Primary Neuroendocrine Carcinoma at an unusual site

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Abstract

Primary Neuroendocrine carcinomas (NEC) of the orbit are extremely rare. The histology of these high-grade, aggressive tumors maybe small cell or poorly differentiated (often large cell) and the diagnosis is usually established by immunohistochemistry. The treatment is multimodality approach and the data is limited. Patients presenting with localized disease is rare and in such cases, radiation therapy with or without resection should be added to combination chemotherapy. Herein we report a case of neuroendocrine carcinoma of the orbit, locally advanced without any distant metastases in a 20-year-old male and non-smoker. We have also reviewed the literature regarding clinical presentation, management options and outcome in primary orbital NECs.

Keywords: Non-smoker, Orbital Neuroendocrine Carcinoma, Platinum-based Chemotherapy, Proptosis

Introduction:

Neuroendocrine tumours (NETs), believed to arise from the enterochromaffin cells, usually originate in the gastrointestinal tract and the lungs.[1] They are a heterogenous group of tumours ranging from the indolent NETs or carcinoid tumors to the aggressive neuroendocrine carcinomas(NECs). NECs are rare and may originate from any organ. More than 80% patients present with metastatic disease and the most common histology is large cell (59%) followed by small cell. The prognosis is poor and the treatment, challenging in view of dearth of literature. The treatment parallels that of small cell lung cancer in view of similar clinical behavior.[2]

Primary NECs are extremely rare and the exact incidence has not been reported. There are few published case reports of small cell NEC metastasizing to the orbit, but there are only three published case reportsof small cell NEC arising from the orbit, so far. Herein we present a case of primary NEC of the orbit, locally advanced without any distant metastases, who has been treated with combination chemotherapy.

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Case Report:

A 20-year-old male, non-smoker, presented with complaints of nasal block and proptosis with total blindness of left eye since 2 months. He had no significant past or family history. A contrast enhanced computed tomography of the orbit done in another hospital was reported as extensive sinusitis and secondary fungal osteomyelitis for which he had undergone functional endoscopic sinus surgery with biopsy and histopathology revealed malignant round cell tumour of the orbit.

He was referred to us with these reports and clinical examination showed significant exophthtalmos with eyeball deviated outwards and no lymphadenopathy. (Figure 1) A review of the biopsy specimen was advised, which showed morphologically malignant small round cell tumour. The immunohistochemistry was positive for synaptophysin, chromogranin, CD 56 and focally positive for cKit (CD 117) with an MiB1 of 95%. The markers for lymphoma (LCA, CD20, CD2 and CD3), melanoma (S100) and Ewing's sarcoma (CD99) were negative. Hence he was diagnosed to haveNEC – small cell type.

Magnetic Resonance Imaging of the paranasal sinuses revealed altered signal intensity lesion, of size 67 x 37 x47 mm involving the left orbit with involvement of the extraocular muscles, abutting the optic nerve and with erosion of the lamina papyracea, lateral pterygoid plate and cribriform plate with extension into both the ethmoid sinuses, nasal cavity, nasopharynx, maxillary sinus, cavernous sinuses and the anterior cranial fossa.(Figure 2) His blood counts and biochemistry panels were normal and computed tomography of the thorax and upper abdomen showed no evidence of lung or liver lesion. He was treated with combination chemotherapy of cisplatin and etoposide. After 4 cycles, patient had remarkable improvement in vision and regression of proptosis (Figure 3) and repeat imaging of the orbit showed radiologically less than partial response, (Figure 4) suggestive of overall responding disease. Radiation therapy was planned to the residual lesion but the disease progressed and the patient has been lost to follow-up.

Figure 1 : Proptosis before treatment

Figure 2 : Intra-orbital mass in CT before chemotherapy

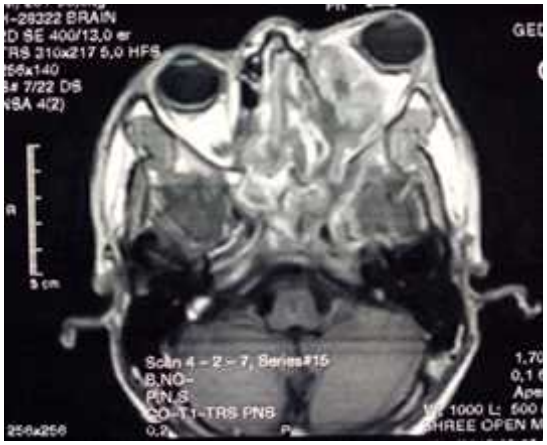
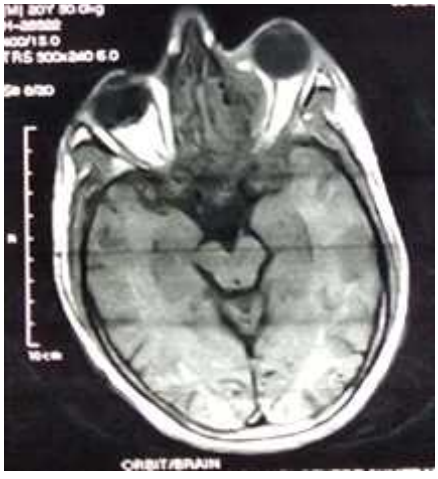


Figure 3 : Resolution of proptosis after chemotherapy

Figure 4 : Regression of mass after chemotherapy



Discussion:

In the latest World Health Organisation (WHO) classification, NECs are a category of poorly differentiated tumours, which express neuroendocrine markers chromogranin A (CgA) and synaptophysin and are high grade. ExtrapulmonaryNECs are characteristically uncommon. According to a population based study, the incidence is 0.84 per 100 000 in NETs with an unknown primary site. The majority of patients (>60%) present with metastatic disease and hence the prognosis is poor.[3]

There are no definite treatment recommendations for extrapulmonary NECs and the treatment is based on extrapolation from treatment of pulmonary small cell carcinomas. Multimodality treatment approach is necessary with platinum based chemotherapy in the front-line setting.There are only three cases of orbital NEC reported till now in literature. In the case report by MacIntosh et al.,a 35 year old woman presented initially with bilateral nasal obstruction and hyposmia, for which she was subjected to functional endoscopic sinus surgery and removal of polypoid masses in the nasal cavity. She later developed left eyelid swelling and limitation of eye movements, and she was diagnosed to have NEC primarily involving the

maxillary sinus with secondary invasion of the orbit with no disease elsewhere. The mass was excised, and patient has responded well to concurrent chemoradiation.[4]

Yamanouchi et al. reports a case of primary NEC of the left lacrimal gland, wherein the 86 year old male patient presented with 3 month history of left upper eyelid swelling. The patient was treated with carboplatin and etoposide for four cycles, followed by surgical excision and 50Gy radiotherapy to margins. The patient was recurrence free for 6 months, after which he developed liver metastasis and was given chemotherapy.[5] Alp Atik et al. reports a case of NEC of both orbits presenting as orbital cellulitis and blindness. The patient had right periorbital painful swelling for 3 weeks and decreased vision. The orbital mass was removed and patient was admisnistered cisplatin and 5 flourouracil, followed by concurrent chemoradiation with cisplatin. The residual lesion was excised and chemoradiotherapy with vincristine, cyclophosphamide and doxorubicin was given. After 2 years, the patient developed local recurrence and succumbed despite intra-arterial chemotherapy with cisplatin.[6]

In conclusion, orbital NECs are very rare and have a dismal prognosis despite multimodality treatment.

References:

1. Modlin IM, Lye KD, Kidd M. A 5-decade analysis of 13,715 carcinoid tumors. Cancer 2003;97(4):934–59.
2. DeVita VT, Lawrence TS, Rosenberg SA, editors. DeVita, Hellman and Rosenberg's Cancer Principles & Practice of Oncology. 11th ed. Philadelphia: Wolters Kluwer; 2019.
3. Rindi G, Klimstra DS, Abedi-Ardekani B, Asa SL, Bosman FT, Brambilla E, et al. A common classification framework for neuroendocrine neoplasms: an International Agency for Research on Cancer (IARC) and World Health Organization (WHO) expert consensus proposal. Mod Pathol 2018;31(12):1770–86.
4. MacIntosh PW, Jakobiec FA, Stagner AM, Gilani S, Fay A. High grade neuroendocrine neoplasm of the antrum and orbit. Surv Ophthalmol 2015;60(5):486–94.
5. Yamanouchi D, Oshitari T, Nakamura Y, Yotsukura J, Asanagi K, Baba T, et al. Primary Neuroendocrine Carcinoma of Ocular Adnexa. Case Rep Ophthalmol Med. 2013;2013:1–4.
6. Atik A, Krilis M, Shannon K. Small cell neuroendocrine carcinoma masquerading as cellulitis and causing blindness via bilateral orbital involvement. Orbit2013;32(3):197–9.