UNUSUAL SIZE OF INTRAVENTRICULAR SPONGIOBLASTOMA IN A CASE OF TUBEROUS SCLEROSIS *

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DURING recent years the main interest in tuberous sclerosis, apart from its ætiology, has been concentrated upon the tumour formation associated with it. The following case is considered noteworthy because of the exceptionally large size of the intraventricular tumour and the complete absence of physical signs until a few hours before death.

PERSONAL CASE

The patient was admitted to the Fountain Hospital for mental defectives on September 6, 1933, at the age of seven years and three months.

History.—She was the only child of Hebrew-Polish parents. Her father was dead of diabetes and her mother, an emotional woman who could speak little English, was 27 at the time of conception. No other members of the family appear to have been subjects of tuberous sclerosis or allied conditions. No definite evidence of psychopathic taint could be discovered in the family.

Gestation and labour were normal. Backwardness was noted during the first year and all 'landmarks' were reached late. The child's mother stated that she was mischievous, destructive to clothes and toys, and cruel to children and animals.

State on Admission.—She was slightly above average height and was adequately nourished. She showed no stigmata of degeneration. Adenoma sebaceum of cheeks and chin was present. The papules were multiple, small, and highly coloured (Pringle's type). There were no fibromata or pigmentary abnormalities on other parts of the body. No central nervous system lesions were discovered; tendon reflexes were normal and equal and there was no spasticity, incoordination or disorder of gait or speech. Pupils reacted normally to light and on accommodation; fundi and discs were normal and there were no signs whatever of raised intracranial pressure. Accurate investigation of the sensory system was precluded by the patient's mental state, but there were no gross lesions. Other systems were normal, except for a sluggish circulation and a tendency to chilblains. Serum Wassermann and Meinicke macro clarification reactions were negative.

Mental State.—The patient was of imbecile grade, her mental age being three, and her intelligence quotient 40. She was scarcely able to sustain the simplest conversation, but could understand easy questions, point to her features, name common objects and count up to four. She showed a tendency to echolalia. Usually she was bright, active and interested in her neighbours and her surroundings. Her disposition was more tractable than is usually found in these cases and there was present none of the characteristic restlessness and resistiveness to attention. She was clean in her habits and able to feed herself. She was subject, however, to occasional 'bad days,' during

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which she was wont to scream for no apparent cause, to be spiteful to other children, to fret and cry to go home and to complain quite untruthfully of ill-treatment at the hands of fellow patients. On these occasions she was tremulous and even mildly ataxic, but showed no other signs of central nervous system lesion.

Her mother's history rather emphasized the spitefulness and troublesome nature of the child, and it appears that her 'bad days' were rather more frequent before admission.

It is common to find periodic alternations of resistiveness and irritability with relative amenability in these cases, but rather unusual for these changes to be regularly of such short duration as a day or so. The cycles are more apt to be measured in months or even years. The 'bad days' of this patient were possibly in the nature of epileptic equivalents.

Fits.—There was a history of infantile convulsions, but no fits occurred between infancy and her terminal attack.

Final Illness.—There was no change in her condition up to the day of her death. After tea she vomited and complained of headache. One and a half hours later she rapidly became comatose and at 7 p.m. was deeply unconscious. Breathing was slow and deep, corneal reflexes were absent and pupils were dilated and fixed. The trunk and legs were held rigidly in a position of extreme extension, while the arms were semiflexed and pronated. Slow athetoid movements, mainly involving the right arm, took place every few minutes. No reflexes could be elicited owing to the extreme rigidity. Papilloedema was absent. At 9 o'clock she became flaccid and moribund and death took place half an hour later.

The decerebrate nature of the attack clearly pointed to an infracortical origin, the lateral ventricle being the most probable site of the lesion.

PATHOLOGICAL EXAMINATION

Kidneys.—Each kidney weighed $2\frac{1}{2}$ oz. Multiple small white tumours were scattered throughout the cortex and at the periphery of both organs and in addition there were several small cysts, filled with clear fluid. The capsules stripped easily and there were no other macroscopic abnormalities. Sections were kindly examined by Dr. R. J. V. Pulvertaft, who reports that the kidneys showed a fair number of small cysts, indicating a mild degree of congenital polycystic kidney. In addition there were a number of areas in the renal cortex which closely resembled normal fat in paraffin sections and stained with Sudan III in frozen sections. They did not show any rotation with polarized light. There would appear to be no doubt that the condition was one of multiple true lipomata. Although pure lipomata of the kidney are an uncommon type of tumour in association with tuberous sclerosis, their occurrence has been noted previously (F. Schob¹⁴).

Liver.—A considerable degree of venous congestion and cloudy swelling was present.

Lungs.—There was terminal congestion at both bases.

The heart, spleen, pancreas, thyroid, pituitary and suprarenals were normal both to naked eye and on microscopical examination.

FIG. 1A.—Right hemisphere.

FIG. 1B.—Left hemisphere.

Brain.—*Macroscopical.*—Weight of whole brain, 1,135 gm. ; cerebellum, 110 gm.

The cranium showed a generalized thinning of the vertex, such as might be associated with a mild degree of hydrocephaly. The membranes showed no abnormality and the pia-arachnoid stripped easily. There was no flattening or dryness of the cerebral hemispheres, or other sign of raised intracranial pressure.

The sclerotic nodules showed up strikingly as smooth, non-umbilicated, pale areas, not appreciably raised above the surface of the surrounding cortex,

FIG. 2.—Tumour in situ. Margin has been outlined.

but distinctly harder on palpation. They were abundant in number, scattered throughout both hemispheres and varying in diameter from $\frac{1}{2}$ to $9\frac{1}{2}$ cm. (figs. 1A and 1B). It will be seen that they are extremely irregular in shape and size and that their boundaries do not conform to those of the gyri.

On separation of the hemispheres a large tumour was seen to be occupying almost the whole of both lateral ventricles, which were very much dilated. In addition to the tumour a considerable amount of blood-stained fluid filled the ventricles. The corpus callosum was reduced to a thin strip, in parts no more than 1 mm. in thickness, and the fornices and septum pellucidum were completely obliterated. The wall of the left lateral ventricle was covered

with typical 'candle-guttering' tumours (fig. 2) and the ependyma on both sides showed gross thickening of granular type.

The remainder of the brain and the retinae presented no macroscopic abnormalities.

Tumour.—Weight, 103 gm.; length, 9 cm.; breadth, 6.9 cm.; depth, 4.9 cm.; cubic capacity, 115 c.cm.

The tumour was lying almost completely free in the ventricular cavity, only a small pedicle attaching it to the ependyma of the right lateral ventricle

FIG. 3.—Tumour viewed from below, showing hæmorrhagic area in right anterior quadrant. (A) Point of attachment in right lateral ventricle.

in the striothalamic region. Of rather soft consistency and irregular shape, its surface was roughened and there was evidence of a recent hæmorrhage at the anterior pole, mainly on its right inferior aspect (fig. 3).

Microscopical.—The histological examination of the brain was of necessity confined to one of the macroscopically typical plaques of the cortex, one 'candle-guttering' and the tumour itself. In the sclerotic plaque were to be seen both glial and ganglionic giant-cells lying either singly or in nests. They were not confined to the cortex, but also formed heterotopic areas in the underlying white matter. The ganglion-cells, even when of normal size, often presented unusual shapes and were to be found quite commonly in the most superficial layer of the cortex. Their orientation within the cortex was

markedly disturbed, many of them lying with their apices directed horizontally or downwards. Diffuse demyelination and fibrous glial proliferation were present throughout the plaque, the latter appearing at the surface as the peculiar and typical 'ruffled-hair' formation.

All these features have been described previously and need no special discussion. It is only necessary to add that in the neighbourhood of the plaques a spongiöse state of the cortex, as described by Bielschowsky² and Schob,¹⁴ could be detected.

A piece of the atrophied corpus callosum showed patchy demyelination and corresponding gliosis.

The 'candle-guttering' presented a typical microscopical picture,

FIG. 4.—Tumour. Note the whorl-like appearance and the nests of giant-cells. Hæmatoxylin-eosin. $\times 90$.

giant-cells and spindle-shaped spongioblasts arranged in strands being a prominent feature. In addition there was a very heavy glial fibrosis. Numerous calcified vessels and free-lying calcified bodies were present, some of the latter showing a stratification not unlike that of amyloid bodies, but giving a negative Lugol reaction.

Tumour.—In contrast with the 'candle-gutterings' the large tumour possessed no definite capsule of connective tissue, glia or ependyma, nor did it show any evidence of calcification. The main feature was the general whorl-like arrangement of the cells (fig. 4). On closer examination these whorls could be defined as strands of uni- and bipolar spindle-shaped spongioblasts, mixed with nests of giant-cells (fig. 5). These giant-cells, which are probably of glial origin, were frequently pear-shaped, although many other shapes were also encountered. The nucleus lay centrally in some cells,

excentrically in others. There also appeared many multinucleate forms of extraordinary size, resembling on account of their homogeneous protoplasm the so-called 'plump' cells. No cells approximating to the neuron type could be discovered and no axis-cylinders appeared in the Bielschowsky-stained sections. Fibrous gliosis was generally of slight degree, only in local areas presenting an outstanding feature. In some parts there was a noteworthy proliferation of thin-walled capillaries, a lesion of which doubtless caused the fatal hæmorrhage.

FIG. 5.—Tumour, showing strands of spongioblasts and pear-shaped giant-cells. Yaburek's silver method. $\times 550$.

DISCUSSION

Tumours of a gliomatous nature accompanying tuberous sclerosis of the brain have been observed by many authors (Schuster,¹⁵ Bielschowsky,² Brushfield and Wyatt,⁴ Berliner, Creutzfeldt,⁵ von Meduna,¹³ Globus, Strauss and Selinsky,⁹ etc.). Recently this coincidence has given rise to the view that there exists a close genotypic relationship between paraventricular spongioblastoma multiforme and tuberous sclerosis. In this regard the investigations of Creutzfeldt,⁵ Bender and Panse,¹ van Bogaert,³ Kufs,¹² Bielschowsky² and Globus, Strauss and Selinsky⁹ are of great importance. They showed that not only in the actual patients affected with spongioblastoma of the brain, but also in other members of their families, more or less well-marked cerebral or extracerebral symptoms of tuberous sclerosis may occur. Accordingly

Bielschowsky comprehends both processes as a foetal spongioblastosis, a term which is extended by Globus, Strauss and Selinsky to 'neurospongioblastosis' on account of the presence of neuronie structures in the spongioblastomas of their cases.

Our own case contributes to this theory inasmuch as the tumour was of the nature of a typical spongioblastoma, and at the same time nearly all the cerebral and extracerebral characteristics of tuberous sclerosis were present, although they did not occur in other members of the family. The collection of such cases is still of importance, as by no means all those on record provide sufficiently clear evidence of the characteristics of both conditions (Kufs¹²). Furthermore, the spongioblastoma of our case is remarkable because of its extraordinary size and its peculiar growth, developing as it did from a very small basis in the striothalamic region into the lateral ventricle, where it was found as a free-lying mass. As regards the findings of Globus, Strauss and Selinsky we failed to discover any neuronie structures within the neoplasm. Moreover, there was no sign of calcification, typical of the 'candle-gutterings,' or of an ependymal covering.

In connexion with so large a tumour the absence of either focal or general signs of raised intracranial pressure until four hours before death must be almost unique; and even in the end the symptoms were not produced by the tumour itself, but by hæmorrhage into it. Globus, Strauss and Selinsky describe a sudden onset of tumour symptoms in the majority of their cases, but an examination of their case-histories reveals that signs attributable to the neoplasm were present for two months in the shortest instance, and varied in duration from this period up to five years. Furthermore, none of their tumours was comparable in size to that of the present case.

It is evident that a combination of three factors was instrumental in allowing the tumour to reach such a huge size unheralded. In the first place its position within the ventricle was, of all sites, the most favourable for growth to occur without involving adjacent tissue or producing pressure signs. Secondly, growth must have been extremely slow, probably extending over the greater part of the child's life; and lastly the condition arose at an age when the skull was most capable of expansion. In some respects the general condition of the cranium was not unlike that due to a mild degree of hydrocephaly. The circumference ($21\frac{3}{4}$ in.) was larger than the normal figure for the child's age ($20\frac{1}{2}$ in.), the vault was very thin, and its internal surface was uneven. The brain, however, showed no signs of excessive pressure and was not compressed against the skull-wall.

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