NEUROBLASTOMA*

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A SURVEY of the literature reveals that about five hundred cases of neuroblastoma have been recorded (Pack, Horning, and Ariel, 1952; Ingalls, 1953; Phillips, 1953).

The commonest site of origin is the suprarenal region, followed by the retroperitoneal area; occasionally other abdominal sites and the mediastinum are incriminated, and many cases do not allow of an anatomical diagnosis of origin (Phillips, 1953). Of all the cases described by these authors only five of 81 reported by Phillips are recorded as arising primarily in the orbit. Phillips remarks that clinical evidence of an orbital primary may be very misleading. No mention of a *post-mortem* examination is made, and it is presumed that a clinical diagnosis alone is offered. Authors who identify retinoblastoma with neuroblastoma and so claim orbital primaries in their cases, have been ignored in this review. The case now reported thus has unusual interest.

Case Report

A boy aged 3 years and 3 months was admitted on October 11, 1955; 4 months previously he had bumped the right side of his forehead, and a month later had been found to have a severe nasal infection (with discharge of mucopus from the right nostril) associated with severe right frontal headache. These symptoms were immediately followed by an acute proptosis of the right eye. His family doctor treated him with two short courses of oral chloramphenicol, which resulted in remission of his condition. In mid-August the right proptosis recurred and on September 30, 1955, a diffuse swelling was noted in the right temporal fossa. An x-ray report accompanied the child when he was referred for a further opinion and treatment; this indicated there to be decalcification or erosion of the sphenoidal ridge. The mother, who appeared to be an accurate witness, stated that the boy had had an extensive birthmark across his chest and on his right upper lid and that these had regressed until all that remained was a faint stain on the right shoulder.

Examination.—He was a well-nourished child. Apart from the skull, orbital, and shoulder lesions no abnormality was discovered. A gross, irreducible, non-tender proptosis with infero-temporal displacement of the right eye was obvious (Fig. 1, opposite).

The tip of a cyst-like mass was palpable through the upper lid under the superior orbital margin and was easily displaced back into the orbit. No bruit was heard, although breath sounds were exaggerated over the right frontal bone. An indefinite soft swelling was discernible in the right temporal fossa, but no fluctuation could be transmitted hence to the orbital mass. Ocular movements were not at all restricted. Slight oedema of the

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FIG. 1.—Proptosis of right eye. The diffuse swelling in the temporal fossa is just discernible in this photograph. The recent wound on the upper lid is the site of the biopsy.

lids was present, but there were no ecchymoses and the eye was white. Corneal sensation was diminished and there was some degree of papilloedema. All other ocular findings were normal, as were the blood reports.

Diagnosis.—Probably sarcoma of the orbit.

Radiologist's Report (Dr. M. Lederman; October 24, 1955).—Definite areas of bony destruction of the right orbit which is larger than the left—suggestive of neoplasm.

Biopsy (October 27, 1955).—At operation a large, smooth-walled cystic mass, bluish in colour, with a tough outer coat, was found in the superolateral region of the right orbit, disappearing back into the depths. The cyst contained a little bloodstained fluid.

Biopsy (November 3, 1955).—Section shows two small pieces of fibrous tissue invaded by masses of round cells, with hyperchromatic nuclei arranged in dense clumps containing small aggregations of cells; one or two of these resemble rosettes. The histological picture suggests a round cell sarcoma, leukaemic deposit or neuroblastomatous and the latter seems the most likely.

High-Voltage Therapy (November 8 and 16, 1955).—3120r, KV 220, was given to the anterior and lateral aspects of the right orbit.

Radiological Examination.—Chest and intravenous pyelograms showed nothing abnormal.

Progress.—Although the child was pale and tired by this time, his condition remained fairly good. Proptosis now was 3 to 5 mm. On January 13, 1956, his general condition had deteriorated and a spinal lesion was suspected. Radiography showed collapse of the dorsal and lumbar vertebrae. High voltage therapy (1100r and 600r) was given to the dorsal and lumbar spine over 16 days. On January 21, 1956, deterioration of his general condition continued and a blood transfusion was given.

By March 9, 1956, he was very wasted and anaemic. No proptosis remained nor any temporal fossa swelling; the eye was white and the fundus normal; ocular movements were in no way restricted. There was no paraplegia but he had considerable pain in his limbs. Sphincter control was unimpaired.

The child died on April 10, 1956.

Post-mortem Report (Dr. D. A. L. Bowen).—The orbital plate of the right frontal bone appeared normal, but posteriorly the greater wing of the sphenoid and the adjacent

pituitary fossa were reddish in colour and softer than normal. This extended to the margin of the temporal bone laterally and to the cavernous sinus medially. On removal of the orbital plate of the frontal bone, a soft oedematous mass of brownish tissue was seen (Fig. 2) which lay above and could not be separated from the superior rectus muscle. It also lay above and to the right of the optic nerve. This mass was thought to be the primary tumour. There was no attachment to the optic nerve itself and the nerve was cut across at the entry to the globe. The brain and spinal cord showed no abnormality.

FIG. 2.—*Post-mortem* photograph showing the soft tumour mass exposed by removal of the superior orbital plate, sphenoidal ridge, and lateral wall of the pituitary fossa, in the basal aspect of the skull, viewed from above.

No tumour was seen in the region of the cervical sympathetic ganglia. The lungs manifested some reddish areas but were otherwise normal.

The peritoneal cavity and the entire gastro-intestinal tract were normal, as were the liver, spleen, gallbladder, and their surrounding areas. No evidence of tumour was found in the adrenals, and the coeliac plexus and the sites of the other abdominal ganglia appeared normal. The mediastinal and abdominal lymph nodes and surrounding areas were normal.

The T.12, L.1, and L.3 vertebrae were collapsed, abnormally red in colour, and softer than the surrounding vertebrae.

FIG. 3.—Photomicrograph ($\times 200$) of section of lumbar vertebra showing replacement of bone by tumour cells in an area of intense infiltration. A few rosettes are to be seen.

Histology.—Tumour tissue was present in the lungs, spleen, liver, pituitary fossa, sphenoid bone, and vertebrae (Fig. 3). The individual cells were small, resembling lymphocytes in appearance, with very scanty eosinophilic cytoplasm, almost the entire cell being occupied by a darkly-staining spherical nucleus having a tendency to be irregular in shape and size. In one vertebral metastasis many cells showed a tendency to form rosettes. One definite rosette was identified (Fig. 4, overleaf), confirming the diagnosis of neuroblastoma. Sections from each lobe of the lungs showed alveoli outlined by tumour cells lying in the alveolar capillaries. In the liver, columns of neuroblastoma cells were present between the liver cells. The splenic pulp contained similar cells. The retro-orbital mass was composed of rather acellular fibrous tissue, showing numbers of pigment-containing macrophages, but no tumour. Both suprarenal glands and coeliac ganglia were normal.

Cause of Death.—Orbital neuroblastoma with spread to sphenoid bone and pituitary fossa, and metastasis in lungs, liver, spleen, and vertebrae.

Discussion

The history and necropsy findings suggest that this neuroblastoma arose in a retro-orbital ganglion. After radiotherapy the orbital portion was

FIG. 4.—Photomicrograph ($\times 680$), higher magnification of Fig. 3, a rosette excellently demonstrated (centre).

destroyed, but haematogenous dissemination had occurred, causing heavy deposits in the liver, lungs, and vertebrae. Despite careful search, no evidence was found of any tumour arising in other possible sites in the thoracic or abdominal ganglia.

An extremely difficult exercise in diagnosis was offered by this case, because of the history of the commencing infection, which followed on trauma, regressing angiomatous skin lesions involving the eye affected, and an orbital lesion with no ecchymosis or limitation of movement and with no other discoverable lesions. On reflection, one investigation might have helped in the early stages, *viz.* a sternal marrow puncture to reveal haematogenous spread of the tumour.

Summary

The first case of neuroblastoma arising primarily in the orbit, with a clinical report and necropsy findings, is recorded.

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