 years. It appears that long survival may follow sub-total removal, but in most series (e.g. that of Ringertz and Nordenstam[4]), sub-total removal is, not surprisingly, prejudicial to the patient's long survival.

DEEP X-RAY THERAPY AND RELATION TO SURVIVAL

Deep X-ray therapy seems to have been given rather haphazardly, 8 cases in this series having received it. As there was only 1 death in this series from tumour recurrence, it is difficult to assess the value of deep X-ray therapy at this stage. Its value has been questioned by many authors, and it would appear that where a total macroscopic removal has been achieved, there is no merit in giving deep X-ray therapy.

MULTIPLE OPERATIONS

Two patients underwent more than one operation. One case, who was alive and well at follow-up $6\frac{1}{2}$ years after his last operation, had a Torkildsen's procedure in April 1952, a sub-total removal in December 1952, and a total removal in March 1957.

Our most recent case, operated on 1 month ago, had a tapping of a cyst and a Torkildsen's procedure performed in Greece 9 years ago. A total removal was performed here, during which procedure a cyst containing about 100 ml. of fluid was encountered.

FOLLOW-UP AND POSTOPERATIVE SURVIVAL

As has been stated, 1 patient died of tumour recurrence $3\frac{3}{4}$ years after sub-total removal. The following table shows the length of survival of the remaining 22 patients, who were all well, with no sign of tumour recurrence, when last seen at the postoperative intervals indicated.

Eleven of the 22 patients were seen, or have been contacted by us, during the past year. They include the 4 longest survivors.

Completed years of survival

No. of years	0-1	1	2	3	4	5	6	8	9	10	11	12	14	20
No. of patients	3	1	1	2	3	2	2	1	1	2	1	1	1	1

SUMMARY

The clinical features, pathology, treatment and prognosis of 25 consecutive cases of cerebellar astrocytoma have been discussed.

We feel that this analysis provides grounds for reasonable optimism when confronted by a child with a posterior fossa tumour.

ADDENDUM

Since submitting this review, the most recent case in the series, who had gross hydrocephalus associated with mental deficiency, has died from meningitis.

We wish to thank the Head of the Department of Neuro-Surgery of the Johannesburg Hospital, Mr. K. Lewer Allen, as well as the other neuro-surgeons concerned in the handling of these cases, for their cooperation and for allowing us access to their clinical records.

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