Clinical and surgical aspects of posterior fossa haemangioblastomata¹

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SYNOPSIS A retrospective study has been carried out on 67 patients with posterior fossa haemangioblastomata. Clinical details are presented, and the problems of diagnosis discussed. A fresh definition of the von Hippel-Lindau complex is put forward. The results of surgery are good for patients with solitary and sporadic tumours.

Haemangioblastomata are histologically benign tumours occurring solely within the neuraxis. The incidence of haemangioblastomata among posterior fossa neoplasms varies from 7.3% to 12% (Olivecrona, 1952; Mondkar *et al.*, 1967; Dastur and Lalitha, 1970; Gleave, 1970). Considerable interest lies in the association of these tumours with the von Hippel-Lindau complex and with erythrocytosis of the peripheral blood.

Our understanding of these tumours still lacks a great deal, both in terms of simple data and in terms of explanations of the curious manifestations exhibited by these remarkable tumours. A retrospective study has been carried out involving analysis of all cases of haemangioblastomata admitted to three neurosurgical units (St Bartholomew's Hospital, the London Hospital, and Addenbrooke's Hospital, Cambridge). The material in the first two mentioned hospitals extends over 22 years and in the last hospital over 11 years. This study involved 76 patients with haemangioblastomata, five with spinal tumours, four with supratentorial tumours, and 67 with posterior fossa tumours. The histological sections from 75 patients were scrutinized. The clinical features and surgical treatment of posterior fossa haemangioblastomata are discussed here, and histopathological and haematological aspects by Jeffreys (1975).

FIG. 1 Age incidence of 67 patients at time of first admission to hospital.

CLINICAL FEATURES

AGE The overall average age of the patients at the time of clinical presentation was 38.4 years (range 12 to 71 years), average 38.4 years for females and 41.5 years for males (Fig. 1). These ages are slightly greater than those reported in other series (Lindau, 1926; Cushing and Bailey, 1928; Perlmutter *et al.*, 1950; Cramer and Kimsey, 1952; Stein *et al.*, 1960). Olivecrona (1952) also found that females tended to present at slightly earlier ages than males. The youngest case was that reported by Krayenbühl and Yaşargil (1958) of a 3 year old child, although Ingraham and Matson (1969) did not find a single case of haemangioblastoma in their large series of tumours occurring in childhood. In the present series 12% of patients presented between the ages of 12 and

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20 years. Patients with a family history of or actually suffering from the von-Hippel-Lindau complex had an average presenting age of 29.6 years compared with an average age for all other cases of 42.1 years.

SEX In this series there were 44 males and 23 females, a sex ratio of 2:1. However, if the figures from other reported series (Lindau, 1926; Cushing and Bailey, 1928; Perlmutter *et al.*, 1950; Cramer and Kimsey, 1952; Olivecrona, 1952; Silver and Hennigar, 1952; Krayenbühl and Yaşargil, 1958; Stein *et al.*, 1960; Robinson, 1965) are added the ratio is 204 males (56.5%) to 157 females (43.5%).

SYMPTOMATOLOGY *Length of history* The average length of time that elapsed between a patient first experiencing a symptom referable to the nervous system and arrival at hospital was 7½ months (range one to 48 months), in agreement with other series which range from eight to 12 months (Cushing and Bailey, 1928; Olivecrona, 1952; Perlmutter *et al.*, 1952; Silver and Hennigar, 1952).

Effect of pregnancy It appears that pregnancy may shorten the length of clinical history. In this series one young woman presented with a haemangioblastoma when three months pregnant, underwent removal of her tumour, and was delivered of a live infant at full term. One other woman experienced her first neurological symptom two months after delivery when she started to take a progesterone preparation as an oral contraceptive. Robinson (1965) found that six out of 12 women in his series experienced their first neurological symptom during pregnancy.

Symptoms The frequency of presenting and secondary symptoms is given in Table 1. Patients presented with two types of headache—the first suggestive of raised intracranial pressure and the second a more localized pain occurring in the occipital and upper cervical regions. The symptomatology in other series is similar. Headache of unspecified location was invariably the most common presenting symptom, occurring in from 84% to 93% of patients (Cramer and Kimsey, 1952; Olivecrona, 1952; Krayenbühl and Yaşargil, 1958; Mondkar *et al.*, 1967).

Signs It will be seen (Table 2) that three signs stand out as regards frequency—papilloedema, ataxia, and nystagmus. In other series papilloedema was the sign that occurred most frequently, the incidence ranging from 56% to 90% (Cramer and Kimsey, 1952; Olivecrona, 1952; Perlmutter *et al.*, 1952; Silver and Hennigar, 1952; Krayenbühl and Yaşargil, 1958; Mondkar *et al.*, 1967). As in other series the signs indicated a posterior fossa tumour,

although there were no neurological features specific for haemangioblastoma.

TABLE 1
SYMPTOMS OF 67 PATIENTS WITH POSTERIOR FOSSA
HAEMANGIOBLASTOMATA AT FIRST ADMISSION*

Presenting symptom	% of pts	Secondary system	% of pts
Raised intracranial pressure	44	Imbalance of gait or limbs	52
Occipital pain	20	Double vision	30
Imbalance of gait or limbs	10	Raised intracranial pressure	21
Lethargy	6	Dementia	9
Anorexia	4	Decreased visual acuity	7
Decreased visual acuity	4	Occipital pain	7
Dementia	3	Tinnitus	4
Attacks of loss of consciousness	3	Difficulty of speech	4
Double vision	2	Anorexia	3
Limb weakness	2	Decreased facial sensation	3
Vomiting without headache	2	Limb weakness	2
		Tingling of limbs	2

* The column on the left allows one symptom for each patient. The column on the right allows any number of subsidiary symptoms for each patient.

TABLE 2
NEUROLOGICAL SIGNS OF 67 PATIENTS WITH POSTERIOR
FOSSA HAEMANGIOBLASTOMATA

Signs	Incidence as % of total number of patients
Papilloedema	70
Ataxia (all forms)	76
Limb and trunk	44
Limb	21
Trunk	11
Nystagmus	62
Palsies of external ocular muscles	30
Facial paresis	21
Dementia	18
Diminished level of consciousness	9
Limb paresis	9
Diminished visual acuity	7
Dysarthria	5
Pareses of lower three cranial nerves	1

VON HIPPEL-LINDAU COMPLEX Hughlings Jackson described the first case of a cerebellar haemangioblastoma in 1872. The first case of what was later to be called the von Hippel-Lindau complex was described by Turner in 1887. At about the same time the first cases of vascular tumours of the retina were described

(Panas and Remy, 1879; Fuchs, 1882). The histology of the retinal tumours was described by Collins in 1894, and it was he who first appreciated that they could be familial. Von Hippel described the clinical appearances of a case in 1904, though he was unable to add the histological details until enucleation of the affected eye was performed in 1911 (Hippel, 1904, 1911). The first family affected with haemangioblastomata of both retina and cerebellum was described by Tresling (1920).

The term haemangioblastoma was introduced by Cushing and Bailey (1928). Lindau (1926, 1930) first pointed out that the tumours of the retina and posterior fossa were histologically identical. He also found that some patients also harboured cysts of the kidney, liver, and pancreas, renal carcinomata, and phaeochromocytoma. The term von Hippel-Lindau complex was first introduced to describe these latter patients by Schuback (1927), though it would seem that Collins (1894) has been done an injustice.

The full extent of a particular patient's disease may be difficult to assess during life and may be revealed only at necropsy. Recently Djindjian *et al.* (1971) have suggested angiography of the head, spinal cord, and abdomen. This is probably unjustified unless there is clinical evidence of the various possible manifestations. However, it is important to screen all patients for retinal haemangioblastoma, renal carcinoma, and phaeochromocytoma.

The term von Hippel-Lindau complex has in the past been rather loosely used. It is suggested that the complex should be defined as follows:

'The von Hippel-Lindau complex is a clinicopathological syndrome in which at least one haemangioblastoma of the neuraxis occurs with at least one intraabdominal example of the following—cysts of the kidney, pancreas or liver, renal carcinoma, or phaeochromocytoma. The term may also be applied to cases with haemangioblastoma of the retina and another haemangioblastoma within the neuraxis. The complex may be sporadic or familial'.

In the present series retinal haemangioblastomata occurred in 6% of patients, corresponding with other series (Cushing and Bailey, 1928; Perlmutter *et al.*, 1950; Cramer and Kimsey, 1952; Olivecrona, 1952; Silver and

Hennigar, 1952; Krayenbühl and Yaşargil, 1958; Djindjian, 1963; Mondkar *et al.*, 1967).

The von Hippel-Lindau complex, as defined above, occurred in 10% of our patients, of which half were sporadic and half familial. A positive family history of haemangioblastoma occurred in 12% of patients. A number of studies of families tainted with haemangioblastoma and the von Hippel-Lindau complex have been reported (MacDonald, 1940; Möller, 1952; Tonning *et al.*, 1952; Courville, 1957; Christoffersen *et al.*, 1961; Shokeir, 1970) and some of these pedigrees stretch over some 100 family members (Silver, 1954; Nicol, 1957; Goodman *et al.*, 1964). It is generally thought that inheritance is autosomal dominant with partial penetrance that varies from 80% (Silver, 1954) to 12% (Goodman *et al.*, 1964).

DIAGNOSIS Plain radiographs of the skull revealed evidence of chronically raised intracranial pressure in 23%, the rest being normal. Isotope encephalography, using Technetium⁹⁹, was positive in 81% of the 16 patients on whom it was performed. Contrast encephalography, usually by the ventricular route because of coincidental papilloedema, was performed on 48 patients. Although in the majority of cases this technique demonstrated a posterior fossa lesion, it could in no way demonstrate the nature of the lesion.

Vertebral angiography by direct puncture was performed 14 times preoperatively and three times postoperatively. Preoperative angiography allowed the correct diagnosis to be made in every case. One of the postoperative angiograms revealed a tumour nodule which had been missed at operation after ventriculography.

The specific features of haemangioblastomata on vertebral angiography have been described (Olsson, 1953; Epstein, 1961; Taveras and Wood, 1964; Hawkins and Melcher, 1966; Wallace *et al.*, 1967; Krayenbühl and Yaşargil, 1968; Skultety *et al.*, 1970; Wolpert, 1970; Jeffreys, 1974). A strong case can be made for vertebral angiography. The preoperative diagnosis can be made with certainty in almost every case. The anatomy of the lesion can be defined accurately so that mural nodules will not be missed at operation. Feeding vessels can be identified, an essential step in the removal of tumours from the floor of the fourth ventricle.

The presence or absence of multiple tumours can be ascertained.

Any adult patient presenting with a history suggestive of a posterior fossa neoplasm of more than three months' duration should be suspected of harbouring a haemangioblastoma. The family history should be carefully checked for haemangioblastoma of the retina or neuraxis and for the von Hippel-Lindau complex. The retina should be screened carefully after the instillation of a mydriatic. If analysis of the peripheral blood reveals a haemoglobin level in excess of 18.0 g/dl the tumour is almost certainly a haemangioblastoma. If the haemoglobin level is between 16.0 and 18.0 g/dl that diagnosis should be considered. In this series the haemoglobin was in excess of 18.0 g/dl in 18% of patients and lay between 16.0 and 18.0 g/dl in 24% of patients (Jeffreys, 1975).

It is possible to state that clinical evidence suggestive of a haemangioblastoma may exist in approximately 60% of patients before radiological examinations are commenced.

TREATMENT

The details of macroscopic and microscopic histology are discussed by Jeffreys (1975): 72% of the tumours were cystic and 28% solid. There were 78 tumours occurring in 67 patients. Multiple tumours occurred in 7% of patients. From a pathological and surgical view it is important to distinguish between recurrence of an incompletely removed tumour and the appearance of a fresh tumour. In principle this distinction is more precise than in practice, unless pre-operative vertebral angiography has been performed. If a tumour occurred after the previous removal of a haemangioblastoma, in a totally different part of the posterior fossa, then this was labelled fresh tumour. A tumour occurring in the same area from which a haemangioblastoma had been previously removed was labelled recurrence. There were 10 (15%) deaths, and 34 (50%) of the patients were followed for five years or more postoperatively.

SURGICAL TREATMENT OF CYSTIC TUMOURS The range of surgical treatment for cystic tumours is not large. The cyst may be drained and the mural nodule excised, or the cyst wall and mural

nodule may be excised together. These two have been labelled radical removal, since excision of the cyst wall is unnecessary. The cyst may simply be drained, usually because the mural nodule has been missed at operation. Of the 42 patients in this group 36 underwent radical surgery with only one recurrence. All of six cysts which were simply drained filled up again. Five of these patients underwent reexploration with successful radical surgery.

There was a variety of postoperative complications—two haematomata, six cases of meningitis, and five cases of hydrocephalus of such continuing severity that ventriculoatrial shunting became necessary. Thirty-seven (88%) patients made good postoperative recoveries such that they returned either to their old occupation or a slightly lighter one. Two patients remained grossly incapacitated, though one of these had also developed chronic renal failure before surgery. There were three deaths in the immediate postoperative period. Four patients, who made good initial recoveries, died later from unrelated causes.

SURGICAL TREATMENT OF SOLID TUMOURS Thirteen of the 20 patients in this group underwent removal of a tumour which was considered radical by the surgeon. None of these recurred. The remainder underwent surgery that was considered to be less than radical because of technical difficulties of haemorrhage, or exposure of tumours lying high in the vermis or cerebellar hemisphere which were often adherent to the under surface of the tentorium cerebelli, or due to the fact that the tumours lay within the medulla oblongata.

There were five deaths in the immediate postoperative period. Ten patients recovered well. There were four deaths from recurrence, all in patients in whom the initial surgery had been inadequate.

SURGICAL TREATMENT OF MULTIPLE TUMOURS Five patients who suffered from multiple tumours within the posterior fossa all underwent more than one operation. One suffered from two cystic tumours, the others all had both solid and cystic tumours. Two patients died postoperatively, both after their third operation; two remain alive after a second operation, and a fifth

TABLE 3

RESULTS OF SURGERY IN OTHER SERIES OF POSTERIOR FOSSA HAEMANGIOBLASTOMATA*

Author	Total cases	Cystic	Solid	Preop. death	Postop. death	Recur-rence	Multiple tumours	Alive and well 3/12 postop.	In-capacitated
Cushing and Bailey (1928)	11	7 (63)	4 (37)	0 (0)	4 (37)	3 (27)	0 (0)	6 (54)	?
Davis (1946)	22	22 (100)	0 (0)	2 (9)	5 (23)	—	0 (0)	7 (32)	?
Perlmutter <i>et al.</i> (1950)	25	25 (100)	0 (0)	0 (0)	2 (8)	1 (4)	0 (0)	17 (68)	5 (20)
Olivecrona (1952)	70	55 (79)	15 (21)	6 (8)	10 (14)	4 (6)	3 (4)	42 (60)	5 (7)
Silver and Hennigar (1952)†	40	34 (85)	6 (15)	0 (0)	8 (20)	?	4 (10)	?	?
Krayenbuhl and Yaşargil (1958)	45	39 (86)	6 (14)	2 (4)	5 (9)	4 (9)	?	29 (64)	4 (8)
Stein <i>et al.</i> (1960)	19	15 (80)	4 (20)	0 (0)	6 (30)	3 (15)	0	10 (52)	0 (0)
Mondkar <i>et al.</i> (1957)	108	76 (70)	36 (30)	3 (3)	16 (15)	10 (9)	10 (9)	93 (86)	?
This series (1973)‡	67	47 (70)	20 (30)	0 (0)	10 (15)	11 (16)	5 (7)	53 (80)	5 (7)

* Actual figures are given for each series. The figures in parentheses denote percentages of the total number of cases in each series. ? Denotes that the information is lacking.

† Thirty-nine of these cases were operated on by Dandy, who described some of the cases in an earlier report (1928).

‡ The results for this present series are given for comparison. In order to do this, the five cases with multiple tumours have been listed as cystic even though some of them had solid tumours as well.

patient died of carcinoma of the breast some years after her third operation for haemangioblastomata.

Multiple tumours present a difficult problem, and each case must be treated on its own merits. Usually one is clinically dominant and needs to be removed. If smaller tumours are reasonably accessible, it would seem wise to remove them also, since they will almost certainly enlarge at a later date.

FIG. 2 Section showing junction of cerebellar hemisphere (above) with haemangioblastoma (below). There is no capsule, though it can be seen that the edge of the tumour is fairly strongly demarcated. H and E, $\times 115$.

RADIOTHERAPY Radiotherapy was given to six patients, four of whom had solid tumours and two cystic. In one cystic tumour the tumour nodule was not removed and the cyst recurred. The other patient also had inadequate surgery and died of further growth of the tumour. In three of the four solid tumours a partial removal was followed by radiotherapy. On the whole, they did well in that they survived seven, eight, and 14 years. However, they all eventually died from further tumour growth.

Three of these five patients suffered from erythrocytosis in the peripheral blood at the time of operation. Although clinically they did well after radiotherapy, in not one of them was the erythrocytosis brought under control and intermittent phlebotomy was necessary to reduce the viscosity of the blood. It would seem that, although radiotherapy may slow down the rate of growth of a haemangioblastoma, it will not suppress the erythropoietic activity of the tumour cells.

DISCUSSION

The basic surgical principles of drainage of the cyst and removal of the mural nodule for cystic tumours and radical excision of solid tumours were laid down by Cushing and Bailey (1928) and by Dandy (1928) and have been generally accepted. The results in other series are tabulated in Table 3. One has to make some allowance for the fact that some series contain a higher propor-

tion of cystic tumours, which tend to have a more favourable outcome, but some generalizations can be made. The incidence of multiple tumours is about 10%. The recurrence rate is about 15%. The mortality rate at operation or in the immediate postoperative phase is about 15% and 70% of the patients did well.

Surgery for tumours lying within the medulla oblongata will always be hazardous, although bipolar coagulation is of inestimable value (Gleave, 1970). These tumours are usually solid, although very small associated cysts may be present. They are not invasive, though small nests of tumour cells may extend for a millimetre or so into the medulla (Fig. 2). Although histologically it would be incorrect to call this a plane of cleavage, it would be reasonable to do so in surgical terms.

If the surgeon finds a cyst at operation and has not performed a preoperative vertebral angiogram it should be drained and the fluid collected for erythropoietin assay, in the event of a mural nodule not being found. The cyst should be widely opened and the walls inspected carefully for a nodule. If none is found, then any areas of induration or discolouration should be excised. If the exploration is still negative, then the surgeon can only stop and close the wound, doing so in the knowledge that simple cysts of the cerebellum are rare (Silverberg, 1971). Once the patient has recovered, a vertebral angiogram should be performed. If a nodule is visualized it can be assumed that the cyst will refill within a few years. It would seem reasonable to re-explore the posterior fossa immediately and remove the nodule.

Many of these patients have hydrocephalus and it would be wise to drain these before opening the posterior fossa. However, only 10% in this series required postoperative ventriculo-atrial shunting and it appears unnecessary to perform a Torkildsen cisternostomy. In those patients with haemoglobin levels in excess of 18.0 g/dl it would be wise to perform a phlebotomy preoperatively to lower the blood viscosity. In those patients with lower levels this will be unnecessary, since the blood loss at operation, if it is replaced with clear fluid, will render the haemoglobin level approximately normal. The haemoglobin level should be checked one month after operation.

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