CASE REPORTS

OLIGODENDROGLIOMA IN AN INFANT OF EIGHT MONTHS

BY

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The relative rarity of intracranial tumours in infants, the site of the tumour and the histological findings render the following case worthy of comment.

Case report

History. Thomas M., aged eight months (date of birth, February 18, 1941), was admitted to hospital on October 4, 1941, with a history of having developed a 'squint' of the left eye two weeks previously and for two days before admission having appeared listless and disinclined to take his feeds. There had been no vomiting and the stools were normal. No previous illnesses were reported.

FAMILY HISTORY. Father was said to suffer from 'chest trouble,' but mother and seven other children are alive and well. Father and two of the children have 'squints' and mother had one miscarriage six years ago.

Examination and progress. On admission the infant was found to be well nourished, weighing 17 lb. 6 oz., with no evidence of dehydration. He was thought to have ptosis of the left eye with strabismus, a rather tense fontanelle, and some slight neck rigidity. Kernig's sign was absent and there was no paralysis. Other examination was negative. Lumbar puncture was performed and a clear colourless fluid not under pressure was obtained. The following is the report on this specimen of cerebrospinal fluid: 'A clear, colourless fluid; total protein 0.04 per cent.; globulin negative; chlorides 0.70 per cent.; sugar normal; cells no increase; cultures remain sterile.' X-ray examination of the chest showed no evidence of disease. His condition remained as described for the next two days. Lumbar puncture was repeated on October 8, with the following result: 'A clear, colourless fluid; total protein 0.06 per cent.; globulin negative; chlorides 0.73 per cent.; sugar normal; cells 10 per c.mm. mainly lymphocytes; no organisms on direct examination; tubercle bacilli were not found; Wassermann reaction negative.' On October 10, the infant became semi-conscious and was found to have a right facial paralysis and right hemiplegia. The fundi were normal. There had been considerable loss of weight and the temperature rose to 101.8° F. Death occurred about 7 a.m. on October 11, the temperature having risen to 104° F. Mantoux reaction 1/1,000, blood Wassermann Reaction, and x-ray examination of the skull were negative.

Post-mortem examination revealed the presence of a small tumour, about the size of a large almond, situated in the mid-brain immediately above the pons varolii. The situation of the tumour can be seen in fig. 1. The upper part of the tumour was cystic and the roof of this cystic part is supported by a small bristle. Apart from the tumour no other abnormalities were found except a patent foramen ovale.

Professor T. B. Davie, Professor of Pathology in the University of Liverpool, has kindly allowed us to quote his report, which is as follows: 'The brain had been split sagittally and the right-hand half was received. This showed a tumour in the upper and posterior part of the crus, the centre of the tumour being level with the upper surface of the cerebellum. The tumour had replaced the posterior part of the crus, the aqueduct of Sylvius, the corpora quadrigemina and the pineal body. The cut surface of the tumour was roughly rounded and approximately 17 mm. in diameter. Its edges were sharply defined and its cut surface was very finely granular and pink in colour, contrasting sharply

FIG. 1.

with the adjacent smooth, white brain tissue. The occlusion of the aqueduct had caused internal hydrocephalus with herniation of the third ventricle in the region of the pituitary stalk.

HISTOLOGICALLY the tumour was highly vascular with numerous wide capillaries. All but the periphery consisted of masses of rounded cells relatively loosely packed with no recognizable arrangement. The cells were relatively uniform in size, about 15 to 20 microns in diameter, with rounded nuclei and pink-staining cytoplasm in haematoxylin and eosin preparations. There were also a certain number of small giant cells about two to three times the size of the rest and containing often one, but sometimes two or three nuclei. No 'boxed cells' were observed. With phosphotungstic acid-haematoxylin there were a very few fine fibrils between the tumour cells but no real matrix. There was no calcification. This part of the tumour appeared to be an oligodendroglioma. At the periphery where the tumour abutted on normal brain the structure differed. The cells were ovoid and closely packed and the histology resembled in every way that of a medulloblastoma.'

The microphotograph (fig. 2) shows the general histological arrangement. On the right-hand side can be seen normal brain tissue and next to this is a band of closely packed medulloblastomatous cells. On the left of the photograph is an area composed of loosely packed oligodendrogliomatous cells. Fig. 3 shows the closely packed medulloblastomatous cells and fig. 4 the loosely packed oligodendrogliomatous cells.

FIG. 2. $\times 60$.

FIG. 3. $\times 350$.

FIG. 4. $\times 350$.

Discussion

The interesting features of this case may be discussed under three heads: (a) Age and incidence, (b) site, and (c) pathology.

Age and incidence. The tumour described occurred in an infant of eight months. In Critchley's (1925) series of 125 cases up to the age of sixteen years only one occurred in the age group 0-1 years, whereas in Bailey and Cushing's (1926) series of classified gliomas, numbering 254, there were twenty-nine medulloblastomas and nine oligodendrogliomas. In this series the average age of twenty-five cerebellar cases was ten years, the youngest being two, the oldest thirty-eight and sixteen occurring in the first decade of life. Among the oligodendrogliomas the youngest case was five years, but the authors make the interesting observation that very possibly all these tumours start in early life. Although ages are not given in detail, the youngest appears to have been a child of two years in the medulloblastoma group and a child of twenty-three months in the group of protoplasmic astrocytomas. In 1927 Bailey described additional cases added to the original series which brought the total to 378 cases, with a total of only twelve oligodendrogliomas. Dickson (1926) described a case of an oligodendroglioma of the fourth ventricle, occurring in a child of six years, in whom the symptoms had lasted for five months, but the child had been diagnosed as suffering from primary optic atrophy at the age of five months. In Cushing's series of 154 children, twenty-four fell in the age group one to five years, but no oligodendrogliomas are mentioned. In 1929 Bailey and Bucy described thirteen cases of oligodendroglioma, one of which was aged five years, and stated that 'these tumours are predominantly situated in the cerebral hemispheres of adults.' In Greenfield and Robertson's (1933) series the incidence of oligodendrogliomas is similar to that found by Cushing, namely nine oligodendrogliomas in 230 cerebral gliomas. In this series there were no infants, the youngest being two children aged sixteen years, one of whom had suffered from hydrocephalus for many years (possibly from infancy) when the tumour may have begun to manifest itself. Martin (1931) described a case in a girl of sixteen who had always had a large head but her symptoms had only been present for ten to twelve months. In Stern's (1937) series of 102 cases, six were in the 0-1 year period, of whom two were tuberculomas. No oligodendrogliomas are mentioned. She suggests that the low incidence of cerebral tumours in infants may be, in part, explained by the fact that most of the published cases come from neurological centres which infants rarely reach.

On the other hand, in this hospital which used to admit an average of 1000 infants per annum, intracranial tumours are excessively rare. From this brief summary it can be seen that an oligodendrogliomatous tumour in an infant is rare, although the history in certain older children suggests that their tumours may have been present from an early age, a theory which finds support in the present case.

Site. In the present case the tumour was situated in the upper and posterior part of the crus (fig. 1), i.e. supratentorial. In Critchley's series almost half were situated in the pons or cerebellum. The nine oligodendrogliomas in Bailey and Cushing's (1926) series were all found in the cerebrum and originated as sub-cortical lesions, the most common situation being the frontal lobes. On the other hand, medulloblastomas occurred most commonly in the cerebellum of children. In Dickson's case the tumour occurred in the floor of the fourth ventricle in the interpeduncular space and caused hydrocephalus of the third

and lateral ventricles. In Cushing's series of 154 children under fifteen years, eighty-five were cerebellar or subtentorial. As has been mentioned Bailey and Bucy (1929) stated that oligodendrogliomas are essentially tumours of the cerebral hemispheres. Martin (1931), who described two cases of oligodendroglioma and reviewed other cases mentioned in the literature, divided such cases into two groups, those occupying the cerebral hemispheres away from the mid-line and those lying across the mid-line and interfering with the circulation of the cerebrospinal fluid. Cases in the former group tend to be relatively 'silent,' irritative symptoms rather than paralytic symptoms being prominent. In the latter group, symptoms tend to appear much earlier with an unfavourable operative outlook. He found the site of election to be the frontal and parietal lobes where calcification, common in such tumours, has time to occur, but rarely occurs in the mid-line cases owing to earlier operation or death. Greenfield and Robertson's (1933) series consisted of five tumours, three of which were cystic tumours of the hemispheres and two were mid-line ventricular tumours and they came to the conclusion that a small medially placed tumour may cause as severe symptoms as a large laterally placed tumour. Of the sixty-two cases in Stern's (1937) series forty-one were subtentorial and nineteen were supratentorial, while two were cases of multiple tuberculomata. In the supratentorial group the majority were laterally situated, whilst in the subtentorial group the cerebellum was the commonest situation. She came to the conclusion that cerebral tumours 'kill by their site of election rather than by their nature or size.' In his opening paragraph Armour (1932) stated that 70 per cent. of all tumours are subtentorial, cerebellar tumours being about twice as common as those in the cerebrum in childhood.

In the present case the tumour, an oligodendroglioma, conforms to the usual supratentorial situation of these tumours, but its supratentorial position renders it somewhat uncommon in a child. The early onset of symptoms in a medially situated tumour is in keeping with the general experience.

Pathology. Bailey and Cushing's (1926) original description of the histological appearance of an oligodendroglioma is as follows: 'The neoplastic cells have spherical nuclei with a heavy chromatin network and are surrounded by a ring of cytoplasm which stains very feebly with ordinary stains. Between the cells is an indefinite material which stains neither for neurofibrillae, neuroglia nor for connective tissue. This material may give the growth somewhat the appearance of a cross-section of a plant. No mitotic figures can be seen. These tumours are prone to become calcified.' In a later paper (1927) Bailey suggested that oligodendrogliomas may be related to medulloblastomas. In one case, which had had repeated operations, the tumour was found to grow with the typical structure of a medulloblastoma. He stated that 'it is not surprising that these tumours should be related to the medulloblastomas for the oligodendroglia along the fibre tracts of the brain develops from medulloblasts which wander into this region and there differentiate into either oligodendroglia or neuroglia.' Reference has already been made to calcification. In the present case x-ray examination of the skull showed no evidence of calcification which may be explained by Martin's theory that a mid-line tumour, causing early death by its situation, may not have time to develop calcification. Greenfield and Robertson found the occurrence of cystic change common in their cases where rapid onset of symptoms in their laterally placed tumours was due to the expansion of cysts associated with slowly growing tumours. The upper part of the tumour in the present case was cystic, which may have had some bearing on the extremely rapid onset of symptoms at so early an age.

The interesting feature of the present case is the combination of an oligodendroglioma with a medulloblastomatous histology at its periphery which tends to confirm the view that an oligodendrocyte is developed from a medulloblast type of cell. It is also a rare example of a supratentorial medulloblastoma.

Summary

A case of a mid-line, supratentorial tumour with an oligodendrogliomatous centre and a medulloblastomatous periphery occurring in an infant of eight months is described, a rare combination of clinical and pathological findings.

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REFERENCES

- Armour, D. (1932). *Lancet*, **2**, 551.
 Bailey, P. (1927). *Johns Hopk. Hosp. Bull.*, **40**, 354.
 —, and Bucy, P. C. (1929). *J. Path. Bact.*, **32**, 732.
 —, and Cushing, H. (1926). *A classification of the tumours of the glioma group*, Phila., 56, 87, 106.
 Critchley, M. (1925). *Brit. J. Child. Dis.*, **22**, 251.
 Cushing, H. (1927). *Amer. J. Dis. Child.*, **33**, 551.
 Dickson, W. E. C. (1926). *Brain*, **49**, 578.
 Greenfield, J. G., and Robertson, E. G. (1933). *Ibid.*, **56**, 247.
 Martin, J. P. (1931). *Ibid.*, **54**, 330.
 Stern, R. O. (1937). *Arch. Dis. Childh.*, **12**, 291.