

MALIGNANT NON-CHROMAFFIN PARAGANGLIOMA IN THE ORBIT*

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THE following case is presented as a probable example of malignant non-chromaffin paraganglioma arising in the orbit. Not unnaturally there has been some hesitation in making this diagnosis since no paraganglionic or chemoreceptor tissue has previously been described in the human orbit, although such tissue is apparently present in the vicinity of the ciliary ganglion within the orbital muscle cone in chimpanzees (Botár and Pribék, 1935) and is reported to occur in association with the ciliary ganglion in monkeys (Paraganglion ciliare of Gosses).

Fisher and Hazard (1952) recorded a non-chromaffin paraganglioma in the left orbit of a 50-year-old white woman with proptosis of insidious onset and slow progression for 1 year. Paralysis of the superior and inferior recti muscles was present together with slight oedema of the retina and blurring of the nasal margin of the disc. Frontal craniotomy revealed a firm, ovoid tumour measuring $4 \times 3 \times 3$ cm. in the upper lateral portion of the orbit, and the tumour, which incorporated the superior rectus muscle into its substance, was completely removed by blunt dissection. Hazard (1962) has informed us that this patient was alive and without evidence of recurrence of the neoplasm 6 years after operation. Microscopically, the growth consisted of epithelial-like cells in sheets and rounded groups separated by small capillaries and larger endothelium-lined blood channels. The epithelial-like cells exhibited vesicular nuclei and their cytoplasm contained eosinophilic granules. Wilder's reticulin stain revealed delicate fibres around the vessels and embracing the groups of tumour cells. Schmorl's chromaffin stain on formalin-fixed tissue was negative. The histological appearance of this tumour was identical with that of non-chromaffin paragangliomata arising in other locations, *e.g.* the jugular body. The authors serially sectioned the retrobulbar tissue from three eyes in an unsuccessful attempt to find orbital paraganglionic tissue. They believed that theirs was the first report of such a neoplasm in the orbit, but they mentioned an illustration by Wolff (1944) labelled "angioma of the orbit", which somewhat resembled a non-chromaffin paraganglioma in appearance.

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Little attention has been given to a report by Hughes and Ambrose (1944) of an "adrenal rest tumour" in the orbit of a 21-year-old woman which caused gradually-increasing proptosis over a period of 2 years. At operation, an olive-shaped, fixed mass measuring 2.5×2.5 cm, was removed from a position behind and slightly above the globe. Sections showed an encapsulated, histologically benign neoplasm composed of cells resembling liver cells or cells from the fasciculated zone of the adrenal cortex, arranged in cords. There were also many areas of small round cells. While accessory adrenal cortical tissue is well known to occur in and about the kidneys and in many sites within the abdominal and pelvic cavities, it would seem difficult to account for its presence in the orbit. In the light of more recent knowledge of the widespread distribution of paraganglionic tissue in the body, it would not strain credulity too far to suppose that this "adrenal rest tumour" was, in fact, a non-chromaffin paraganglioma arising in the orbit.

An additional case of orbital non-chromaffin paraganglioma has recently been seen in Adelaide, Australia. The patient was a 4-year-old boy with a slowly enlarging, ovoid, encapsulated tumour which appeared to originate in the lateral rectus muscle (Tye, 1961).

Case Report

A man aged 38 years, admitted to the Ram Lal Eye and E.N.T. Hospital, Amritsar, on April 7, 1958, had developed redness and watering from the right eye 5 months previously. This was accompanied by diminution of vision and prominence of the right eyeball. He used some drops but the trouble went on increasing until he came under our observation.

Nothing relevant found in his personal, past, and family history.

Examination.—The eyeball was proptosed and pushed inwards. Outward movements were moderately restricted. In the inter-palpebral area the conjunctival vessels were prominent and tortuous. There was no diplopia. The visual acuity was reduced to 6/36. Fundus examination revealed no abnormality.

Operation.—On April, 29 1958, a lateral orbitotomy was done and the tumour was removed and sent for histopathological examination.

A report by Arthur Purdy Stout, received through the Pathology Department, Medical College, Amritsar, mentioned the possibility of non-chromaffin paraganglioma of the ciliary ganglion and organoid granular cell myoblastoma of malignant type.

Progress.—The redness and prominence of the right eyeball disappeared, the visual acuity improved to normal and the patient was discharged from the hospital.

Just under 1 year later he reported again with the right eyeball proptosed and turned in.

Examination.—There was proptosis of the right eye, lateral rectus paralysis with marked inturning of the eyeball, and puffiness of eyelids, but no tumour was detected. There was no diplopia and the visual acuity was 6/6.

Operation.—On March 18, 1959, he was operated on to correct the squint, as a result of which his eye became straight but remained prominent.

Progress.—3 months later, he felt intermittent pain behind the right eyeball, and the visual acuity was markedly reduced, and he was admitted for the third time on August 3, 1959.

Examination.—The orbital margins were normal, the interpalpebral fissure was markedly widened, and the eyeball was proptosed (Fig. 1.) The skin of the lids was stretched. There was no congestion or rise in temperature. The conjunctiva over the growth was moderately congested with prominent blood vessels. In the inter-palpebral area the growth was ulcerated and encrusted and could be palpated all round the eyeball. It was firm, tender and did not bleed on touch. The cornea was slightly hazy. The pupil was dilated and non-reactive to light. The iris pattern was normal. The fundus could not be seen because of the hazy cornea. The visual acuity was reduced to perception and projection of light. The intra-ocular pressure was 50 mm. Hg (Schiötz).

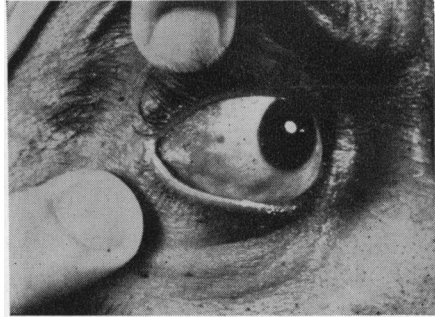


FIG. 1.—Proptosis and congestion in interpalpebral area.

Laboratory Investigations.—Orbital x-rays showed no abnormality. Total leucocyte count, 7,000/cu. mm.; polymorphs, 65 per cent.; lymphocytes, 34 per cent.; bleeding time, 2 min.; coagulation time, 3 min.

Exenteration was done and a piece of the growth was sent to Mr. C. H. Greer at the Royal Victorian Eye and Ear Hospital, Melbourne, Australia, who suggested a diagnosis of secondary hypernephroma. One month after the exenteration radium was applied.

In view of the pathological report, the patient was sent to the Department of Surgery, V. J. Hospital, Amritsar, for examination of the kidneys so as to find the primary growth but after a plain x ray of the abdomen, intravenous pyelography, retro-peritoneal insufflation, and intravenous pyelography with retro-peritoneal insufflation, the surgeon reported that there was no hypernephroma or any evidence of growth in the retro-peritoneal region.

Progress.—On February 1, 1960, the patient again reported to the hospital complaining of pain in the right orbit and forehead.

Examination.—There was a tender, firm, and almond-sized nodule in the right lower lid. The skin over it was healthy and mobile but the nodule was adherent to the surrounding structures. The temperature was normal. This tumour was removed and specimens were sent to the Department of Pathology, Medical College, Amritsar, the Department of Pathology and Bacteriology, M.U. Institute of Ophthalmology, Aligarh, India, and the Department of Pathology, Royal Victorian Eye and Ear Hospital, Melbourne, Australia.

Result.—During his last stay in the hospital, the patient became very weak and cachectic. He was given blood transfusions and a high protein diet which he refused and lost weight. On March, 24, 1960, he left the hospital against medical advice.

Three attempts were made to contact him but no reply was received, and we presume that he has since died.

Pathology

The following reports were received:

- (1) Medical College, Amritsar—Malignant paraganglioma deposits.

(2) Department of Pathology and Bacteriology, M.U. Institute of Ophthalmology, Aligarh—Rhabdomyosarcoma.

(3) Royal Victorian Eye and Ear Hospital, Melbourne, Australia—Malignant non-chromaffin paraganglioma. (Detailed report by C. H. Greer):

The first specimen, received in 10 per cent. formalin on October 9, 1959, measured 3×1.5 cm. and was pink, firm, and lobulated. It was embedded in paraffin wax and sections were stained with haematoxylin and eosin, phosphotungstic acid-haematoxylin, Masson's trichrome stain, and Gordon and Sweet's reticulin stain. Glycogen staining by Best's carmine technique showed fine purplish granules in a scattered minority of the cells while Gomori's stain for chromaffin substance was negative. Sections (Fig. 2) showed a neoplasm composed of large polygonal and cuboidal cells arranged in cords and variable sized groups, which were supported and enclosed by a fine collagenous and reticulin network carrying capillaries (Fig. 3, opposite). The cell groups were further intersected by larger endothelial-lined blood channels. The cell cytoplasm, which often exhibited a distinct boundary line, was finely vacuolated or contained fine eosinophilic granules which tended to lie in the base of the cell nearest a capillary channel. With Masson's stain these granules appeared brown. The nuclei were variable in size and shape. Only a few were vesicular in appearance, many contained a deep blue or purple nucleolus, and the majority exhibited a wrinkled nuclear membrane and a coarse irregular chromatin

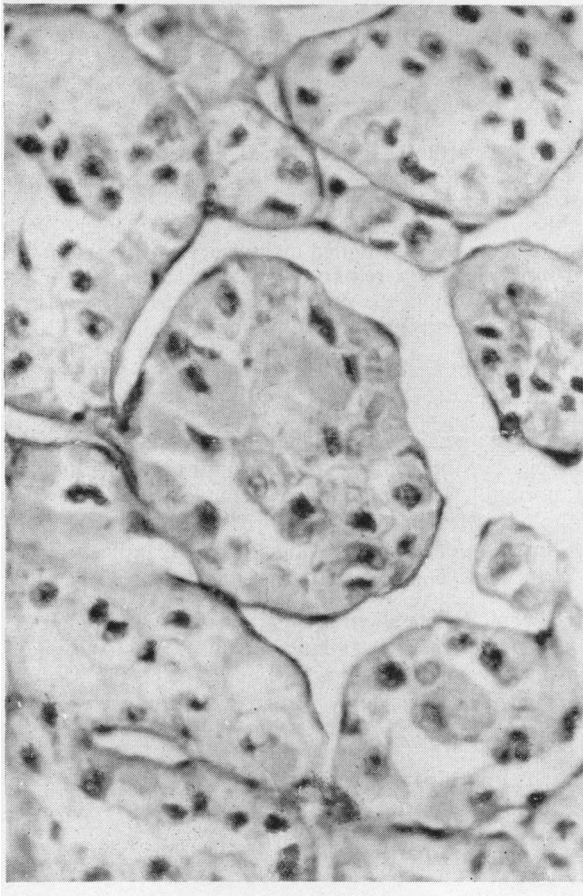


FIG. 2.—Photomicrograph of first specimen, showing large tumour cells in close relationship to wide endothelial-lined blood channels. Haematoxylin and eosin. $\times 450$.



FIG. 3.—Photomicrograph of first specimen, showing reticulin network enclosing cell masses (unstained). Gordon and Sweet's reticulin stain. $\times 450$.

pattern. No mitotic figures were seen. Neoplastic cells were present within veins at the perimeter of the growth which had also invaded the adjacent orbital fat. A diagnosis of secondary hypernephroma was made, but the degree of nuclear irregularity was noted as abnormal. It was subsequently learned that no primary renal tumour was found.

A further specimen received on March 4, 1960, measured $6 \times 4 \times 3$ mm. and was part of an almond-sized nodule from the right lower lid. Sections again showed an organoid growth with the same granular epithelial-like cells arranged in nests in intimate relationship to small capillary vessels (Fig. 4, overleaf). The cells varied considerably in size and exhibited multinucleate forms. Many of the cells contained fine light-brown granules which did not stain for iron (Prussian blue reaction), melanin (Fontana silver stain), or bile pigments, and were probably lipochrome granules. Gomori staining for chromaffin substance was again negative. Sections from this and the previous specimen were submitted to Dr. R. Motteram, Pathologist at the Peter MacCallum Clinic, Melbourne, who thought the appearance consistent with a tumour of the paraganglioma alveolar soft-part sarcoma group.

Discussion

The tumour reported here certainly seems to belong to that group of neoplasms called non-chromaffin paragangliomata or chemodectomata, the

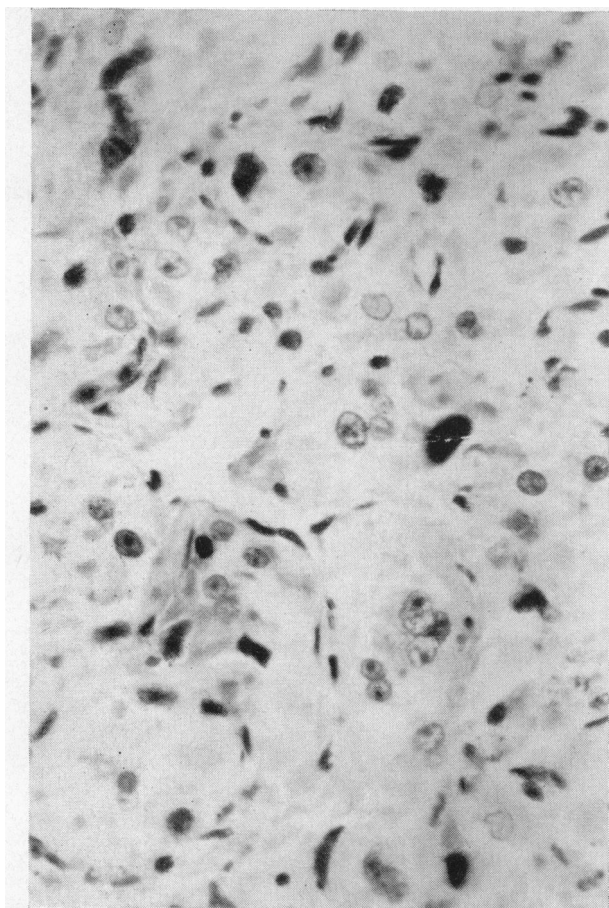


FIG. 4.—Photomicrograph of second specimen, showing multinucleate tumour cells. Haematoxylin and eosin. $\times 450$.

best known of which arise from the carotid, jugular, tympanic, and vagal bodies. It is becoming increasingly apparent that non-chromaffin paraganglionic or chemoreceptor tissue is much more widespread in the body than was formerly thought. Thus, Smetana and Scott (1951) illustrated such tissue in Hunter's canal and Evans (1956) stated that chemoreceptor organs of simple type occurred in relation to blood vessels within the viscera, muscles, and other tissues.

Authentic records of metastases from non-chromaffin paragangliomata of the head and neck are very rare. The fourteen malignant non-chromaffin paragangliomata reported by Smetana and Scott (1951) arose mainly in the thigh muscles and retroperitoneal tissues, but these were a selected series from more than thirty neoplasms of similar character in the files of the Armed Forces Institute of Pathology. Clinical and/or pathological evidence of metastases, predominantly to the lungs, was present in the majority of these fourteen cases. It is of interest that misdiagnoses in this series in-

cluded hypernephroma, hepatic cell carcinoma, malignant myoblastoma, adrenal carcinoma, amelanotic melanoma, liposarcoma, and haemangiosarcoma.

Christopherson, Foote, and Stewart (1952) reported a series of twelve tumours of unknown histogenesis which they called alveolar soft-part sarcomata. The histological structure of these tumours closely accords with the characteristic basic pattern of the non-chromaffin paraganglioma and is strikingly similar to that of the orbital tumour which is the subject of this report, particularly in their illustrations of Cases 1, 3, 4, and 10. Furthermore, distant metastatic spread, which occurred in approximately half of these alveolar soft-part sarcomata, most commonly affected the lungs. The authors noted the impressive histological resemblance of their tumours to paragangliomata, but seem to have rejected a paraganglionic origin because such tissue was not known to occur in the muscles of the extremities where most of their tumours originated.

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