Peripheral primitive neuroectodermal tumor of the orbit in Graves' ophthalmopathy – A rare presentation

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Abstract:

Graves' ophthalmopathy is the most common cause of both unilateral and bilateral proptoses in adults. Peripheral primitive neuroectodermal tumor (pPNET) is a small round cell malignant lesion of neuroectodermal origin which very rarely affects the orbit. In this case report, we have discussed about a young woman with existing Graves' ophthalmopathy who presented with worsening proptosis; computed tomography imaging revealed an irregular mass lesion in the right orbit without bone erosion. Biopsy and immunohistochemistry of the mass lesion revealed features of primitive neuroectodermal tumor (PNET). The tumor was MIC-2 gene positive, and on follow-up, no recurrence was noted after successful surgical resection. PNET of the orbit is very rare, and to our best knowledge, this is the first case of peripheral PNET in patent with Graves' ophthalmopathy.

Keywords:

Graves' ophthalmopathy, primitive neuroectodermal tumor, proptosis, small round cell

Introduction

Proptosis in adults is commonly due to thyroid eye disease, and various lesions can complicate the existing eye condition and should be suspicious when the complaints worsen. Primitive neuroectodermal tumor (PNET) typically affects the central nervous system; PNETs involving other systems are diagnosed as peripheral PNET and mostly affect young adults without any sexual predilection. PNET of the orbit is extremely rare, and <10 cases have been reported so far.[1] Diagnosis is based on biopsy showing rosettes/pseudorosettes and positive immunohistochemistry (IHC). The association of orbital PNET with Graves' ophthalmopathy has not been previously reported and should be included as a possibility in young patients.

Case Report

A young woman (32 years) who is a diagnosed case of Graves' disease presented with complaints of worsening protrusion of the right eye with orbital pain and double vision for 2 months. On examination her visual acuity in both eyes were 6/6, proptosis noted in both eyes with Hertel's exophthalmometer reading of 24 mm in the right eye and 20 mm in the left eye measured at 100 mm with signs of thyroid eye disease like Joffroy's sign, Dalrymple's sign were positive. On palpation, a nontender firm, fixed globular mass, nonpulsating with irregular surface of size 3 cm × 3 cm, is noted in the superotemporal quadrant. Blood investigations including complete hemogram with erythrocyte sedimentation rate and peripheral smear were done (normal limits). Thyroid profile showed levels suggestive of hyperthyroidism. Computed tomography (CT) imaging revealed a soft-tissue irregular mass in the superotemporal region of the right orbit without any evidence of bony erosion along with bulkiness all four rectus muscle noted [Figure 1].

No evidence of any lymph node involvement and metastatic workup was negative. The patient line of management was planned as per the biopsy report. Lateral orbitotomy of the right orbit was done, and *en bloc* excision of the lesion was done. The lesion was removed completely without any residual tissue. Grossly, the tumor is well encapsulated and weighs 10 g. The tissue

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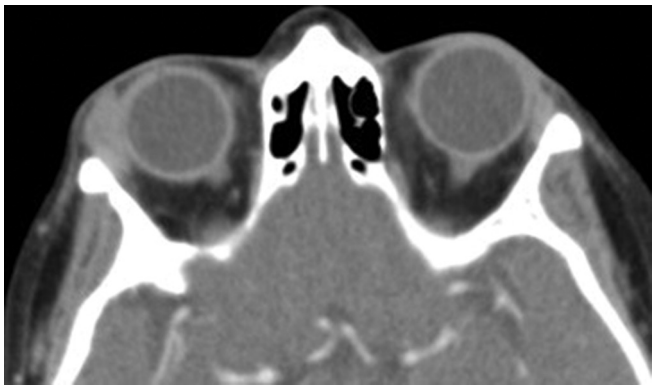

Figure 1: Axial computed tomography image of the orbit/brain showing soft-tissue lesion in the superotemporal region of the orbit

was fixed with 10% neutral buffered formalin and fragment is embedded in paraffin, the sections from it are stained with hematoxylin and eosin. Histopathological examination revealed small round cells having eosinophilic cytoplasm arranged in sheets. Few cells were seen around blood vessels suggestive of pseudorosettes [Figure 2].

IHC studies were done for neuron-specific enolase (NSE), leukocyte common antigen, and MIC-2 gene using avidin-biotin technique. MIC-2 and NSE were positive in IHC. Diagnosis of peripheral PNET of the orbit is made with the above findings. PNET with MIC-2 positive is usually less malignant and so the patient was advised for serial close follow-up with oral painkillers for the initial few weeks postoperative period and no other treatment modalities employed. On follow-up, the patient complaints gradually subsided with only minimal eye pain and no diplopia. On serial follow-up for 2 years with CT imaging performed every 6 months, no evidence of recurrence has been made out.

Discussion

Proptosis describes an abnormal protrusion of an organ but is generally applied to the eyeball; exophthalmos refers specifically to the eyeball only.[2] Thyroid eye disease is the most common underlying cause of proptosis in adults, but on rare occasions, other lesions can coexist and worsen an existing condition. Graves' ophthalmopathy is a state of inflammation with lymphocyte infiltration and so many cases of lymphoma associated with Graves have been described.[3] To our best knowledge, PNET of the orbit is very rare, and this is the first case of Graves with peripheral PNET of the orbit.

Peripheral primitive neuroectodermal tumor (pPNET) comes under Ewing sarcoma type of tumors. The genetic modification found among PNET includes translocation of chromosome 22, commonly seen in young people or adolescence. Histopathology is characterized by small, round, blue cell tumor with sheet-like arrangement of cells, pseudorosette formation. IHC studies for the sample typically show MIC-2 positivity and various IHC positivity seen in few cases of PNET include NSE, synaptophysin, and S-100. MIC-2 gene

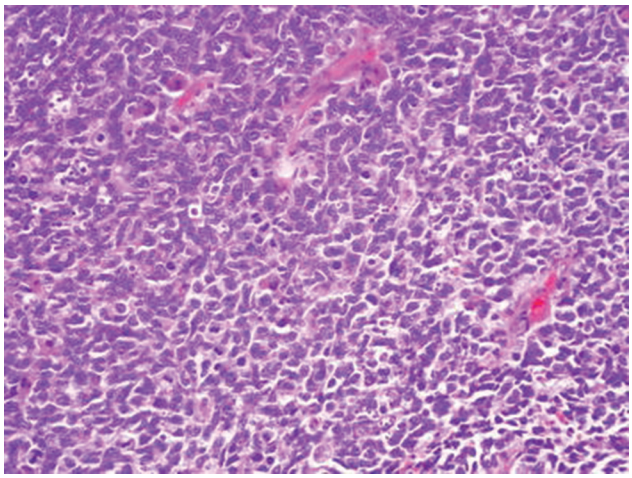

Figure 2: Histopathological examination of section showing cells with eosinophilic cytoplasm and few pseudorosettes

is a pseudoautosomal gene located in q arms of X and Y chromosomes; various proteins have been contributed by MIC-2 gene like neuraminidase and protease.[4] The first case of intraconal pPNET with MIC-2 positivity has been described by Alyahya GA *et al*., where a child also had microphthalmia.[5] MIC-2 gene positivity helps to differentiate from other small, round blue cell tumors which is often highly malignant with poor prognosis.

In our case report, a young woman with Graves' ophthalmopathy with proptosis and other thyroid eye signs presented with worsening of complaints. Examination revealed a mass lesion in the superotemporal quadrant of the right eye which also is confirmed by the help of CT imaging and complete excision carried out via lateral orbitotomy. Histopathology and IHC revealed features of small, round blue cell tumor with MIC-2 gene positivity which is suggestive of pPNET. The tumor is MIC-2 positive and PNET associated with it is usually less malignant, and since the tumor is removed completely by lateral orbitotomy following lateral cantholysis and canthotomy without removal of lateral orbital rim, the patient is kept on serial close follow-up without any other treatment employed. On follow-up, complaints resolved and no recurrence has been found on serial monitoring with imaging. CT of the orbit, brain, and paranasal sinuses was performed every 6 months to watch for any recurrence, and the patient did not develop any recurrence after 2 years of follow-up. Prompt intervention is required in cases with worsening of proptosis because the lesion can be sight threatening; compressive optic neuropathy, vascular occlusion of the eye, glaucoma due to elevated episcleral venous pressure, and corneal lesion due to exposure keratopathy are various causes of sight loss. Tamer C *et al*. and Sen *et al*. previously have reported a case of orbital pPNET and its treatment by excision, but they were not associated with thyroid eye disease.[6,7] To our knowledge, our case report is the first to show pPNET orbit in a young woman with Graves' ophthalmopathy.

In conclusion, the case report highlights the existence of pPNET orbit in a young woman with Graves' ophthalmopathy and the importance of biopsy with IHC in diagnosing the lesion, and to our best knowledge, this is the first case to be reported. Worsening complaints in Graves' ophthalmopathy requires attention and prompt workup for diagnosing associated pathology.

Declaration of patient consent

The authors certify that we have obtained appropriate patient consent forms. In the forms, the patient has given her consent and other clinical information to be reported in the journal. The patient understands that her name and initials will not be published and due efforts will be made to conceal her identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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