is nonobstructive and is considered to be a developmental anomaly.

In the case under discussion, infundibular stenosis was limited to the left kidney, which weighed 175 grams. It was slightly enlarged, its surface was smooth, and the cortex was minimally reduced in width. The calyces were uniformly distended and communicated with a normal pelvis via small, round, sharply defined lumina. Multiple small concretions lay in the lowest calyx.

On microscopic examination of the calyces, the most significant finding was an increase in the size and number of the smooth muscle fibers of the lower calyceal sphincters. At this level the muscle bundles of the calyx and adjoining pelvis had a thick, coarsely woven texture (Fig. 1). The kidney parenchyma was well preserved, and in none of the sections was there any evidence of recent or remote infection.

The available literature dealing with this restricted form of hydronephrosis caused by obstruction, whether functional or anatomical, is very limited, and in none of the reports has hypertrophy of the lower calyceal sphincters been mentioned. Although hypertrophy of the calyceal ring leading to infundibular stenosis might readily explain the hypertrophy and dilatation of the calyces, the actual mechanism responsible for this overgrowth of smooth muscle remains unanswered. Watkins,[2] Moore,[3] and Williams and Mininberg[4] have suggested achalasia as a possible mechanism, but they were the first to point out that such a suggestion is pure speculation.

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ESTHESIONEUROBLASTOMA: A LIGHT AND ELECTRON MICROSCOPIC STUDY

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Abstract

The electron microscopic features of an olfactory esthesioneuroblastoma are described. The tumor cells had well developed neuritic processes containing neurotubules and neurofibrils. In addition, neurosecretory granules, similar to those seen in adrenal neuroblastomas, were present in the main cell body as well as in the neuritic processes. The neurites were also well demonstrated by light microscopic examination when stained by the Palmgren silver method. The importance of demonstration of these processes in establishing a firm diagnosis is stressed. Electron microscopic demonstration of neurites and secretory granules in a nasal tumor is diagnostic of an esthesioneuroblastoma.

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[redacted]

Only one other paper could be found in the English literature in which some ultrastructural features of a nasal neuroblastoma are illustrated.[5]

CASE REPORT

[redacted] He had no history of pain but had noticed a watery discharge from the nostril and slight proptosis of his left eye. Two years previously he had had an operation on his nose in another country but no further details are available.

On examination a fleshy tumor was found in the superior part of the nasal cavity. It was filling the left choana and extending into the postnasal space. [redacted] but no other clinical features of note. Tomograms showed a soft tissue mass in the nasal cavity on the left side and destruction of the medial orbital margin and possibly of the medial wall of the left maxillary antrum (Fig. 1). All the paranasal sinuses were noticed to be opaque. Tomography of the base of the skull showed no bony erosion and a brain scan was unremarkable.

A biopsy of the tumor was reported as showing an undifferentiated carcinoma. A left Caldwell-Luc and left sphenoethmoidectomy were performed. The medial wall of the maxillary antrum was bulging into the antral cavity which was free of tumor. The middle and inferior turbinates were removed, and tumor tissue was excised piecemeal from the anterior, middle, and posterior ethmoidal cells. The sphenoidal sinus was found to be free of tumor. Histologic examination demonstrated tumor in all the ethmoidal cells as well as in the middle turbinate. The tumor was again reported to be an undifferentiated carcinoma. Three days later a left frontoethmoidectomy was performed and tumor was removed from

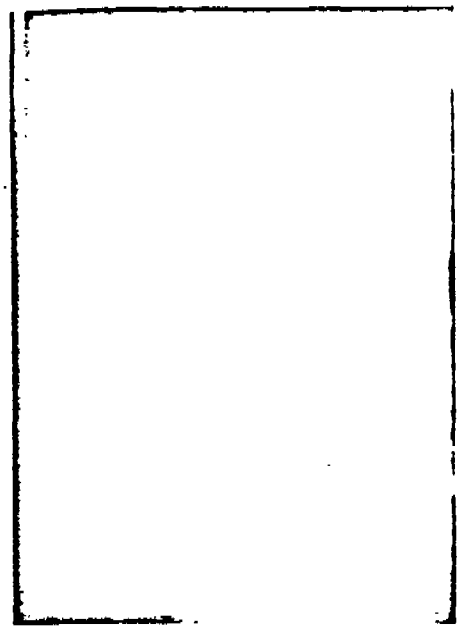

Figure 1. Tomogram showing soft tissue shadow in the left nasal cavity, destruction of the medial orbital margin, and clouding of the paranasal sinuses.

the frontal sinus. On this occasion a histologic diagnosis of esthesioneuroblastoma was made. In August and September the patient was given a course of radiotherapy to a maximal tumor dosage of 5520 rads. He was then discharged.

In November he was found to have a polyp attached to the right middle meatus. A 1.5 by 1.5 cm. polyp was excised and showed the features of an esthesioneuroblastoma. One week later a right sphenoethmoidectomy was performed. Friable tumor was found in the ethmoid and was removed from its attachment to the cribriform plate. The superior and middle turbinates and part of the vomer and rostrum were excised. Three 10 mg. radium tubes were inserted into the region of the roof of the nasal cavity. Microscopic examination confirmed the presence of tumor in the ethmoidal and sphenoidal sinuses. The patient was discharged nine days later and returned home to Angola. In view of the extent of the lesion and failure of response to radiotherapy, the prognosis was considered to be very poor.

PATHOLOGY

Methods

[redacted] (10 per cent formalin). Minced fragments of the tumor were immediately transferred to phosphate buffered glutaraldehyde and postfixed in Palade's solution. The tissue was then dehydrated in graded alcohols and embedded in Araldite. Ultrathin sections were cut, stained with aqueous uranyl nitrate and lead acetate, and examined with an AEI–GEC 6B electron microscope.

Light Microscopic Examination

[redacted] (Fig. 2), whereas in others obvious infiltration of lamellar bone was noted.

[redacted] (Fig. 3). Within this stroma a few ducts and acini of minor salivary gland origin were observed.

[redacted] The cytoplasm [redacted] of

Figure 2. Photomicrograph showing intact respiratory mucosa covering anastomosing cords of tumor cells. (Hematoxylin and eosin stain. ×200.)

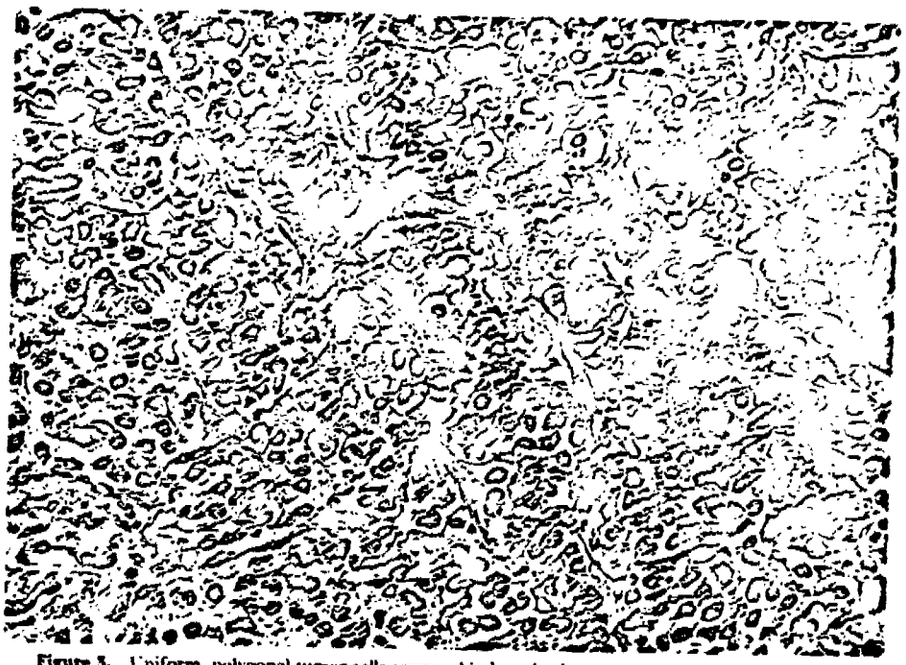

Figure 3. Uniform, polygonal tumor cells arranged in broad columns, separated by delicate fibrovascular stroma. (Hematoxylin and eosin stain. ×320.)

Figure 4. High power photomicrograph showing tumor cells with regular oval nuclei, prominent nucleoli, and a cytoplasm with a fibrillar appearance. Cell membranes are indistinct. (Hematoxylin and eosin stain. ×800.)

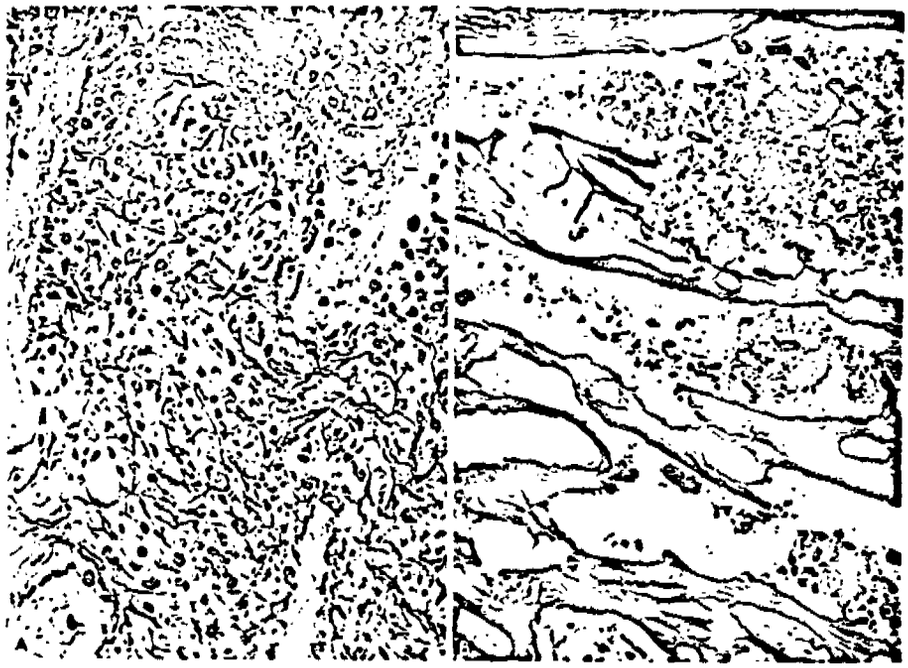

Figure 5. *A*, Abundant delicate neurofibrils form a meshwork within islands of tumor cells but are absent in fibrovascular septa. (Palmgren's silver stain. ×200.) *B*, Coarse reticulin fibers in fibrovascular septa surround islands of tumor cells but are not present within these islands. (Gordon-Sweet reticulin stain. ×200.)

as indistinct (Fig. 4). [redacted] nd numbered about six per 50 high power elds. (3 [redacted] o [redacted] The Palmgren stain [redacted] (Fig. 5*A*). iese fibrils were not present in the fibrocular septa. [redacted] he [redacted] s. [redacted] t in the rovascular septa but was completely absent thin the cords and islands of tumor (Fig. 5*B*). e reticulin fibers were coarser than the urofibrils and tended to form bundles her than a delicate meshwork. [redacted]

ectron Microscopic Examination

The tumor cells were compactly arranged, d the plasma membranes of opposing cells showed focal areas of thickening suggesting specialized surface attachment plates (maculae densae), but true desmosomes were not observed (Fig. 6). [redacted] (Figs. 6 to 8). When sectioned longitudinally, they could be followed for a considerable distance. They contained numerous fine filaments, which ran parallel to the long axis of the cell process (Figs. 6, 7). In transverse section they appeared as dots of uniform size and rather evenly distributed (Fig. 8). [redacted] (Figs. 6, 7). When sectioned longitudinally, they appeared as a double layered membrane, whereas transverse sectioning showed a ringlike structure (Figs. 6 to 8). Some neurofilaments and tubules were also present in the cytoplasm of the main cell body but in much smaller numbers than in their neuritic extensions. [redacted] (Figs. 6, 7, 9). These granules were round and fairly uniform in

Figure 6. Electron micrograph showing longitudinally sectioned neurite with neurotubules (short arrows) and neurofilaments in close proximity to secretory granules. Maculae densae are present between opposing plasma membranes (long arrows). (×52,500.)

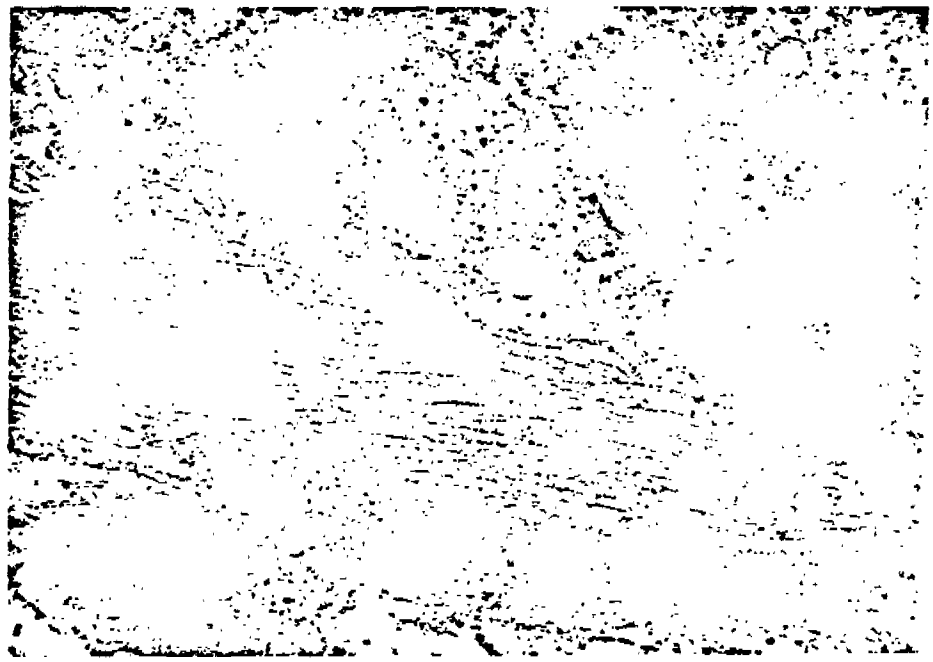

Figure 7. Electron micrograph showing longitudinally sectioned neurite containing numerous fine neuro
 filaments and occasional neurotubules (arrows). Secretory granules are seen in an adjacent cell body. (×70,000)

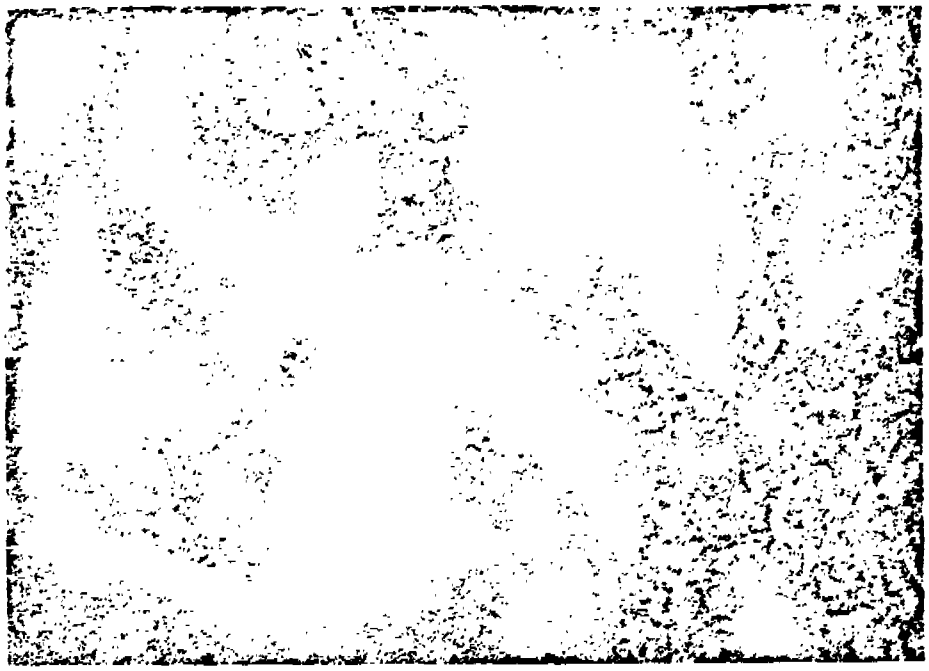

Figure 8. Obliquely sectioned neurite in which some of the tubules appear as ringlike structures. (×40,000.)

size, measuring up to 1000 Å in greatest diameter. They had a distinct limiting membrane and an electron dense core. A prominent electron lucent area was present between the limiting membrane and the electron dense core. Within the cytoplasmic processes the granules were found in close association with the tubules and filaments (Fig. 6).

Cytoplasmic organelles were sparse. There were moderate numbers of mitochondria and dilated profiles of smooth endoplasmic reticulum. The mitochondria were slighdy enlarged and showed focal swelling of some of the cristae (Fig. 9).

DISCUSSION

[redacted] and was first described by Berger et al.[4] in 1924 under the name, "L'esthésioneuroépithéliome olfactif." This tumor contained well formed rosettes. In 1926 Berger and Coutard[5] reported a variant of the above tumor and termed it "L'esthesioneurocytome olfactif." This tumor lacked the rosettes. [redacted]

[redacted] and is composed of anastomosing trabeculae of rather uniform cells. These may resemble epithelial cells, as in our case, and be mistaken for an undifferentiated carcinoma, or they may resemble lymphoreticular cells and the tumor then may be misdiagnosed as malignant lymphoma. When present, rosettes are helpful, although even these may be mistaken for the glandular structures of an adenocarcinoma. We agree with Obert et al.[7] that in the absence of neurofibrils a nasal tumor cannot be diagnosed as a neuroblastoma with certainty.

Gerard-Marchant and Micheau[8] stressed that axons do not show up clearly in the usual routine staining methods, and they considered this to account for the fact that 17 of the 45 cases of esthesioneuroblastoma in the literature that they reviewed had initially been incorrectly diagnosed. The first two biopsies performed on our patient had also been incorrectly diag-

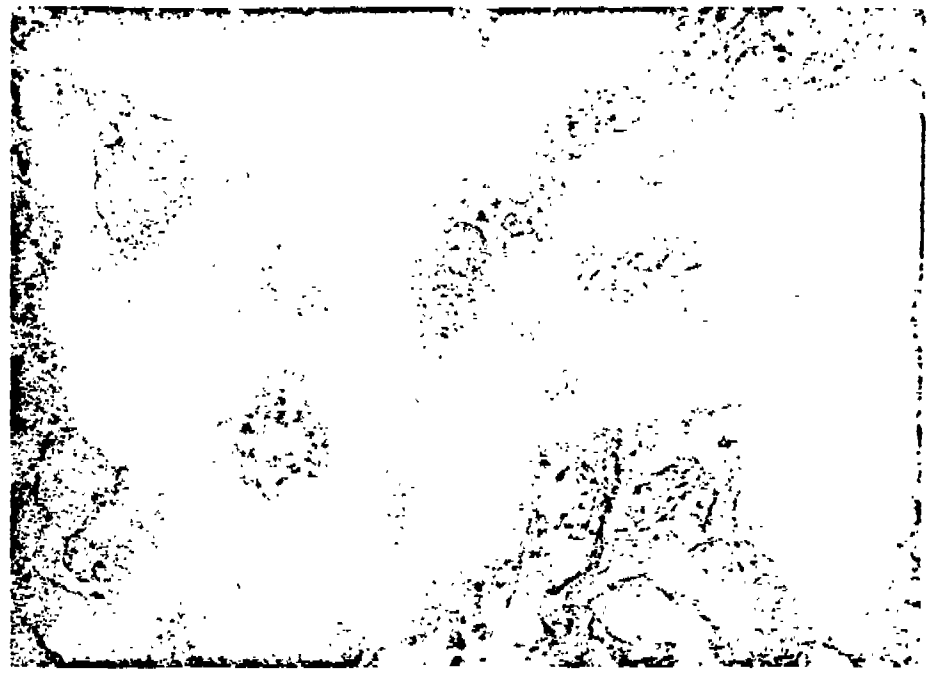

Figure 9. Numerous membrane bound neurosecretory granules in the cytoplasm of the tumor cell. Mitochondria are enlarged and show focal swelling of some of the cristae. (×70,000.)

nosed as undifferentiated carcinoma. Although most cases in the literature mention the presence of fibrils or fibrillar material associated with the tumor cells, we have been disturbed by the frequency with which these fibrils have been accepted as neurofibrils on the basis of hematoxylin and eosin staining alone. The Palmgren silver stain for neurofibrils conclusively demonstrated a feltwork of neurofibrils associated with the tumor cells in our case, and contrasted well with the reticulin stain, which demonstrated only connective tissue fibers in the fibrovascular stroma. McGavran[2] also stressed the difficulty in recognizing this neoplasm and suggested that ultrastructural examination, even of formalin fixed tissue, could be of considerable help.

[redacted]

In that paper the presence of numerous cytoplasmic processes and membrane bound neurosecretory granules was demonstrated in sections prepared from formalin fixed tissue. The nature of the cytoplasmic processes was not discussed and they were apparently not recognizable as axons. Our electron microscopic studies demonstrate the presence of neuritic processes arising from the tumor cells. These processes are characterized by the presence of an admixture of neurofilaments and neurotubules. In addition, the cytoplasm of the tumor cells contains moderate numbers of neurosecretory granules; these are also present within the neuritic processes. The presence of neurosecretory granules and neuritic processes has also been demonstrated ultrastructurally in adrenal neuroblastoma cells and chick embryo and sympathetic ganglion cells grown in vitro.[9] The granules in the nasal tumor were about the same size as those in the cells from the sympathetic ganglia and from the neuroblastoma but smaller than those noted in pheochromocytoma cells.

[redacted]

Neuritic processes were noted in the undifferentiated neuroblastic cells as well as in the mature ganglionic type of cell. Morphologically similar granules have been found in the carotid body and glomus jugulare tumors. The membrane bound dense core granules seen in carcinoid tumors of the alimentary

act are similar but tend to be larger and more leomorphic and are not associated with neuro- laments or neurotubules.[12] Our electron icroscopic findings thus confirm the neurog- ous nature of the tumor and its resemblance the adrenal neuroblastoma. The presence dense core neurosecretory granules suggests e possibility that some of these tumors may e found to produce catecholamines.

Kolze[13] found the urinary level of 3-methoxy-4-hydroxymandelic acid to be normal in a patient with an olfactory esthesioneuroblastoma. Unfortunately urinary catecholamine levels were not determined in our patient, but this test should be performed in all patients suspected of having this tumor. It would also be interesting to see whether future ultrastructural studies of this tumor confirm the existence of several histologic variants.

[redacted] 7, 14, 15

Another possible site of origin is the ganglion of Loci of the nervus terminalis, a structure composed of sympathetic fibers and ganglion cells in the anterior aspect of the olfactory mucous membrane.[16] Origin from the organ of Jacobson[17] and the sphenopalatine ganglion[18] would anatomically be inconsistent with that of the majority of the tumors.

[redacted]

nd were noted in three of 18 cases reported Hutter et al.[19] In 1966 Skolnick et al.[15] sented an extensive review of 97 cases. rvical node metastases occurred in 11 pa- nts and distant metastases in 11. The lung s the most frequent site of distant metas- es. Schenck and Ogura[20] noted cervical le metastases in three of eight patients seen their institution over a 22 year period.

The effectiveness of therapy is difficult ssess because of the relatively small num- of cases reported. The extensive review skolnick et al.[15] demonstrated a 52 per cent year survival rate in 50 patients who had n followed for five years or more. They ommended surgical resection as the treat- nt of choice with irradiation reserved for sistence of tumor. However, the tumor is med by some authors to be fairly radio- sitive so that local excision followed by iation therapy is frequently recom- ded.[1, 13, 21] No convincing relationship been demonstrated between the histologic earance and the prognosis.

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