BLOODVESSEL TUMOURS OF THE BRAIN WITH PARTICULAR REFERENCE TO THE LINDAU SYNDROME

BY

G. S. HALL, BIRMINGHAM

INTRODUCTION

LUSCHKA, who in 1854 recorded the first cerebral angioma, distinguished two types : (1) those arising by sequestration of small portions of the embryonic capillary system, and (2) the true tumour formations arising from vascular tissue. Previous to Luschka's description, tumours of both types had been recognized elsewhere in the body, and because of their essentially cavernous nature had been named 'cavernous angiomas' by Rokitansky. Dandy, in a critical review of the venous abnormalities and angiomas of the brain, states that distinction between the two types is determined by the relative preponderance of connective tissue and vascular spaces, and concludes that there is little, if any, fundamental difference between them ; as a result he prefers to adopt the old nomenclature of cavernous angioma.

The researches of Lindau have, however, firmly established the clinical and pathological individuality of that type of vascular tumour which seldom occurs in any part other than the hindbrain, and which may be associated with angiomatosis retinae (von Hippel's disease), cystic disease of the pancreas and kidney, and rarely—in the fully developed form of the condition—with hypernephroma, tumours of the epididymis, and angiomatosis of the liver.

Since Lindau's original publication several workers, Cushing and Bailey in particular, have drawn attention to this group of cases, which because of their histological picture have been named 'hæmangioblastoma.' These are believed to be true neoplasms of the bloodvessel elements—in contradistinction to the angiomatous malformations, which (according to Cushing and Bailey and others) are, as their name indicates, probably malformations and not true tumours, and contain between their vascular loops traces of nervous tissue. Of these angiomatous malformations, the venous type tends to be associated with hæmangiomatous lesions of the skin, usually in the trigeminal distribution, as has been particularly stressed by Parkes Weber, Harvey Cushing and many more.

Both conditions, the angiomatous malformations and the hæmangioblastomas, arise from some developmental defect ; Lindau has expressed the view that the associated lesions, to which his name has become attached, are due to a maldevelopment of the mesoderm in the third month of foetal life.

It is remarkable that these two conditions—both due to some developmental defect in the cerebral vascular tissue—would appear to be so distinct. The angiomatic malformations are essentially benign, non-familial, unassociated with any visceral anomalies, occur most commonly in the cerebral hemispheres, apparently never give rise to cyst formation, and tend to be associated in the more common type—the venous form—with congenital nævi of the skin in the form of port-wine marks on the face. The hæmangioblastomas are true tumours, in some instances a familial history is obtainable, they occur almost entirely in the hindbrain, frequently give rise to cyst formation, are unaccompanied by any skin lesion and may be associated with visceral anomalies and angiomatosis retinae (von Hippel's disease).

It is difficult in the present state of our knowledge to see why these two types of lesions should be so distinct. That the syndrome described by Lindau is well defined is shown by the constancy with which the recorded cases adhere to his original clinical and pathological description. Thus the occasional familial and hereditary tendency is well illustrated not only by some of Lindau's original cases, but also by the more recently recorded ones of Möller, Cushing and Bailey, Hartman, Collier and others. Since the publications of Lindau, the association of angiomatosis retinae with the syndrome has been from time to time reported, by Cushing and Bailey, Möller, Rochat, Nicolato, Viegts, Atkinson and others. The site of election of the lesion in the cerebellum or medulla oblongata is such that Lindau believes that they do not occur elsewhere in the nervous system, apart from rare simultaneous involvement of the spinal cord; Cushing and Bailey state ' . . . It can be seen that the list of true bloodvessel tumours in the cerebrum is an exceedingly meagre one. We have met with no example ourselves . . . ' They are sceptical of the authenticity of recorded cases in which the lesion has been found above the level of the tentorium cerebelli. In 1931, however, Barnard and Walshe reported an undoubted case in which the lesion was found in the right temporal lobe; Rochat has also reported a similar case. Russell has described a unique case of spinal compression due to a capillary hæmangioma of the cervical cord associated with syringomyelia. The occurrence of cyst formation is frequent and well known, while its precipitation has been presumed to follow slight trauma, as was first emphasized by Sargent and Greenfield; it is probably the cyst formation and not the tumour nodule which more often initiates cerebral symptoms.

An extensive study of the literature has revealed only four instances of the occurrence of cutaneous hæmangiomatic lesions in the Lindau syndrome: one of Lindau's patients had a capillary angioma on the wrist; in the cases recorded by Aust and by Tschenzaw there was a small one on the forehead, while the patient of Fabritius had several small ones. This rarity of cutaneous lesion is remarkable when it is remembered that the nervous system is of ectodermal origin.

From the above considerations it would seem profitable to ascertain the

possible occurrence of cases which exhibit features common to the two conditions.

Concerning angiomatosis retinae (von Hippel's disease), Lindau states that 25 per cent. of the cases develop cerebral symptoms: these without exception appear to be due to a hæmangioblastoma of cerebellum or medulla oblongata. Treacher Collins distinguished unusual tortuosity or abnormal branching of retinal vessels from that condition in which a large retinal vessel disappears into a raised angiomatous mass at the periphery of the fundus. Lindau showed that this latter group may be associated with similar vascular and cystic growths of the hindbrain: the former group is often associated with angiomatous formations in skin and mucous membrane, and sometimes with symptoms suggesting tumour formation of an angiomatous character, pressing on the cerebrum. Both venous capillary hypertrophy of the choroid and angioma of the ciliary bloodvessels and of the choroid have been described in association with cutaneous vascular lesions—usually of the face (Sturge, Horrocks, Parkes Weber, Paton and Treacher Collins). Parkes Weber and Cushing associate unilateral buphthalmos or congenital glaucoma with cutaneous and cerebral hæmangiomatosis, and retinal hæmangiomatosis with the Lindau syndrome. There appears to be no recorded case of angiomatosis retinae in which a vascular lesion of the skin has been present; but of those cases in which it has formed part of an angiomatosis of the nervous system, Lindau, Aust and Tschenzow have each reported an instance in which a small cutaneous nævus has existed.

With reference to the visceral lesions which may be present, Russell distinguishes between the cavernous hæmangiomas—which usually occur above the tentorium cerebelli and in her seven cases were unassociated with cyst formation—and the true capillary hæmangiomas or hæmangioblastoma. In two cases of the former type, visceral lesions of the Lindau syndrome type were found in the form of cysts in the kidney and liver.

Thus it would seem possible, as further cases are recorded, that atypical features may be encountered which may indicate a possible association between the angiomatous malformations and the hæmangioblastomas.

For this reason it has been thought desirable to place on record one such case which, even though pathological investigation was denied, possessed several distinctive clinical features which rendered it unique.

PERSONAL CASE

D. C. C., a well-developed boy of 16 years, was admitted to hospital on August 25, 1934. There had been no other similar case in the family history.

History of Illness.—He was well until he slipped down the bottom two steps of a flight of stairs four years ago; he fell on his buttocks and did not strike his head. Apart from his feeling a little shaken, no ill effects were observed until the following day, when he felt unwell and sick and had a headache. Later in the day he vomited and thereafter he vomited daily, almost regularly after each meal. He also noticed that whenever he turned his eyes to the left without moving his head 'everything used to

move to the right' without the occurrence of any diplopia. During the three months in which he stayed in bed he had frequent giddiness, and whenever he sat upright 'everything went black' and he felt faint though he never lost consciousness.

He returned to school after an absence of six months: by this time the vomiting had ceased, but after a short interval it returned and thereafter he had regularly occurring morning vomiting.

In January 1934 he noticed that the left eye was moving from side to side when he looked to the left, and that he felt intensely giddy on looking vertically upwards or on attempting to lie flat in bed. At about this time he was examined by a competent ophthalmic surgeon and no papilloedema was found.

He wrote with his left hand until one year ago; he then noticed a constant numb feeling in the tip of the left forefinger and a sense of cramp in the left middle finger, which resulted in the pen's slipping from his hand; he thereafter took to writing with his right hand. For six months he had observed complete inability to recognize objects by touch with his left hand and had distrusted the hand in holding things.

For some considerable time he had held the neck stiff to avoid looking directly forwards or upwards. Slight numbness of the left toes had been present for two months. The only other incident of interest in the history is that two days after the initial onset of symptoms his motions were black.

State on Admission.—He was a bright intelligent boy, rather tall for his age, who carried his head rigidly inclined forwards and slightly extended, and even when lying in bed would not permit the cervical rigidity to relax. Over the front and back of the upper midthoracic region was a diffuse light purplish-coloured capillary nævus which extended into the anterior and posterior cervical regions and across the axillæ on to both upper arms. Here the lesion existed in the form of several small isolated areas, not extending below the elbows with the exception of a few tiny areas on the flexor aspect of the right forearm and over the extreme periphery of the palmar surface of the right thumb. Over both anterior deltoid regions could be seen several large subcutaneous veins, which had their origin in the palms of the hands, whence they could be traced upwards along the flexor aspect of each upper limb. In places the skin lesion was bright red; there was also a small capillary nævus to the right of and above the umbilicus.

The *cranial nerves* were normal with the following exceptions. The fundi showed early bilateral papilloedema; the edges of both optic discs were obscured and the veins engorged and tortuous in places; these signs were more marked on the left side, where there was to be seen on the temporal margin of the optic disc a small, round, pinkish, non-pulsatile nodule, into which a large vessel—apparently an artery—entered and disappeared from view (fig. 1). This nodule appeared to be in the retina and had the appearance of an angioma. The pupils were dilated and apart from the right one being slightly the larger and reacting less well to direct light than the left were otherwise normal. There was a coarse, sustained, horizontal nystagmus with a rotary element on full left lateral conjugate deviation; this nystagmus was more marked in the left eye. On full right lateral conjugate deviation there was visible a fine, quick and well-sustained nystagmus.

Examination of the *motor system* revealed the following abnormalities. At rest the left hand lay with the fingers slightly flexed into the palms; the fingers were rarely still owing to the occurrence of involuntary movements of a faintly athetoid type. When the upper limbs were held outstretched the abnormal posture and involuntary movements of the left hand were well seen; the hand assumed the posture characteristic of chorea with the fingers hyperextended and the hand pronated and slightly flexed. Both upper limbs were hypotonic, the left more markedly so; there was a slight bilateral terminal tremor in the finger-nose test, also more obvious

on the left side where motor power was ill-sustained and a little impaired. Both lower limbs were hypotonic ; apart from motor power being less well sustained on the left side where dorsiflexion of the foot was a little weak, there was no other abnormality.

All tendon-jerks were brisk—a little more so on the left side ; the lower abdominal reflexes on both sides were not obtainable ; the plantar responses were both flexor.

Sensory examination revealed complete position loss and astereognosis of the left hand ; there was partial position loss of the toes of the left foot.

FIG. 1.

In walking the boy carried the head rigidly inclined forwards and the left limbs showed a bigger excursion of movement without there being any ataxia.

There was no bruit on auscultation of the skull, radiographic examination of which revealed evidence of increased intracranial tension with no other abnormality.

While the patient was under observation his condition remained unchanged apart from increase of the degree of papilloedema.

An analysis of his physical signs suggested that the gross position loss of the left hand was the cause of the astereognosis and that such sensory loss was not incompatible with an infratentorial lesion ; this was considered the most likely situation of a lesion that could produce the symptoms of intermittent hydrocephalus of which his story was so suggestive. In addition his

sensory loss was apparently of late onset and therefore more likely to have no localizing value. It may be recalled that two of the cases reported by Cushing and Bailey had such sensory loss; Riddoch has also referred to one such similar case of his own. The lesion was thought to be situated either in the left cerebellar hemisphere or in the fourth ventricle, and in view of the vascular lesions present in retina and skin, the confident diagnosis of a bloodvessel tumour of the brain was made. Moreover, though skin lesions appear to be excessively rare in the Lindau syndrome, it was felt that the case in question was an instance of that condition.

Operation was undertaken by Mr. F. A. R. Stammers on October 17; a

FIG. 2.

subtentorial decompression was performed and the arches of the atlas and axis were removed. On reflexion of the dura mater a remarkably tensely distended multiloculated cyst overlying the medulla oblongata was found; this on needling yielded about 12 c.cm. of clear yellow fluid which underwent spontaneous coagulation. Examination of this fluid revealed a protein content of 1.3 per cent. On deflation of the cyst the anticipated tumour nodule was found; it lay between the left cerebellar hemisphere and the medulla oblongata and its lower pole was anchored by three large tortuous vessels which entered it after running vertically upwards alongside the medulla oblongata. The tumour was a lobulated mulberry-like mass of the size and shape indicated in the diagram (fig. 2). No attempt to remove the

tumour was made. It was decided to try to devascularize it by means of deep X-ray treatment, after which a second operation should be performed for its removal: the wound was accordingly closed. To our keen disappointment the boy developed a fatal pneumonia, of which he died on the fourth day following operation. It is greatly to be regretted that no post-mortem examination of any kind was possible.

COMMENT

It is of interest to note the initiation of symptoms following slight trauma and that the cyst was multiloculated and contained xanthochromic fluid—a frequent finding in the syndrome described by Lindau. Whether the black stools which the boy is said to have passed at the onset of symptoms indicates that he had true melæna, it is impossible to say; no record of any case reported in the literature has been found in which vascular lesions of the alimentary tract have been present. That he had some abdominal disturbance is suggested by the history that for several months in 1933 the upper part of the abdomen was very distended—so much so that he was treated for an enlarged liver and spleen, though as far as can be ascertained these viscera were at no time palpable.

The central position of the retinal angioma would appear to be quite unusual, as in both angiomatosis retinæ and in those cases of the Lindau syndrome in which a retinal lesion has been present, the angioma is almost always found at the extreme periphery of the fundus. Niccol and Foster Moore have recently described an example of the former condition in which the lesion adjoined and partly overlay the temporal edge of the papilla.

In spite of the absence of histological confirmation of the diagnosis, it is felt that this is sufficiently certain to enable one to record the case as one of the Lindau syndrome in which the presence of an extensive skin lesion was a remarkable feature.

SUMMARY

1. Bloodvessel tumours of the brain are briefly discussed and the chief features of the angiomatous malformations and the hæmangioblastomas are described and contrasted.

2. Attention is drawn to the occurrence of cases in which features common to both types of lesions occur.

3. A case is described which on clinical grounds is believed to belong to the group of cases described by Lindau. The existence of an extensive skin lesion rendered the case unique and is believed to indicate an association between the angiomatous malformations and the true bloodvessel tumours of the brain.

It is a pleasure to express my thanks to Dr. A. P. Thomson for permission to report this case, which was admitted to the Birmingham General Hospital under his care, and to Dr. Stanley Barnes for his helpful interest.

BIBLIOGRAPHY

- ATKINSON, W. S., *Trans. Amer. Acad. Ophthalm.*, 1932, 7, 510.
 BARNARD, W. G., and WALSH, F. M. R., *Jour. Path. Bact.*, 1931, 34, 385.
 COLLIER, W. T., *Brit. Med. Jour.*, 1931, 1, 194.
 CUSHING, HARVEY, *Jour. Amer. Med. Assoc.*, 1906, 47, 178.
 CUSHING, H., and BAILEY, P., *Tumours arising from the Blood-vessels of the Brain*, 1928.
 CUSHING, H., and BAILEY, P., *Arch. of Ophthalm.*, 1928, 54, 447.
 DANDY, W. E., *Arch. of Surgery*, 1928, 715.
 HARTMAN, E., and SOURDILLE, G., *Ann. d'ocul.*, 1931, 168, 881.
 HORROCKS, P., *Trans. Ophthalm. Soc. U.K.*, 1883, 3, 106.
 LINDAU, A., *Acta Pathol. et Microbiol. Scandin.*, Supplement 1, 1926.
 MÖLLER, H., *Acta Ophthalm. Scand.*, 1929, 7, 244.
 NICCOL, W., and FOSTER MOORE, R., *Brit. Jour. Ophthalm.*, 1934, 18, 454.
 PARKES WEBER, F., *Proc. Roy. Soc. Med.*, 1928-29, 22, 431.
 PATON, LESLIE, and TREACHER COLLINS, E., *Trans. Ophthalm. Soc. U.K.*, 1919, 39, 157.
 RIDDOCH, G., *Proc. Roy. Soc. Med.*, 1931, 24, 383.
 ROCHAT, G. F., *Nederl. Tijdschr. Geneesk.*, 1927, 1, 1124.
 ROCHAT, G. F., *Klin. Monats. f. Augenheilk.*, 1931, 86, 23.
 RUSSELL, D., *Proc. Roy. Soc. Med.*, 1931, 24, 383.
 RUSSELL, D., *Jour. Path. Bact.*, 1932, 35, 103.
 SARGENT, P., and GREENFIELD, J. G., *Brit. Jour. Surg.*, 1929, 17, 65.
 STURGE, W. A., *Trans. Clin. Soc.*, 1879, 12, 162.
 TREACHER COLLINS, E., *Proc. Roy. Soc. Med.*, 1931, 24, 372.
 VIEGTS, H. A., *Jour. Nerv. Ment. Dis.*, 1933, 77, 457.