Case Reports

Cerebral and Cerebellar Gliomas in a Case of von Recklinghausen's Disease with Adrenal Phaeochromocytomas

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The simultaneous occurrence of gliomas in the cerebellum and cerebrum of the same individual is rare. Of the possible mechanisms responsible, that of multiple primary tumours arising independently has always failed to gain much support. Russell and Rubinstein* pointed out that this concept would be more acceptable if it were possible to demonstrate multifocal benign cerebral astrocytomas, but to their knowledge this had never been established; in the majority of cases reported the tumours were of so malignant a nature that the deposits could well be metastatic.

In the case we describe a diffuse astrocytic glioma of the cerebrum and mesencephalon was accompanied by nodules of glial tumour in each of the cerebellar hemispheres in a patient with cutaneous von Recklinghausen's disease and bilateral phaeochromocytomas of the adrenal medulla.

Case Report

50794, D.C., a 58-year-old white female, was referred for neurosurgical opinion to Mr. Valentine Logue at the Maida Vale Hospital for Nervous Diseases on May 3, 1962, from the Amersham General Hospital, where she had been admitted for the investigation of headaches, progressive dementia, and unsteadiness of gait which she had suffered for some 6 months. Lumbar puncture had yielded normal cerebrospinal fluid. On arrival at Maida Vale Hospital she volunteered no complaints but admitted on direct questioning to using words incorrectly, occasionally inventing neologisms, and impairment of memory for recent events. No family history of disease of the nervous system or skin could be obtained, but it was noted that one of her three children bore nodules on the skin of his face.

Examination. The patient was fully conscious and reasonably co-operative, but her intellectual impairment was such that only a very simple conversation was possible. She was disoriented in time and place and while there was some degree of expressive dysphasia, she could use her pen correctly (she was right-handed) and read letters and numerals.

The fundi were normal; there was bilateral ptosis and the pupils were dilated—the left larger than the right. Reaction to light was normal. There was marked impairment of voluntary gaze in all directions. There was no true nystagmus. The jaw jerk was exaggerated. A right-sided grasp reflex was present and a tetraparesis with spasticity more marked on the right and weakness more marked on the left side; the right plantar reflex was extensor, the left equivocal. Sensation to painful stimuli and sense of vibration were unimpaired, but other modalities could not be tested. Gait could not be examined. The heart, lungs and abdomen were normal. Blood pressure was 150/90. There were multiple café au lait spots and pedunculated nodules in the skin of limbs and trunk. A clinical diagnosis of midline glioma and von Recklinghausen's disease was made.

 Investigations. Haemoglobin was 12.3 gm. per cent (84 per cent). Count of white blood cells was 12,100 per c. mm. (differential: neutrophils 84 per cent, eosinophils 1 per cent, lymphocytes 12 per cent, monocytes 5.5 per cent, basophils 0.5 per cent) and a sedimentation rate of 5 mm. per hour (Westergren). Wassermann reaction was negative. Electroencephalography showed an abnormal record reported as "suspicious of an anteriorly placed midline lesion" (Dr. M. Painter). Roentgenograms of chest and skull were normal. Bilateral carotid angiography (May 8, 1962) suggested considerable ventricular dilatation. Ventriculography (May 9) confirmed the hydrocephalus and showed narrowing of the back of the 3rd ventricle from side to side. Air would not pass through the aqueduct. Myodil ventriculography showed that the aqueduct was narrow and irregular. The report (Dr. G. H. du Boulay) concluded that the appearance of the aqueduct could be explained only on the basis of an infiltrating brain-stem lesion or congenital narrowing, and the narrow back of the 3rd ventricle would be consistent with an infiltrating lesion. Protein in the ventricular fluid was less than 10 mg. per cent.

Course. During the week following admission the patient's condition deteriorated. On May 9 Mr. Logue considered that the radiographic findings were most probably caused by a brain-stem glioma but a midline meningioma of the clivus or bilateral acoustic neurinomas were possibilities that had to be excluded. However, the latter was an unlikely diagnosis in view of the normal amount of protein in the cerebrospinal fluid and the absence of symptoms of the 8th nerve.

Operation. It was decided as a last resort to explore the lesion and, if inoperable, ventricular drainage of the hydrocephalus would be instituted. The same afternoon exploration was made through a posterior temporoparietal flap. The temporal lobe was elevated, the tentorium was incised and no lesion of the cranial nerves or clivus was found. The pons appeared swollen. It was felt that no surgically treatable lesion was present and closure was made. The ventricles were drained.

The patient expired on the night of the operation.

Necropsy was performed within 24 hours of death. The external appearances were typical of von Recklinghausen’s disease with many café au lait spots (largest 7
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mm. in diameter) and approximately 50 soft pedunculated tumours of the skin (largest 3 cm. in diameter); the majority of these lesions were on the front of the chest and abdomen. No relevant changes were found in any of the viscera except the adrenal glands. These were enlarged (right weighed 75 gm. and left 25 gm.) by the presence of tumours of similar appearance (Fig. 1). In each of the glands the adrenal cortex and medulla were normal up to the point at which the cortex was stretched over the tumour, forming most of the intact capsule investing the growth. The cut surface of each tumour was terra-cotta brown streaked with dark areas of haemorrhage (the right was 5 cm. in diameter, the left 3 cm.). When placed in 10 per cent formalin, the brown colour of the tumour diffused at once into the fixative.

Both hemispheres of the brain (total weight 1425 gm.) were swollen and there was a moderate degree of herniation of the cerebellar tonsils; the uncus was grooved on both sides. No tumours were present on nerve roots. On the under surface of the left cerebellar hemisphere there was a hard, very pale grey nodule 7 mm. across, whose centre was 10 mm. lateral to the midline. On the under surface of the right cerebellar hemisphere there was a similar nodule 5 mm. across, 20 mm. from the midline. The spinal cord and nerve roots were examined and removed via the anterior approach; no abnormality was seen. After fixation in formalin the brain was sliced in the coronal plane; in the anterior slices there was oedema of both hemispheres, but more in the left than in the right and the septum pellucidum was shifted across the midline towards the right side. There was diffuse, pale grey, glial hypertrophy or tumour involving the thalamus on both sides, which extended to the subthalamic nuclei (Fig. 2). The head of the right caudate nucleus was replaced by a gelatinous glial mass about 8 mm. in diameter. The exact confines of the process could not be determined. The mid-brain was swollen from infiltration by pale grey firm tissue that was especially obvious around the narrow aqueduct; this did not appear to extend below the level of the mid-pons.

Histology. Microscopical preparations of several levels of spinal cord, nerve roots, posterior root ganglia and various viscera show no relevant changes. The tumours of the skin are typical neurofibromas with elongated cells containing slender nuclei distributed through a faintly collagenous matrix. The adrenal tumours are composed of solid cords of large polygonal cells, often with a bulky cytoplasm filled with granules staining brown in haematoxylin and eosin preparations after formalin-chromate fixation and blue by Gomori's method. Fine strands of connective tissue separate groups of neoplastic cells. A few multinucleated giant cells are present but cells in mitosis are very rare. The tumours show all the characteristics of pheochromocytomas and no features that suggest malignancy.

The cerebral tumour is a diffuse astrocytic glioma (Fig. 3). The neoplastic cells have small oval or rounded vesicular nuclei and, for the most part, the body of the cell is indistinguishable. A few cells, however, are typical "gemistocytes" and rarely are there multinucleated cells. Some fine short glial fibres accompany the neoplastic cells, but the over-all picture is of paucity of glial

Fig. 1. Phaeochromocytoma of the right adrenal gland.

Fig. 2. Coronal section of cerebrum showing diffuse enlargement of both thalami by a glial tumour. The head of the right caudate nucleus is replaced by a glistening nodule.