Phaeochromocytoma and cerebellar haemangioblastoma

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Certain tumours which are believed to be of neuro-ectodermal origin are occasionally found to occur in the same patient.

About 20% of patients with angiomas of retinae (Von Hippel, 1904) have cerebellar or spinal cord haemangioblastomata (Lindau, 1926), and neurofibromatosis is sometimes found in association with Von Hippel-Lindau's disease. Lindau (1931) mentioned that tumours of the kidneys and adrenal glands could be found with the condition, but no more details were given. Hume (1960) collected from the literature cases of phaeochromocytoma occurring with neurofibromatosis and added four personal cases. He was able to describe 37 cases and estimated that neurofibromatosis occurred in 4% of patients with phaeochromocytoma.

The association of phaeochromocytoma with Von Hippel's or Lindau's disease appears to be rather more unusual. Details of previously recorded cases are given in the Table.

That there is sometimes a familial element is strongly suggested by the remarkable cases of Chapman and Diaz-Perez, and by the work of Tisherman, Gregg, and Danowski (1962) who studied a family of 199 persons. They found seven phaeochromocytomata, two cases of Von Hippel-Lindau's disease, and 22 possible *formes frustes* of neurofibromatosis with café-au-lait spots of greater diameter than 1.5 cm.

Nicol (1957) studied Lindau's disease occurring in five generations of one family and decided that the mode of inheritance suggested an autosomal dominant factor. Incomplete manifestation occurred in certain instances since some individuals showed the disease although their parents were apparently unaffected.

Carman and Brashear (1960) studied 25 cases of phaeochromocytoma in 10 families and believe that the familial cases are due to a dominant gene.

This brief review of the literature suggests that there is an association between the conditions of

Von Hippel-Lindau's disease, neurofibromatosis, and phaeochromocytoma.

The combination in one patient of Von Hippel's or Lindau's disease and phaeochromocytoma appears to be particularly unusual and only seven such cases have been mentioned in the literature before this report.

TABLE
CASES OF VON HIPPEL-LINDAU'S DISEASE
AND PHAECHROMOCYTOMA

Author and Case No.	Age and Sex	Phaeochromocytoma	Other Lesions
Wolf and Wilens (1934)	33 M	Left (three)	Cerebellar cystic haemangioblastoma, three spinal haemangioblastomata, syringomyelia, syringobulbia, pancreatic cysts, kidney tumour
Mandeville and Sahyoun (1949) Case 1. Glushien <i>et al.</i> (1953) Meredith and Hennigar (1954) Case 10. Chapman <i>et al.</i> (1959) Case 4 Hume (1960) Case A. H. Glushien <i>et al.</i> (1953) Case 2.	55 F	Left	Haemangioma of fourth ventricle Neurofibromatosis
Glushien <i>et al.</i> (1953) Case 3.	24 M	Left	Angiomas of retinae, cervical ribs, horseshoe kidney
Chapman <i>et al.</i> (1959) Case 5. Hume (1960) Case L. S.	34 F	Left	Angiomas of retinae, skin naevus and pigmentation
Chapman and Diaz-Perez (1962) Case 1. Chapman and Diaz-Perez (1962) Case 2.	24 F	Right	Three haemangiomas of medulla
Present case	48 F	Bilateral	Cerebellar haemangioblastoma
	36 M	Bilateral	Cerebellar haemangioblastoma
	17 M	Left	Cerebellar haemangioblastoma

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CASE HISTORY

The patient was first admitted to the Middlesex Hospital on 9 April 1963, at the age of 15, under the care of Professor A. Kekwick.

He complained of frontal headaches which were worse on waking in the mornings and had been present for two years. In the six months before admission, he had noticed that he tired easily and became breathless on exertion. His blood pressure was found to be 280/160 mm. Hg. and he was referred to the Middlesex Hospital for investigation.

His past history was unremarkable, and his blood pressure had been recorded in 1960 as 120/65 mm. Hg.

On admission, full examination showed no abnormality except hypertension. Haemoglobin was 94%; white cell count, 8,000 with a normal differential count. Serum electrolytes and urea were all normal. Urea clearance was normal. A chest radiograph was normal. E.C.G. showed left ventricular hypertrophy and strain. An aortogram was performed through a catheter inserted at the right femoral artery, when the renal arteries were shown to be of normal calibre, but the left suprarenal gland was seen to be enlarged. Urinary catychol amines were estimated at the equivalent of 320 μ g. of noradrenaline per litre, and in a second specimen, at 1,680 μ g. of noradrenaline per litre. An intravenous phentolamine test reduced the blood pressure to 160/90 mm. Hg in one minute.

At operation, performed by Mr. C. J. B. Murray on 26 April 1963, a tumour of the left suprarenal gland, measuring 8 cm. by 5 cm., was removed. The patient's blood pressure after operation fell to 135/90 mm. Hg and his recovery was uneventful. Urinary catychol amines were repeated and found to be equivalent to less than 50 μ g. of noradrenaline on two occasions.

He was readmitted on 9 April 1966. One month previously, he began to complain of severe occipital headaches, often associated with vomiting without previous nausea. He began to have some blurring of vision and horizontal diplopia and his parents noted unsteadiness of gait and clumsy speech. In the week before admission, his gait had become much worse and he tended to stagger and fall to the right. His speech became more slurred and he complained of severe headache.

On admission, he was found to be very drowsy, and when roused was dysarthric. The optic fundi showed early papilloedema with small haemorrhages. He had horizontal and vertical nystagmus, bilateral sixth nerve weakness, a mild right facial weakness, and gross ataxia of the right arm and leg. Both plantars were extensor. The pulse rate was 60 and his blood pressure 190/110 mm. Hg. Haemoglobin was 111%, white cell count 8,000 with a normal differential. Radiographs of the skull showed no abnormality.

Air and Myodil ventriculography showed gross symmetrical dilatation of the lateral ventricles. The aqueduct was displaced considerably towards the left by a right cerebellar hemisphere tumour. After two days' ventricular drainage, posterior fossa exploration was carried out by Mr. J. Andrew. A large, smooth-walled cystic cavity was found in the right cerebellar hemisphere.

FIG. 1. *Phaeochromocytoma. Haematoxylin and eosin* $\times 280$.

FIG. 2. *Haemangioblastoma. Vascular nodule in the wall of the cyst. On the outer aspect is a portion of cerebellar tissue. Haematoxylin and eosin* $\times 20$.

FIG. 3. *Haemangioblastoma. Haematoxylin and eosin* $\times 280$.

Projecting into it from the lateral side was a typical mural nodule of a haemangioblastoma, which was removed. Following the operation the patient made an uneventful recovery. The cerebellar signs cleared completely and his blood pressure settled at 120/80 mm. Hg.

No family history of phaeochromocytoma, haemangioblastoma, or angiomatosis retinae could be obtained.

PATHOLOGY

After fixation in formalin the cut surface of the bisected adrenal tumour showed variegated yellow tissue with areas of haemorrhage.

Microscopically, the tumour showed the characteristic appearance of a phaeochromocytoma with cords and masses of large cells, with pale granular cytoplasm intimately related to thin-walled blood vessels and sinusoids. There was no penetration of the capsule or other evidence of malignancy (Fig. 1).

The cerebellar tumour was a dark coloured cyst, measuring $2 \times 1.3 \times 1$ cm., containing jelly. A small portion of the cerebellum was attached.

Microscopically, a small nodule in the wall of the cyst was shown to consist of a fine mesh of blood vessels

and capillary channels as well as several blood spaces of larger size. Between the capillaries were stromal cells with pale homogeneous cytoplasm (Figs. 2 and 3).

SUMMARY

A patient is described in whom a phaeochromocytoma and a cerebellar haemangioblastoma were found together. This is the eighth case in which Von Hippel's or Lindau's disease has been found in association with a phaeochromocytoma.

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