Unilateral pseudouveitis revealing a pancreatic neuroendocrine carcinoma: A case report

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Abstract

Neuroendocrine tumors have a wide range of malignant potential. These tumors infrequently metastasize to the orbit. We report the case of a 61-year-old man who presented with unilateral recurrent panuveitis related to choroidal metastasis. Explorations led to the diagnosis of pancreatic neuroendocrine carcinoma as the primary tumor.

Unilateral pseudouveitis revealing a pancreatic neuroendocrine carcinoma: A case report

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Abstract

Neuroendocrine tumors are a heterogeneous group of tumors with a wide range of malignant potential that tend to have a relative prolonged course. These tumors infrequently metastasize to the orbit. Ocular metastases from pancreatic neuroendocrine tumors (PNETs) have never been reported in the literature.

We report the case of a 61-year-old man who presented with progressive deterioration of general condition with unilateral recurrent episodes of non-granulomatous panuveitis of the left eye related to a choroidal metastasis. Radiological imaging and histopathological analyses led to the diagnosis of metastatic pancreatic neuroendocrine carcinoma as the primary tumor.

Choroidal metastases from neuroendocrine tumors are extremely rare, but compromise patients' well-being because of visual impairment. Uncommonly, these metastases can be the first manifestation of unknown tumors, warranting further investigations to detect the primary cancer.

Keywords

Pancreatic; neuroendocrine; tumors; carcinoma; choroidal; metastasis

pseudouveitis

Introduction

Pancreatic neuroendocrine tumors (PNETs) are a heterogeneous group of tumors that arise from the endocrine tissues of the pancreas and comprise only 1%–2% of pancreatic tumors [1,2]. However, their incidence has significantly increased over the past few decades due to the improvement and the wide-spread use of diagnostic imaging [3] . Only 10% of all PNETS are associated with hereditary genetic endocrine tumor syndromes, other cases are sporadic[4,5].

PNETs are classified as functional or non-functional tumors depending on the presence of clinical syndrome caused by the hypersecreted hormones and in most of cases they are non-functional [6].

Aggressiveness of these tumors is very unpredictable ranging from slow-growing to invasive forms [7].

Metastatic disease mostly affects liver, lymph nodes and bones [8]. Ocular metastases from neuroendocrine tumors are exceedingly rare and can simulate other primary or metastatic lesions [9]. We report a case of pancreatic neuroendocrine carcinoma revealed by choroidal metastasis.

We report a particular observation of a 61-year-old man in whom choroidal metastasis was the revealing manifestation of a metastatic pancreatic neuroendocrine carcinoma.

Observation

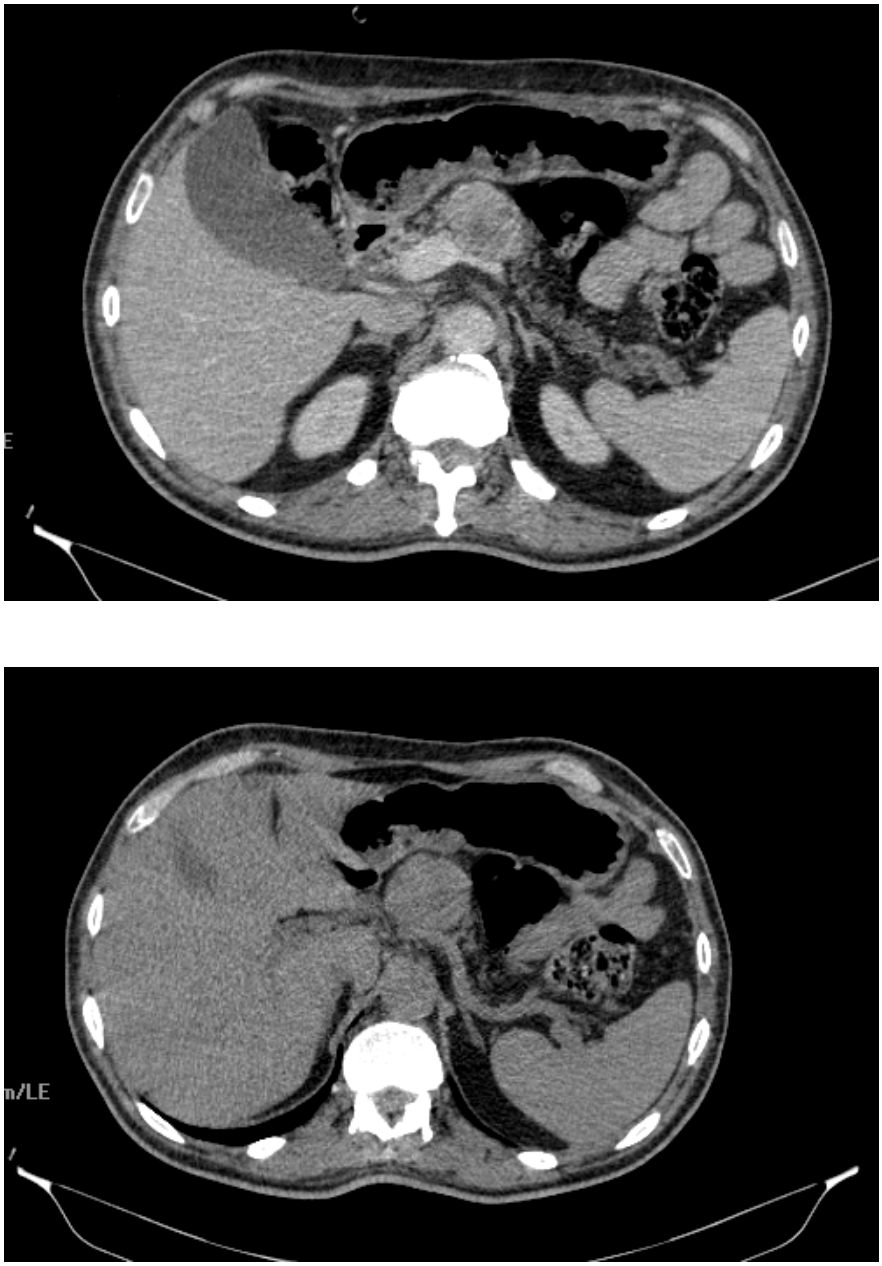
We report the case of a 61-year-old man, non-smoker, with a 5-year history of diabetes mellitus type 2, treated with Metformine and basal insulin, who presented with recurrent eye redness, ocular pain and progressive decrease in visual acuity of the left eye. Ocular symptoms were evolving for six months and were associated with clinical deterioration with a significant weight loss of 30 kilos in six months.

Physical examination was normal. The patient was afebrile with normal vital signs. There were no general symptoms, meningeal syndrome or cutaneous eruption. All biological parameters were normal.

Ophtalmological examination showed decreased visual acuity with 8/10 vision on the right eye and 3/10 vision on the left. There were features of non-granulomatous panuveitis: left anterior uveitis with hypopion, posterior iris synechia and dense diffuse vitritis without retinal detachment. The right eye was quiet, with no evidence of intra-ocular inflammation.

Orbital ultrasonography showed circumferential left choroidal echogenic and heterogeneous tissular thickening suggestive of metastases.

Thoraco-abdominopelvic computed tomography was performed in order to search primitive neoplasm. An invasive heterogeneous tumor mass at the level of the pancreatic body measuring 48*36 mm, with upstream pancreatic atrophy and a marked dilatation of the Wirsung duct was detected (figure 1). Multiple nodules disseminated through liver parenchyma, spontaneously hypodense without bile duct dilatation were also noted.



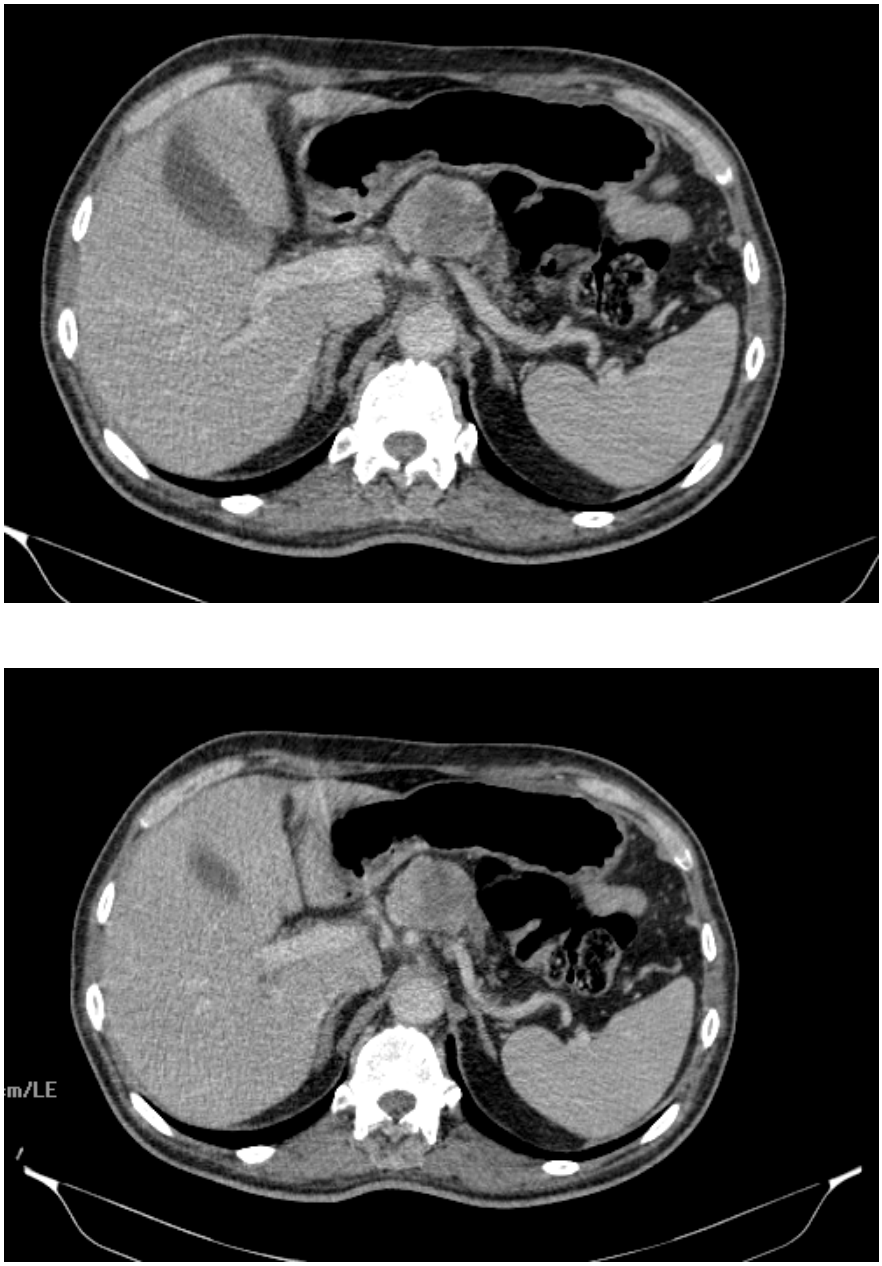
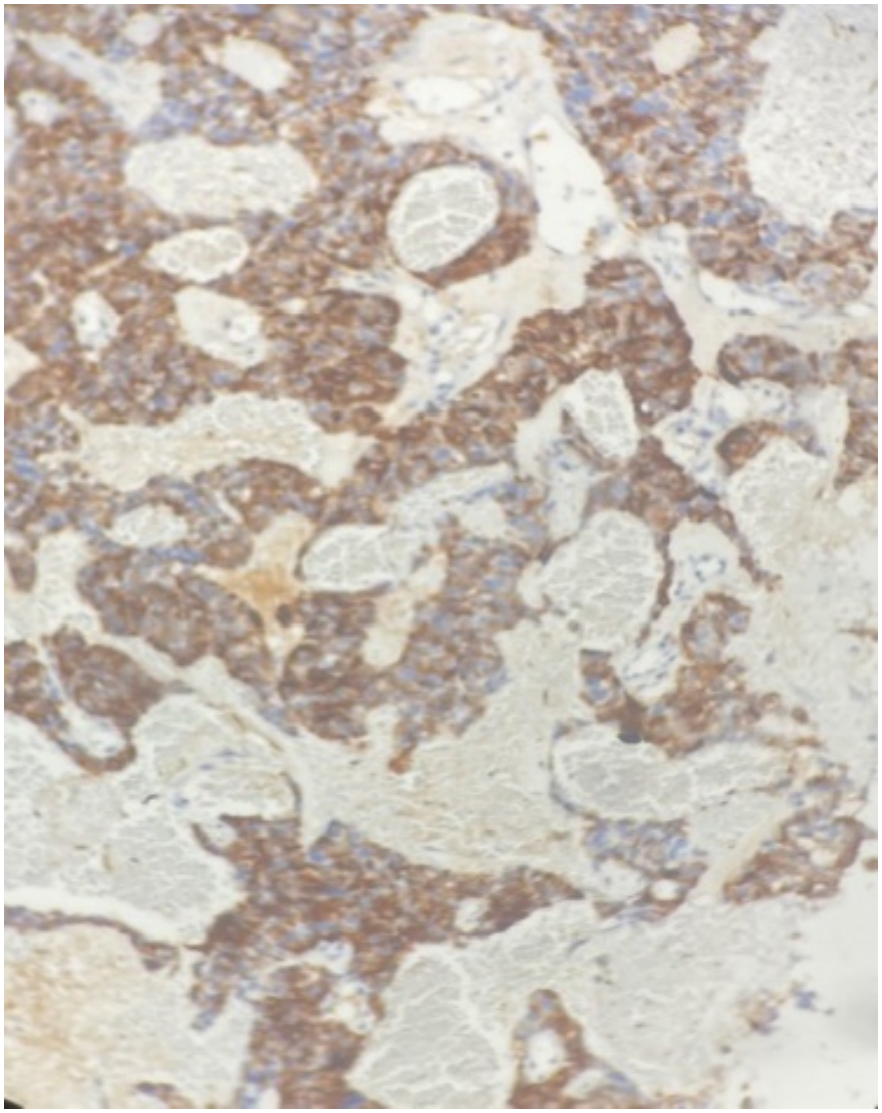
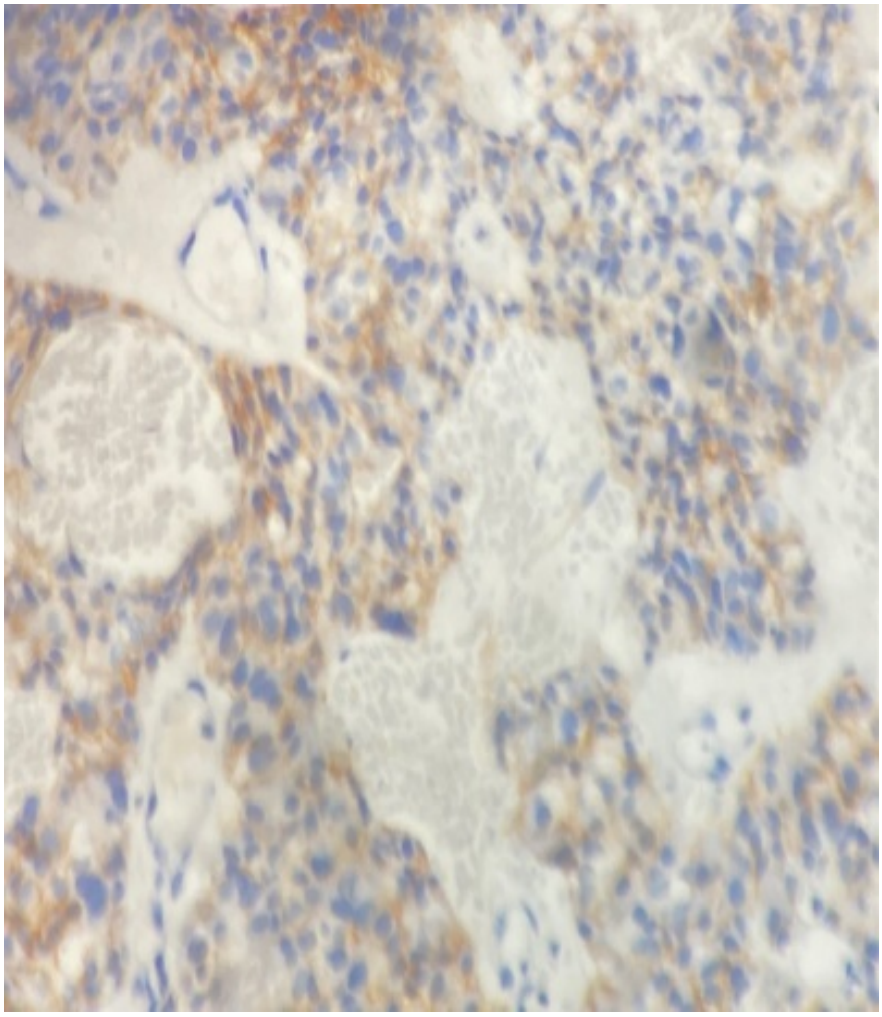
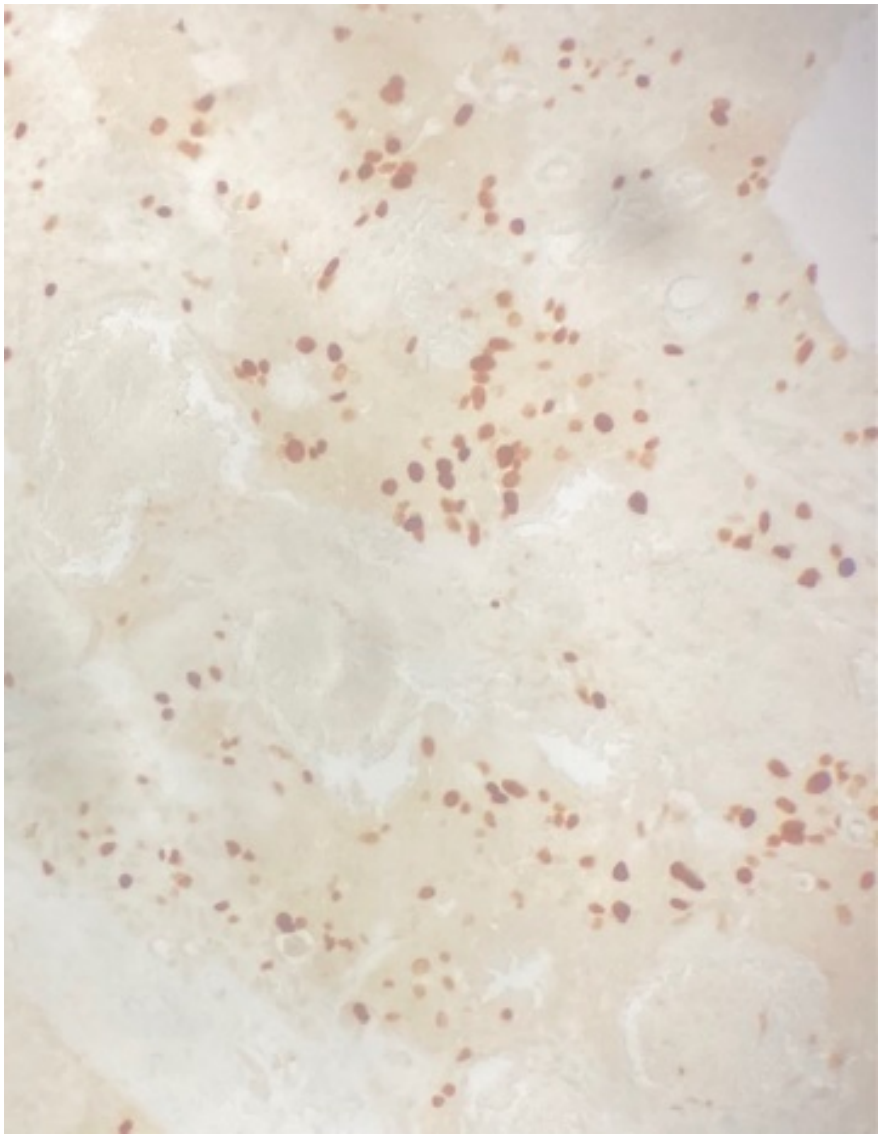


Figure 1: CT sections showing pancreatic tumor, upstream pancreatic atrophy and hepatic metastasis.

Anatomopathology report of the CT guided biopsy showed a largely necrotic carcinomatous proliferation organized in trabecular structures. Tumor cells were rounded or polyhedral, with an eosinophilic cytoplasm, large vesicular nuclei and highly irregular nuclear contours. On immunohistochemical analysis, tumor cells stained diffusely for chromogranin and synaptophysin. The Ki67 showed a proliferative index of 30 % confirming the diagnosis of a pancreatic neuroendocrine carcinoma (figure2).







a

b-

c-

Figure 2 : anatomopathological sections with immunohistochemical analyses: a- neuroendocrin différenciation and positive chromogranin immunostain, b- positive CD56 immunostain, c- ki67 prolifératives index of 30%.

Chemotherapy regimen as an initial treatment based on a combination of Etoposide (VP16) and cisplatin (CDDP) was planned.

Discussion

PNETs can be clinically divided into functional and non-functional depending on their hormonal activity [10,11]. Non-functional PNETs (NF-PNETs) comprise up to 90% of all PNETs and are often asymptomatic.

The lack of hormonal syndromes makes \soutthe clinical symptomatology discrete and non-specific [12]. Clinical features are due to mass effect exerted by a growing tumor and include weight loss, jaundice and abdominal pain [11]. As a result, these tumors are most often diagnosed later during the course of the disease, revealed by signs of local invasion or distant metastasis [10]. In fact, 32 to 73 percent of NF-PNETs are metastatic at the moment of diagnosis [10,13]. Like in the case of our patient who had an unexplained weight loss and in whom malignant pancreatic neuroendocrine carcinoma was diagnosed late in the metastatic stage.

The most commun area of metastasis is the liver [14]. Other sites including bones, spleen, peritoneum and brain have been reported [15,16].

It was long believed that metastatic tumors in uveal tissue were relatively rare but several studies had shown that ocular metastases are reported to be the most common intraocular malignancy, even more frequent than primary uveal melanoma [17,18], occurring through haematogenous spread by carotid and ophthalmic artery [19]. Some reports suggest that the incidence is underestimated. The prevalence of metastases estimated from post-mortem examination ranged from 4 to 10% with a clear predominance of the choroid because of its rich vascular supply [20,21].The most frequently found primitives are lung and breast cancers [22–24]. Uveal metastases from neuroendocrine tumors have only rarely been reported [25], and more rarer from pancreatic ones. In a series of 410 patients with uveal metastases, the primary cancer was a neuroendocrine tumor in only 9 cases (2,2%). The site of the primary neuroendocrine tumor was the bronchial tract in seven patients, the esophagus in one, and the thymus in one [9].

The most common reported complaints are ocular pain, blurred vision and proptosis [26].

Classically, the diagnosis of ocular metastases is evoked in case of a prior history of malignancy. However, these metastases can rarely be diagnosed prior to the detection of the primary tumor. Many patients with a disseminated stage cancer are debilitated and may not complain of visual symptoms, and minor visual problems may be dismissed as trivial or related to treatment these patients take. This may contribute to the higher than expected incidence. In 230 consecutive autopsies of patients who died of cancer of all types, Bloch and Gartner1 found a 12% incidence of ocular involvement.[27] In another small series of 15 cases of ocular carcinoid metastasis, the primary neoplasm was unknown and clinically silent in three cases [28]. In our case, the patient had unilateral eye redness and progressive decrease of visual acuity due to the choroidal metastasis that led to the diagnosis of metastatic pancreatic neuroendocrine carcinoma.

Data regarding survival after the diagnosis of ocular metastases of neuroendocrine tumors are limited. In a series of 13 patients with orbital carcinoid metastases, Mehta et al [29] showed that the overall survival was 72% at 5 years and 38% at 10 years. These findings suggest that patients with neuroendocrine tumors may have prolonged survival despite metastatic dissemination [30]. Early diagnosis and appropriate treatment in order to preserve their vision and quality of life are crucial. Numerous therapeutic modalities are proposed including beam radiotherapy, systemic chemotherapy and surgical excision [31]. External irradiation is an efficient treatment for orbital metastases that improves the visual acuity [32]. It is especially useful for symptomatic patients with single lesions [33]. However, data regarding response of uveal carcinoid metastases after palliative radiation is not available. Chemotherapy has also proven its efficacy in several cases. Fan et al [34] reported a significant regression of both choroidal and visceral metastases after the initiation of cisplatin and etoposide chemotherapy in a 65-year-old woman diagnosed with metastatic bronchial neuroendocrine carcinoma. Authors recommended the use of cisplatin and etoposide in the treatment of aggressive metastatic neuroendocrine carcinoma [35]. Moreover, the combination of chemotherapy and radiotherapy seems to be an efficient therapeutic option. In a series of six patients with ocular metastases from carcinoid tumors, treated with chemotherapy and external radiation, all patients responded well to that treatment and did not require surgical excision [36]. In many studies, chemotherapy has been considered as to be equally as effective as radiation therapy for treatment of ocular metastasis based on clinical lesion regression (decrease in tumor size, elevation, pigment clumping, and fluid resorption) and improved visual acuity. Common practice has been to wait at least 6 weeks to see the effects of systemic therapy on lesion regression. [37]

Concerning the case of our patient, who had an aggressive pancreatic neuroendocrine tumor metastasized to the liver and eye, oncologists opted for cisplatin and etoposide chemotherapy.

Conclusion

Choroidal metastases from neuroendocrine tumors are particularly rare, but compromise patients' well-being because of visual impairment. Since neuroendocrine tumors tend to have a prolonged course, early identification and treatment of choroidal metastasis is a fundamental issue to enhance quality of life. The present case serves as a reminder that unilateral recurrent uveitis should be well explored with orbital ultrasound or ideally magnetic resonance imaging and that identification of orbital metastases warrants further investigation to detect the primary tumor and initiate the effective treatment.

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Conflict of interest

All authors declare that they have no conflicts of interest.

Author's contribution

FC and AAH contributed to conception and design, acquisition and interpretation of data, and manuscript creation and drafting; IN and HM contributed to the critical revision of the article for important intellectual content; all authors were involved in the management of this patient, the revision of the manuscript, and approved the final version.

Ethical approval

Ethical approval for this case report was not required.

Consent

A written informed consent was obtained from the patient for the publication of this report.

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