Primary Carcinoid Tumor of the Orbit

A Clinicopathologic Study With Histochemical and Electron Microscopic Observations

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- A patient with a primary carcinoid tumor of the orbit is described. No other tumor had been found during the 15-year interval since the onset of unilateral proptosis. Symptoms of the carcinoid syndrome were absent, and the urinary levels of 5-hydroxyindoleacetic acid were normal. Histologically, the bulky, noninfiltrating tumor compressed but did not invade the optic nerve. The argyrophilic cells were arranged in solid lobules and formed abundant, rosettelike structures. Pleomorphic neurosecretory granules were demonstrated by transmission electron microscopy.

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Thousands of cases of carcinoid tumors have been reported in the literature. Carcinoids are the most common tumor of the appendix and the most frequent type of "bronchial adenoma." Metastasis to lymph nodes, liver, bone, and skin have been well-documented. Ocular or orbital involvement, however, has been rare. Only 20 cases have been reported. We describe a patient with a primary carcinoid tumor of the orbit. To our knowledge, no other such well-documented case has been reported. This case is tabulated in another report, but clinicopathologic details are reported herein for the first time.

REPORT OF A CASE

A 71-year-old woman was seen because her right eyelids protruded so notably (Fig 1) that they abutted against her spectacles. A slowly progressive, right exophthalmos had been diagnosed by examinations made 11½ and three years earlier. The eye had lost all vision one year prior to the latter examination. The patient was advised to have further diagnostic testing and a neurosurgical examination but she did not follow this advice. The general physical examination at the time of admission disclosed no abnormalities except for the massive proptosis of the right eye. Orbital roentgenograms and computed tomography (Fig 2) showed enlargement of the right orbit and a large, noncalcified intra-

Fig 1.—Left, Notable proptosis of right eye of 11½ years' duration (AFIP Neg 80-6853-2). Right, Lateral view (AFIP Neg 80-6853-1).
The clinical history suggested a retrobulbar tumor (Fig 2) adherent to dura of optic nerve (N) (AFIP Neg 81-18843). The patient denied ever having had symptoms of the carcinoid syndrome and, postoperatively, the urinary 5-hydroxyindoleacetic acid (5-HIAA) levels were normal. The patient refused further diagnostic tests. She is well more than three years after exenteration and has no evidence of metastatic disease.

Macroscopic examination disclosed a large orbital mass that appeared to be so intimately attached to the optic nerve that a primary tumor of the optic nerve was suspected.

All of the tissue was embedded in paraffin. Samples of the large orbital neoplasm (Fig 3) were studied by the use of paraffin sections stained with hematoxylin-eosin, PAS, alcian blue, mucicarmine, Fontana-Masson, Dianazonium fast red, Sevier-Munger, and the Grimelius methods for argentaffin and argyrophilic granules. Histologically, the retrobulbar tumor compressed the atrophic and gliotic optic nerve, but it was entirely extradural, and there was no intrinsic involvement of the nerve. The neoplasm exhibited a mixture of the following histologic patterns: basaloïd, trabecular, tubular, and rosetted (Figs 4 through 7). In areas with well-developed rosettes, the tumor resembled a retinoblastoma (Figs 6 and 7).

The tumor cells were of two types in almost equal proportions. The first had a moderate amount of clear cytoplasm containing fine, faintly eosinophilic granules and a central, lightly basophilic nucleus with finely stippled chromatin. The second possessed an eosinophilic cytoplasm and a densely basophilic nucleus. Both cell types showed minimal nuclear pleomorphism with small, indistinct, or absent nuclei, and round or ovoid outlines. The mitotic index was 1/70 high-power fields. In some areas tumor cells displayed an intensely positive argentaffin reaction (Fig 8), and there was a more diffusely positive argyrophilic reaction. Small foci of PAS-positive material were found within the tumor cells. Focal accumulations of extracellular mucopolysaccharide were present. Except for a decreased number of retinal ganglion cells, the intraocular tissues appeared to be normal.

Using a published technique, tissue was prepared for transmission electron microscopy. Numerous pleomorphic intracytoplasmic membrane-bound neurosecretory granules were present (Figs 9 and 10). They ranged in size from 100 to 500 nm. Most of the granules were electron-dense but some had a lighter matrix. Most were round or oval but dumbbell and crescent shapes were also present. The Golgi complex, the mitochondria, and the roughsurfaced endoplasmic reticulum were focally abundant. Few desmosomes were seen.

COMMENT

The histologic differential diagnosis of a primary orbital carcinoid tumor includes amelanotic melanoma, paraganglioma, and metastasis from oat cell carcinoma, retinoblastoma, neuroblastoma, or nonorbital carcinoid. All but the latter can be eliminated using established clinical, histologic, and ultrastructural criteria. To differentiate the tumor in our case from a metastasis of a nonorbital carcinoid, the clinical and histologic
data from 11 recently reported metastatic orbital or ocular carcinoids and the published reports of four others were reviewed.

Clinically, our case differed radically from those of known orbital metastasis from carcinoids. In all of 15 patients described there was a histologically confirmed nonocular primary carcinoid. Nine of the metastatic tumors were in the choroid and six were in the orbit. The primary tumor had been discovered one month to nine years before the orbital or ocular metastasis in 12 patients. Elevated urinary levels of 5-HIAA and/or symptoms of the carcinoid syndrome were found in four of these patients. The primary tumor was detected two months to two years following the onset of ocular symptoms in three patients, but not until autopsy when clinically undetected ileal carcinoids were found in two of them. Elevated urinary levels of 5-HIAA and/or symptoms of the carcinoid syndrome were present in two of these three patients.

Histologic material was reviewed from four metastatic orbital carcinoids. Each tumor was composed of light and dark cells that were indistinguishable from those observed in the primary orbital carcinoid. An infiltrative pattern with abundant connective tissue and areas of tumor cells arranged in single file were present in three of the metastatic cases. Argentaffin granules were present in each tumor. The fourth metastatic carcinoid had a lobular pattern with small amounts of fibrous tissue. Its cells were nonreactive to silver stains.

The ultrastructural characteristics of the primary orbital carcinoid were indistinguishable from those of primary ileal carcinoids and their choroidal metastases. The neurosecretory granules in foregut carcinoids are round or ovoid. They are more pleomorphic in midgut tumors.

Primary carcinoid tumors of the small intestine have a number of unusual features. Most of the tumors are less than 1 cm and tumors larger than 3.5 cm in diameter are extremely rare. Metastasis usually develops
from primary tumors that are smaller than 2 cm in diameter. Radiologic contrast studies are helpful in detecting these tumors, but because of their small size and deep location, more than half of the tumors are missed. These tumors are easily overlooked even at autopsy unless careful examination is made. Symptoms of the carcinoid syndrome (episodic flushing, diarrhea, asthma, and edema of the lower extremities) are common. These symptoms may be present for 20 years before the primary tumor is located. When there are no systemic manifestations, however, it is extremely rare to have evidence of extraabdominal metastasis occurring years before detection of the primary tumor.

Carcinoid tumors arise from Kulchitsky's cells, which are normally found in the gastrointestinal tract, the bronchi, the thymus, the uterus, and the genitourinary tract. Bronchial carcinoids were described prior to the discovery of Kulchitsky's cells in the bronchi. These cells have not been described in the normal orbit, ovary, or testicle. A few cases of primary carcinoid tumors of the ovary and testicle have been reported. These facts, coupled with the noninfiltrative pattern of the tumor cells, and the absence of other carcinoid tumors during a 15-year period following the onset of proptosis, strongly support our belief that, in the present case, the orbital tumor was a primary carcinoid. Only continued follow-up study and a meticulous autopsy can absolutely establish this fact beyond dispute.

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References