CIRCUMSCRIBED CEREBRAL TUMOURS IN YOUNG INFANTS

BY

DOROTHY S. RUSSELL, M.D.,
Member of Scientific Staff, Medical Research Council,

and

RICHARD W. B. ELLIS, M.D., M.R.C.P.

(From the Bernhard Baron Institute of Pathology and the Children's Department, London Hospital.)

The following three cases are reported because of the rarity of intracranial tumours in young infants and because of the histological problems that have arisen from their study. They also present some interesting clinical features.

Case reports.

Case 1.—LEFT CEREBRAL GLIOMA IN A STILL-BORN INFANT. Still-born at term. The mother was 28 years of age; she had had four children who were alive and well, and no miscarriages. Pregnancy had been normal except for frequency of micturition during the later months. Strong labour pains began on May 24th, 1925. On the following day instruments were unsuccessfully applied by a private doctor. The mother was then admitted to the London Hospital under Dr. Russell Andrews; an anæsthetic was given at 11.45 a.m. on May 26th, 1925, and a 7 lb. still-born fœtus was delivered without instruments. The fœtus was in the right occipito-posterior position when the first examination was made, and in the right occipito-anterior position when delivered.

NECROPSY (S.D. 1188. 1925). A limited necropsy was carried out by a member of the gynæcological staff. The following notes only are available.

The specimen of intracranial tumour was obtained from a well developed female infant. The sutures of the skull were widely separated. There was great internal hydrocephalus. A solid spherical mass (8.5 × 7.5 × 6 cm.) occupied the left cerebral hemisphere. The cerebral cortex and white matter were reduced to a layer, in places only 0.5 cm. thick, over the surface of the tumour and could easily be separated from it. The leptomeninges appeared normal except for a few areas of hæmorrhagic staining. The outer margin of the tumour was lobulated and the cut surfaces presented a homogeneous pinkish grey or white surface resembling brain matter. The centre was occupied by closely packed capillaries, and contained both an opaque yellow patch (2 cm. in diameter) and a cavity containing blood clot.

MICROSCOPICAL EXAMINATION.—Three paraffin blocks were prepared from representative parts of the tumour. Sections were stained with hæmatoxylin and eosin, Weigert's hæmatoxylin and van Gieson's mixture, Weigert's fuchselin and neutral red, Mallory's phosphotungstic acid hæmatoxylin after treatment with Zenker's fluid, Laidlaw's method for reticulum, and Fincher's modification of Hortege's silver carbonate method for astrocytes⁶. No material had been reserved for frozen sections.

The tumour was clearly separable from the surrounding brain tissue which was compressed and not invaded by the tumour cells. In most areas it was composed

of interlacing bundles of closely packed cells supported by a scanty stroma of blood vessels (Fig. 1). The cells were remarkably uniform; they were of spindle or oat shape when seen in longitudinal section, and appeared in cross section as small circles or polygons. Their nuclei were oval or rod shaped: each had a fairly stout membrane and a delicate chromatin net of irregular mesh. The nodes were variable both in size and distribution; in many instances they were grouped near the nuclear membrane, but in others were more evenly distributed. There were from one to three small nucleoli. Many mitoses were present. The cytoplasm was moderately voluminous and contained stringy eosinophil material streaming at either pole of the nucleus into a fairly long process. These processes, in phosphotungstic acid hæmatoxylin and in silver preparations, sometimes contained delicate glial fibrils. In other places, using the same stains, an appearance of condensation was seen at the

FIG. 1. Case 1.—Area showing general character of tumour. (Hæmatoxylin and eosin: $\times 500$).

margin of the cytoplasm, forming a deeply stained tail towards the end of the process. Blepharoplasten were not present. The cells tended to ensheath blood vessels longitudinally, but were sometimes arranged at right angles to them. In many vessels an excess of endothelial cells was present.

There were many areas of degeneration and necrosis; about these a pallisading of the tumour cells was sometimes seen. Collections of amorphous hæmatoxyphil particles were present in some of the necrotic areas. With Laidlaw's method there was little reticulum in the tumour: it was confined to the blood vessels and their immediate neighbourhood.

COMMENT.—From the available data it is probable that the tumour in this case gave rise to difficulty in delivery and was therefore responsible for foetal death. Histologically it has features that characterize it as a glioma: the reticulum was limited to the walls of blood vessels; the cells had the

appearance and arrangement of glial cells, and the fibrils present in some of them were delicate, lay definitely within the cell, and were demonstrable with silver carbonate as well as with phosphotungstic acid hæmatoxylin. Gliomata are sometimes circumscribed but are more often diffuse. The circumscribed are usually the more benign types of tumour. It is obvious, however, from the degree of cellularity and the number of mitoses that the tumour under discussion was of rapid growth. Already, in the course of intra-uterine life, it had reached an impressive size. The histological appearance was not typical of any of the commoner types of glioma. According to the character and arrangement of the cells the tumour is here regarded as a polar spongioblastoma. It is clear, however, that it has little in common with the polar spongioblastomas described by Bailey and Eisenhardt² and by Penfield⁹, but is probably closely related to the malignant tumour of the third ventricle in a child described by Cairns and Russell³ (Case 1 of their series) under this title.

Case 2.—PRIMARY SARCOMA OF CEREBRUM. V. H., male, aged 5 months. Full term, normal delivery, artificially fed. Parents alive and well. One sibling died from pneumonia at the age of 8 months. The infant appeared normal in every way until six days before admission to the London Hospital (March 27th, 1932). During that period he suffered from sudden attacks of projectile vomiting which bore no close relationship to feeding. The bowels were not open for five days. No other symptoms were noted; the feeds were taken well and the infant did not appear ill.

On admission the infant was well developed and nourished, weighing 14 lb. 3 oz.; the temperature was 100° F., the pulse rate 120 and the respiration rate 30. The infant reacted quite normally for his age, sitting up unsupported, grasping for objects and following a light with his eyes. He moved his limbs freely and his cry was normal. The anterior fontanelle was widely patent and bulging; the circumference of the head was 17½ in. There was no neck rigidity and Kernig's sign was absent. The discs and fundi were normal. There was no demonstrable paralysis nor alteration of muscle tone. The knee jerks were present and equal. The reaction to pin-prick on trunk and limbs was normal. No signs of disease were found in the heart, lungs or abdomen.

On April 28th, lumbar puncture was performed. 8 cc. xanthochromic fluid, obtained under slightly increased pressure, contained 13 white cells per c.mm. with red blood cells in the stained film. No micro-organisms were seen. Protein 0.15 per cent. Wassermann reaction negative. On May 1st lumbar puncture was repeated: the fluid showed 32 white cells per c.mm. (mononuclears predominating) with many red cells. Right ventricular puncture gave 3 to 4 c.c. xanthochromic fluid under increased pressure, followed by fluid containing fresh blood. Left ventricular puncture gave 20 c.c. clear fluid under considerably increased pressure showing no deposit of blood on standing, 2 lymphocytes per c.mm., protein 0.065 per cent. Repeated ventricular punctures continued to show xanthochromic or blood-stained fluid from the right, and clear fluid under increased pressure from the left ventricle, the latter becoming blood-stained in the last puncture before death.

Projectile vomiting continued irregularly during 7 days in hospital and the temperature rose irregularly to 104° on May 3rd, 1932, the day before death. Head retraction and coarse lateral nystagmus were noted two days after admission, and the general condition deteriorated very rapidly from this time, the infant ceasing entirely to respond to pin-prick or to light. The limbs became progressively more spastic, and there were frequent clonic movements of the right arm. The patient died in coma on May 4th, 13 days from the onset of the first symptom. Repeated examinations of the discs before death showed no papilloedema. A clinical diagnosis of internal hydrocephalus and cerebral hæmorrhage, ? cerebral tumour, was made.

SUMMARY OF NECROPSY (P.M. 197. 1932). Internal hydrocephalus: primary intracranial endothelio-sarcoma. A slightly wasted male infant with sunken eyes. Foramen ovale patent to probe. Œdema of lungs. Irregular pale grey area (2 cm. diam.) in posterior border of lower lobe of left lung. Moderate parenchymatous degeneration of liver and of kidneys. Slight œdema of spleen. Mucous catarrh of dilated stomach. Focal dilatation (6 cm. circumf.) of colon. Well developed glandular thymus. Middle ears clean.

WEIGHTS (in grammes): Heart, 28·4; liver, 177·2; kidneys, 42·5; spleen, 7·1; brain, 843·4; suprarenal bodies, 4·1; pituitary gland, 0·125; thyroid gland, 0·95; thymus, 6·3; pancreas, 4·9.

MACROSCOPIC EXAMINATION OF BRAIN (after hardening in formaldehyde). The cerebral convolutions were greatly flattened. On the right there was a diffuse area of bluish discoloration involving the angular and lower part of

FIG. 2. Case 2. —Rightside of brain to show size and position of tumour.

the post-central convolutions. A firm, sharply circumscribed tumour (6·5 cm. from before backwards, by 4·5 cm. from above downwards, by about 6·5 cm. from side to side) occupied the centre of the brain, lying slightly more to the right than the left (Fig. 2). It replaced the lower border of the genu and anterior half of the corpus callosum, the septum lucidum and fornix, extending on the right to involve the head of the caudate nucleus, optic thalamus and mesial part of the right corona radiata. The tumour bulged down into and greatly expanded the cavity of the third ventricle, and appeared to obstruct completely the foramina of Monro. It occluded and expanded the body and all except the extreme tip of the anterior horn of the right lateral ventricle. The choroid plexus of this ventricle was incorporated with the growth anteriorly, but appeared normal elsewhere. The posterior and descending horns of the ventricle were enormously distended. On the left the basal ganglia were hollowed out to form a bed for the left border of the tumour, and the mesial surface of the left frontal lobe was concave to accommodate the bulging opposing surface of the right frontal lobe and the underlying tumour. The left ventricle also

was distended, but to a less extent than the right. The corpora quadrigemina and pineal body were flattened and distorted beneath the posterior border of the tumour.

The outer surface of the tumour was greyish white, opaque and rather friable. The cut surfaces were variegated. The greater part was greyish white, slightly translucent and finely granular. There were many small, poorly defined areas (up to 0.4 cm. diam.) of reddish-brown hæmorrhage near the periphery, and near the centre was a larger area (3.5 cm. diam.) of hæmorrhage and necrosis. In the centre of the portion in the right anterior horn was a diffuse area (1.5 cm. diam.) of slaty-grey fibrosis, streaked in places with opaque yellow, and a few small cystic areas (up to 1.5 by 0.8 cm.) with glairy contents.

The spinal cord appeared normal except for slight brown hæmorrhagic staining of the arachnoid membrane and pia. In the upper part of the sixth thoracic segment was an ill-defined area (0.25 cm.) of grey pearly thickening of the pia adjacent to the right posterior root.

MICROSCOPICAL EXAMINATION.—Paraffin sections were prepared from three blocks

FIG. 3. Case 2.—Area to show general character of tumour. (Hæmatoxylin and eosin; $\times 300$).

taken from representative parts of the tumour, and from the sixth thoracic segment of the spinal cord. A fourth block of the tumour was used for frozen sections. Paraffin sections were stained by the methods already enumerated with the addition of Bielschowsky's method (Davenport's modification) for neurofibrils. Sections cut on the freezing microtome were stained with Scharlach R and hæmatoxylin, by Penfield's modification of Hortega's method for oligodendroglia and Cajal's gold chloride sublimate method for astrocytes. Spare sections were also stained by Hortega's method for astrocytes after storage for a fortnight in formol-bromide.

In most places the tumour was clearly separable from the adjacent brain. Both frontal cortex and ependyma were compressed and stretched over it and evidence of invasion was restricted to a few places in which ependyma and subependymal glia were replaced by tumour tissue.

Most of the tumour cells were round or polygonal, and were arranged loosely in acini of various sizes separated by a scanty stroma of blood vessels (Fig. 3). The cells varied considerably in size. They had a fairly abundant, faintly eosinophil

vacuolated cytoplasm and a relatively large round or oval nucleus, which was often indented in one or more places and was occasionally cup-shaped. The nuclear membrane was moderately stout and well defined, the nucleoplasm pale and clear and traversed by an exceedingly delicate chromatin net beset with a very few small nodes. One or two large nucleoli lay near the centre. Many mitotic figures were present. These cells had no demonstrable affinity for either gold or silver when stained by the methods mentioned.

With Laidlaw's stain for reticulum, a conspicuous network of delicate fibrils enclosing small groups of cells was found, particularly near the anterior margin of the tumour (Fig. 4). This reticulum was not accounted for by any extra vascularity or organization of the tissue in the regions where it was most abundant. In other parts of the tumour it was less abundant although everywhere there was more than is usually encountered in gliomas.

Slight variations in structure were demonstrated in different parts of the tumour.

FIG 4. Case 2.—Area in anterior part of tumour showing distribution of reticulum. (Laidlaw: $\times 110$).

Thus, in the anterior part, where reticulum was most abundant, the cells were arranged in small syncytial groups or short trabeculae separated by an oedematous stroma of collagen and reticulum (Fig. 5). In this area mitoses were conspicuous. Near the ventricle the cells were closely packed and occasional strands of elongated spindle cells were present. Within the cytoplasm of these one or two delicate fibrils were sometimes seen with phosphotungstic acid hæmatoxylin. Also in the neighbourhood of the ependyma was seen an area in which there was a conspicuous perithelial arrangement of the tumour cells round small blood vessels. Here too mitoses were conspicuous.

Large areas of hæmorrhage and smaller foci of degeneration and necrosis were scattered throughout the tumour; in these necrotic areas were collections of extracellular fatty material and fat granule cells which corresponded, in silver preparations, to the distribution of amœboid microglia.

In the sixth thoracic segment there was a crescentic area of infiltration by polygonal tumour cells in the pia over the right posterior column and adjacent root. The cells were loosely packed and were supported by a considerable stroma of thin collagen fibrils. The adjacent spinal cord appeared normal.

LUNG.—In pale grey area in the posterior border of the lowest lobe of the left lung the alveoli were crowded with large foamy macrophages. A few similar cells were present in the lumina of the respiratory bronchioles and in some of the smaller bronchi. There was but little focal inflammatory infiltration of the interstitial tissue consisting of large lymphocytes and a few neutrophil leucocytes. Occasional collections of bacteria in alveoli and bronchioles were not associated with any cellular reaction. The histological picture was not that of a pneumonia; it might possibly have been accounted for by the inhalation of a small quantity of milk.

COMMENT.—Owing to the extreme readiness with which separation of the cranial sutures and expansion of the anterior fontanelle can occur in early infancy, the signs and symptoms of intracranial tumour at this age are liable to differ somewhat from those observed when the condition arises after the skull has become more rigid. This is well illustrated by the present case.

FIG 5. Case 2.—Area in anterior part of tumour showing cells in syncytial groups and short trabeculae. (Hæmatoxylin and eosin: $\times 275$).

Although the tumour was probably of rapid growth the extremely short history and paucity of signs until a terminal stage had been reached are remarkable in view of the large size of the growth. Thus the presenting symptom was projectile vomiting of cerebral type which occurred for the first time thirteen days before death. When the infant was first seen, six days after the onset of the vomiting, the only physical signs of disease were bulging of the anterior fontanelle and an increase in the circumference of the skull to three-quarters of an inch in excess of the average for the age. Papilloedema was absent up to the time of death, and though this sign is not a constant finding with intracranial tumours, especially with those

above the tentorium, even at a later age, its entire absence with a tumour of this size is exceptional. Clinical deterioration was rapid after the first symptoms were observed.

The presence of internal hydrocephalus of obstructive type was shown before death by obtaining repeated samples of ventricular fluid under increased pressure. That the obstruction involved the foramina of Monro was demonstrated by the dissimilarity in the specimens obtained from the two ventricles: the fluid from the left ventricle was clear whereas the right ventricular and lumbar fluid was xanthochromic or blood-stained. These clinical observations were confirmed by post-mortem examination. The xanthochromia of the fluid in the right ventricle and spinal canal was probably the result of independent hæmorrhages into the lateral and third ventricles respectively. The observation of hæmorrhagic staining of the spinal meninges supports this explanation.

The appearance, arrangement and staining reactions of the cells in the intracranial tumour in this case and the amount of reticulum present rule out the possibility that it is a glioma. The lack of any specific differentiation on the part of the tumour cells, however, makes it difficult to name. There is no evidence that it is a teratoma. The pineal body was intact. The relative abundance of reticulum suggests that it is a tumour of mesodermal origin. If so, it must be regarded as originating from the tela choroidea, or from the stroma of one of the choroid plexuses, or from the perivascular sheath of one of the perforating vessels. Inasmuch as all these structures are derived from the pia it would be correct to regard the tumour as a malignant endothelioma or sarcoma. An alternative possibility that the tumour is a carcinoma of the choroid plexus must also be considered. In support of this is the conspicuous perithelial arrangement of the cells about a central vascular core in one part of the tumour, the patchy distribution of reticulum and lastly the tendency of the reticulum fibrils to enclose groups rather than individual cells. In secondary carcinoma of the brain the amount of reticulum is exceedingly variable even if the different specimens examined are derived from the same type of primary tumour, for example carcinoma of the lung. In one specimen of this type the amount of reticulum present in the metastasis was considerable, even though remote from the meninges, and was comparable to that observed in this tumour. The reticulum in the metastasis, however, could be attributed to the proliferation of spindle fibroblasts amongst the tumour cells, whereas in the tumour under discussion a cellular stroma of this kind could not be detected. It must be concluded therefore that the reticulum was produced by the activity of the tumour cells.

Thus in the light of the available evidence it is reasonable to regard this tumour as a primary sarcoma or malignant endothelioma of pial origin. The focus of tumour cells in the pia of the thoracic spinal cord was interpreted as a metastasis from the main tumour. Such metastases are of frequent occurrence in all the commonly recognized kinds of glioma³, but have not previously been recorded in circumscribed tumours of this kind. The

presence of these metastases in the spinal canal depends less upon the intrinsic malignancy of the primary tumour than upon the close contiguity of the tumour to the subarachnoid cerebro-spinal pathway.

Case 3.—PRIMARY SARCOMA OF CEREBRUM. K. B., male, aged 1 year 11 months. The infant, an only child, was born at term after a prolonged labour and weighed 10½ lbs. He was breast fed for 10 months and apart from pertussis at 1 year was quite well and developed normally up to the age of 1 year and 8 months (Dec. 31st, 1932). At this time there was vomiting of sudden onset which occurred each morning for two weeks and then ceased. The child then developed a divergent strabismus of the left eye for which glasses were prescribed at an eye hospital. The general condition was good until one month before death, when the child was suddenly

FIG. 6. Case 3.—Mesial aspect of right hemisphere showing tumour in parieto-occipital region.

unable to sit up or walk and became increasingly drowsy. There was loss of appetite and constipation for two weeks.

On March 16th, 1933, the child was admitted to the Hospital for Sick Children, Great Ormond Street, under Dr. Frew. He was drowsy and irritable when roused. He continually rubbed his nose. The general nutrition and development was good. The head was obviously enlarged with separation of the sutures and a circumference of 21½ in. The scalp veins were dilated especially over the left temple. Both discs appeared pale and the margins definitely blurred; there was some engorgement of the vessels, with marked congestion around the discs. The pupils were central, but reacted very sluggishly to light. There was a slight divergent strabismus of the

left eye. The arm jerks were normal; the abdominal reflexes and the knee and ankle jerks were not obtained. Extensor plantar reflexes were obtained on both sides. The pulse rate was 120 and the volume good. The blood pressure was 110/45. There were scattered râles in both lungs posteriorly, but no other physical signs of disease. Lumbar puncture (March 18th) yielded clear fluid of normal composition under increased pressure.

The infant became comatose on the day following admission and showed slight spasticity of the left arm. The temperature rose to 104° and the pulse rate to 160; there was appreciable increase in the circumference of the skull. Death occurred on the fourth day in hospital. A clinical diagnosis of cerebral tumour was made.

NECROPSY.—We are indebted to Dr. R. C. Lightwood for the following note:—

A fairly nourished infant with considerable degree of post-mortem change. Cranial sutures wide with no erosion of bones of skull. Flecks of calcareous deposit in dura over vertex and at base. No hydrocephalus. Liver fatty. Spleen, heart, lungs, kidneys and suprarenals, post-mortem changes only. Weights: body, 11.34 kgrm. (length 94 cm.); heart, 60; liver, 200; spleen, 35; kidneys, 32 grm.

The right half of the brain was received after hardening in formaldehyde. The posterior half of the right cerebral hemisphere was replaced by a hard globular growth (7 cm. from side to side, by 11.3 cm. from before backwards, by 10 cm. from above downwards). This presented a flat nodular surface (9.5 by 10 cm.) beneath the leptomeninges covering the mesial surface of the parieto-occipital lobe (Fig. 6). Here the brain tissue had almost entirely disappeared but could occasionally be identified as a thin translucent layer between the meninges and the surface of the tumour. Anteriorly the brain formed a sharp crescentic border round the tumour and posteriorly there was a small cap of the occipital lobe (2 cm. deep), which, however, had been almost entirely detached from the tumour. The right lateral ventricle and basal ganglia, the corpus callosum and callosal gyrus were pushed forwards and compressed. The corpora quadrigemina also were compressed into a pyramidal mass (0.9 cm. from before backwards by 0.6 cm. high). The pineal body was not present in this half of the brain.

The exposed portion of the tumour was opaque, greyish white and extremely firm. In places the texture resembled that of a cauliflower, but mostly was composed of smooth nodules and flat bosses from 0.5 to 1.5 cm. in diameter. On section, the cut surfaces were everywhere solid and extremely firm: the tissue was composed in part, and especially at the periphery, of white glistening tissue, slightly translucent. In the centre were a few areas (up to 2 cm. diam.) of lemon-tinted gelatinous material flecked with brownish-red streaks and dots. Also near the centre were a few sunken slaty grey areas of fibrosis. The greater part of the tumour was variegated with glistening white areas, similar to the peripheral zone, interspersed with more extensive diffuse grey patches of translucent appearance which were thickly beset with fine hair-like dark red streaks and dots. Most of these streaks and dots were surrounded by a narrow zone of pearly white tissue making them conspicuous to the naked eye. These grey areas were flexible and extremely firm.

MICROSCOPICAL EXAMINATION.—Representative blocks from the periphery and more central parts of the tumour were embedded in paraffin. The block from the periphery was first cut on the freezing microtome and sections were stained with Scharlach R and hæmatoxylin, by Hortega's method for pineal parenchyma, and by Penfield's modification of Hortega's silver carbonate method for oligodendroglia, and Cajal's gold chloride sublimate. The remainder of the block was then embedded in paraffin. Paraffin sections were stained by the methods already enumerated.

The tumour was markedly cellular, but varied greatly in density in different parts. The periphery was composed of closely crowded round or polygonal cells; in the deeper areas these aggregated round cells were separated into masses of varying size and shape by broad zones in which parallel spindle cells were more

sparsely arranged in an abundant fibrillar or sometimes hyaline stroma of connective tissue (Fig. 7). These strands of spindle cells broke up into thinner trabeculae which penetrated everywhere into the collections of round cells. No sharp demarcation was found between the round and spindle celled zones: transitions existed everywhere between the two types of cell. Their nuclei also were of similar structure. In the round cells the nucleus also was round or, less commonly, lobed and had a delicate membrane and clear pale nucleoplasm traversed by an irregular net of chromatin. The chromatin content varied greatly: in some instances there were a few small nodes only, in many others the nodes were large and irregularly distributed. Many also were hyperchromatic. There were from one to three small nucleoli. The nuclei of the spindle cells were elongated but were in other respects similar.

No intra-cytoplasmic fibrils were demonstrated with phosphotungstic acid hæmatoxylin. There was, however, an abundance of fine elastic fibrils which were

FIG. 7. Case 3.—To show general character of tumour. (Hæmatoxylin and eosin: $\times 85$).

distributed between the spindle cells and formed a more feebly stained and often beaded intercellular net in many of the round-cell areas. With Laidlaw's method a great abundance of both fine and coarse reticulum fibrils was demonstrated. The distribution however was uneven: in the cellular peripheral zone the fibrils were scanty but they became increasingly abundant as the deeper parts were approached. They formed dense bundles in the spindle-cell areas and a pericellular net in many of the deep collections of round cells.

Irregularly shaped areas of degeneration and necrosis were present in the deeper parts. The blood vessels were sparse but are conspicuous by reason of their dilatation and engorgement.

All the metallic impregnation methods produced negative results.

COMMENT.—In this case the clinical history is again of relatively short duration though the contrast of the clinical picture with that seen in older

subjects is less striking than in Case 2. Vomiting occurred for the first time three months before death, and papilloedema was present when the child was admitted to hospital. Whereas in Cases 1 and 2 the tumour had caused a considerable degree of internal hydrocephalus, in this case there was no hydrocephalus because the tumour had not interfered with the flow of cerebrospinal fluid from the ventricles. The increase in the size of the head which occurred is to be attributed to pressure from the growth of the tumour.

Microscopically the tumour appears to be a fibrosarcoma. The naked eye appearances suggested that it might be a teratoma, but this diagnosis was not supported by the histological examination. The spindle cells in the tumour are clearly fibroblasts. They have produced an abundance of collagen, reticulum and elastic fibrils. That the round cells are of a similar nature appears certain because there are transitions between them and the spindle cells, their nuclei are of similar character and they also are frequently separated by delicate elastic and reticulum fibrils. The tissue of origin is either the cerebral leptomeninges or the pial investment of a perforating vessel. The tumour in general bears little resemblance to the meningiomata that arise from the dura mater in later life. There is, however, a conspicuous tendency for the round cells to be arranged concentrically around vessels. A further point of resemblance lies in the production of elastic fibrils. Mallory⁸ found great variations in the amount of elastic produced in the dural endothelioma or, as he called it, the arachnoid fibroblastoma. He observed that in some it 'occurs as a fine to coarse reticulum which is distributed fairly evenly everywhere between the cells,' and also that 'the stain of the fibrils varies. It is intense in those which are fully developed but grades downwards to almost nothing in those which are newly formed. This variation of intensity of stain and character and distribution of the fibrils indicates that they are the product of the tumour cells.'

Discussion.

The cases here reported clearly show that progressive expansion of the skull in a young infant may in rare instances be caused by a large circumscribed tumour of the cerebrum. Such a tumour may be a glioma (Case 1), or a sarcoma (Cases 2 and 3). Teratomata may also occur in a similar situation and produce similar results⁵. The macroscopic features of such tumours suggest that early recognition of the condition followed by radical surgical treatment might be of benefit to the patient. Unfortunately the readiness with which the expansile skull of the infant compensates for raised intracranial pressure may result in the condition being far advanced before the patient comes under medical observation. Moreover, the impossibility of making a full neurological examination in young infants increases the difficulty of reaching an accurate diagnosis.

The histological problems raised by these cases have already received comment. In Case 1 the tumour is a glioma and has been called a polar spongioblastoma. Although it appears to be recognized⁷ that gliomata may

occur in the new born, we have no personal knowledge of any detailed description of such a tumour. That reported here is the sole example of its kind in a series of 358 intracranial gliomata examined in this laboratory. The incidence and topography of gliomata in the early years of life has been described by Cushing⁴. It is generally agreed that they are commoner below the tentorium than above in children under 15 years. Our own figures agree fairly well with those of Cushing. Thus 55 of our total of 358 gliomata were in subjects of 15 years or under. Of these 12 only were situated in the cerebral hemispheres. The distribution in the different age groups is as follows: below 1 year, 1 cerebral (Case 1) and 2 subtentorial; 1-5 years, 1 cerebral and 8 subtentorial; 5-10 years, 4 cerebral and 19 subtentorial; 10-15 years, 6 cerebral and 12 subtentorial. In two cases, omitted from this analysis, there was a diffuse gliomatosis of the leptomeninges without any demonstrable primary tumour.

The tumours in Cases 2 and 3 are not gliomatous: they probably have arisen from the pia and are sarcomatous. In Case 3 there is more certainty in reaching this conclusion than in Case 2: fibroblasts undoubtedly are the type cell of the tumour in Case 3. In the tumour of Case 2 the cells are endothelioid rather than fibroblastic in character. But as the primary tumours of the dura mater in older subjects show even greater divergence in histological structure, it cannot be considered that the dissimilarity of the tumours in Cases 2 and 3 in any way invalidates our conclusions concerning their nature.

The occurrence of these circumscribed sarcomata of the brain has already been demonstrated by Bailey¹. In certain of his cases, however, the possibility that the intracranial tumour was metastatic could not be dismissed because the necropsy was limited to an examination of the head. In our two cases this possibility can be dismissed. This kind of tumour has also been commented upon recently by Cushing⁵. He reaffirms that, apart from a true diffuse sarcomatosis of the meninges in childhood, there are also circumscribed enucleable tumours that should be regarded as sarcomatous. It is remarkable, however, that these tumours can be removed without subsequent recurrence of the growth, a circumstance that belies their malignant histological appearance. Undoubtedly, as Cushing observes, this kind of tumour deserves further study.

Summary.

1. Three circumscribed tumours of the cerebrum occurring in early infancy are reported from both clinical and pathological aspects.
2. Attention is drawn to the modification of the clinical picture which may occur from the readiness with which the skull expands at this period when the intracranial pressure is raised. In general, the clinical history tends to be of short duration and deterioration is rapid after the infant first comes under observation.

3. The tumour in the still-born infant in Case 1 is a glioma: a polar spongioblastoma. In Cases 2 and 3 the tumours are both regarded as sarcomata of pial origin. This diagnosis appears certain in Case 3, but is tentative in Case 2.

It is a pleasure to thank Doctors Russell Andrews, Maitland-Jones and Frew for permission to use the clinical notes of the cases under their care. We also thank Professor H. M. Turnbull and Mr. Hugh Cairns for their help and criticism in the preparation of this paper.

REFERENCES.

1. Bailey, P., Arch. Surg., Chicago, 1929, XVIII, 1359.
2. Bailey, P., & Eisenhardt, L., *J. Comp. Neur.*, Philade., 1932, LVI, 391.
3. Cairns, H., & Russell, D. S., *Brain*, Lond., 1931, LIV, 377.
4. Cushing, H., *Am. J. Dis. Child.*, Chicago, 1927, XXXIII, 551.
5. Cushing, H., *Intracranial Tumours*, Baltimore, 1932.
6. Fincher, E. J., *Am. J. Cancer*, 1932, XVI, 918.
7. Kaufmann, E., *Lehrb. d. speziellen Path. Anat.*, 6th Edition, Berlin, 1911, 1168.
8. Mallory, F. B., *J. Med. Res.*, Boston, 1920, XLI, 349.
9. Penfield, W., *Nelson's Loose-leaf Surgery*, N.Y., 1932, II, 327.