A 57-year-old man with a history of hepatic adenocarcinoma was referred 3 years after his diagnosis with a choroidal tumor in the right eye. Results of a transscleral excision biopsy revealed the tumor to be an amyloid-rich neuroendocrine metastasis. The patient subsequently developed cushingoid features and investigations revealed ectopic corticotropin syndrome, an elevated urinary 5-hydroxyindoleacetic acid level, and neuroendocrine metastasis in several locations. The choroidal neuroendocrine metastasis stained negative for serotonin and corticotropin. The source of the ectopic corticotropin and the location of the primary tumor have not been found. This case demonstrates that disseminated neuroendocrine tumors may rarely cause ocular lesions before systemic endocrine sequelae arise.

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Neuroendocrine tumors are derived from amine precursor uptake and decarboxylation cells of the diffuse neuroendocrine system. Most neuroendocrine tumors develop in the gastrointestinal tract, pancreas, and lung, although they can develop anywhere in the body. We describe a patient who had an asymptomatic choroidal neuroendocrine metastasis as the initial manifestation of systemic disease. The location of the primary tumor is unknown.

**REPORT OF A CASE**

A 57-year-old man was referred to an ophthalmologist following a routine examination by his optician that revealed a choroidal tumor in his right eye. Three years previously he was examined because of symptoms of prostatism and incidentally was found to have multiple lesions on liver ultrasonography. The liver biopsy specimen at that time was described as metastatic adenocarcinoma, with the primary lesion considered to be of pancreatic or intestinal origin. However, despite extensive investigations, the primary source could not be found and no treatment was deemed feasible.

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The patient subsequently developed cushingoid features. He also developed cutaneous hyperpigmentation. Biochemical investigations confirmed the diagnosis of Cushing syndrome caused by ectopic corticotropin production. In addition to a high serum corticotropin and high urinary free cortisol levels, the patient had a high 24-hour urine 5-hydroxyindoleacetic acid level. Computed tomographic examination of the chest revealed no pulmonary lesion, but abdominal computed tomography showed that the liver was almost completely replaced by tumor. The pancreatic head was bulky but no discrete tumor was seen. Metastases were also seen in the sacrum. A second liver biopsy specimen revealed neuroendocrine tumor.

The patient was treated with oral ketoconazole, which blocks adrenal steroidogenesis; metyrapone,
which blocks cortisol synthesis; and mitotane, an adrenolytic agent that also blocks cortisol synthesis. In addition, the patient received insulin to control his diabetes. A few months later, the patient developed weakness and wasting in his right arm. A magnetic resonance imaging scan of the cervical spine and upper chest revealed numerous metastases throughout the thoracic and cervical spine. The patient received palliative radiotherapy. He is continuing medical treatment.

The clinical presentation of neuroendocrine tumors underestimates their incidence, because many are asymptomatic. The majority of neuroendocrine tumors (95%) arise in the gastrointestinal tract, pancreas, and lung.1 Unusual sites of occurrence include the maxilla, larynx, and trachea. Metastasis usually develops in the lung, liver, spleen, bone, and lymph nodes. Metastasis to the eye and orbit is rare and represents only 2% of all ocular metastatic tumors.2

The histology of this tumor was similar to a medullary carcinoma of the thyroid; however, no calcitonin was found. Thyroid imaging did not reveal a focal lesion. Features of a typical carcinoid tumor were lacking on clinical and histological findings. Furthermore, the chemical pathology did not correspond to the immunohistochemistry; corticotropin and serotonin markers stained negative in the choroidal tumor. This observation suggests that the ocular tumor differed from the bulk of the extraocular metastases and may reflect the heterogeneity of the cells of the neuroendocrine system and perhaps the presence of a multiple endocrine neoplasia syndrome.

The clinical behavior of this tumor is unusual. The site of the primary tumor can usually be identified through clinical investigation.3 In our case the primary tumor has never been identified. Another unusual feature is the development of Cushing syndrome caused by ectopic corticotropin. This systemic effect is a rare long-term management problem and is associated with more malignant neuroendocrine tumors, such as small-cell carcinomas of the lung.4

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