Perineuritis or infiltration of optic nerve sheath? A presentation of diffuse large B cell Gastric lymphoma

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Optic perineuritis is an inflammatory disorder involving the optic nerve sheath. It is currently considered as a part of idiopathic orbital inflammatory disease which also includes dacryoadenitis, orbital myositis, superior orbital fissure, and cavernous sinus syndrome (Tolosa hunt syndrome). As it is idiopathic, it is considered a diagnosis of exclusion. Another important differential is optic nerve lymphoma. Isolated optic nerve lymphoma associated with systemic involvement has been described in literature. We report a case that presented as third nerve palsy but later on developed central retinal vein occlusion and was ultimately diagnosed as primary gastric lymphoma of diffuse large B cell type.

Key words: Gastric lymphoma, optic perineuritis, orbital inflammatory disease

Orbital inflammatory disease (OID) may present with pain, localized swelling, ocular motility defects depending on the structure involved. Optic perineuritis (OPN) is a type of orbital inflammation that specifically involves optic nerve sheath (ONS) along with surrounding muscles and fat. MRI features in OPN is classically seen as "tram track sign". Important differential diagnoses of "tram track sign" are meningioma, optic nerve lymphoma, and metastasis.[1] We report a case that presented as OPN and was eventually diagnosed to have primary gastric cell lymphoma.

Case Report

A 76-year-old male patient presented with complaint of sudden onset of drooping of left eye (LE) lid along with deviation of the LE. There was no history of any systemic illness. His best corrected visual acuity was 20/200 in both the eyes which corroborated with the presence of cataract. Both the pupils were 3 mm in size with no RAPD, with normal fundus examination. There was complete ptosis with limitation of adduction, elevation and depression in LE. The ocular movements in right were full and rest of the examination was normal. The 4th, 5th, and 6th cranial nerves were normal. Based on examination, a diagnosis of LE pupil sparing oculomotor nerve palsy was made. Considering the age of the patient he was evaluated to rule out a possible ischemic aetiology. His blood pressure, lipid profile, blood sugar was within normal levels, but he had elevated serum homocysteine levels (30 μmol/L). Patient was prescribed folic acid 1 mg, pyridoxine 10 mg and cyanocobalamin 400 mcg per day. However, two weeks later, the patient presented with acute onset visual loss in LE associated with upper lid swelling and pain. His current vision in LE was light perception only. Fundus examination showed central retinal vein occlusion (CRVO) [Fig. 1]. The oculomotor nerve palsy had also progressed to involve pupil leading to anisocoria [Fig. 2]. The consensual reflex of the other eye was also affected. Suspecting a compressive or an inflammatory aetiology, an urgent contrast enhanced MRI of orbit and brain was obtained. It showed diffuse enhancement of the ONS up to the apex with mild surrounding fat tissue stranding which was suggestive of OPN [Fig. 3]. There was mild enhancement of proximal extraocular muscles also. Brain MRI was normal. Further workup was done to rule out any inflammatory disorder. It revealed elevated ESR (37 mm/h) and CRP (22.7 mg/L). Other tests including CBC, chest X-ray, mantoux test, VDRL, HIV, HBsAg, anti-HCV, P- ANCA, C-ANCA, ANA, serum ACE, and calcium levels were normal. A provisional diagnosis of OPN with pupil involving oculomotor nerve palsy with CRVO was made. In view of the age, raised CRP and radiological features of the patient, Positron-emission tomography (PET) scan was also ordered simultaneously to screen for malignancy. It remarkably showed high uptake at the greater curvature of the stomach suggestive of either a gastric ulcer or carcinoma. It also showed mild uptake in the left ONS but no uptake was seen in the brain. Endoscopic biopsy of the gastric lesion confirmed the diagnosis of diffuse large B cell lymphoma. The histopathological report revealed infiltration of lamina propria by large atypical lymphoid cells and destruction of most of the crypts. It was positive for CD 20, CD 10, BCL6 immune markers [Fig. 4]. MUM1 immune marker was negative. CECT abdomen was done which showed involvement of mesenteric node in the vicinity of lesion. CSF Analysis with cytology was also planned for the patient to rule out leptomeningeal involvement but patient refused any further management.

Discussion

Ocular motility disorders are part of OID. However, in our case, old age, absence of inflammation and sparing of pupil at the initial

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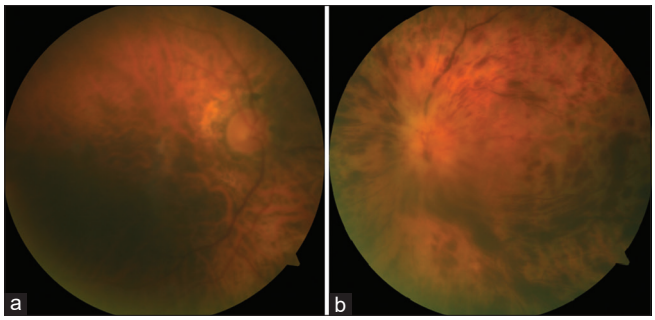

Figure 1: (a and b) Fundus pictures of both the eyes showing CRVO in the LE (b)

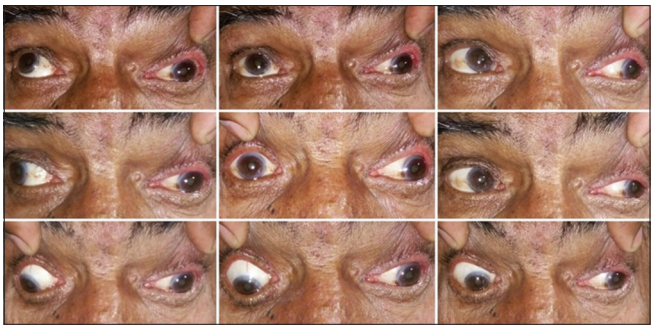

Figure 2: Nine gaze picture of the patient showing left eye pupil involving complete oculomotor nerve palsy

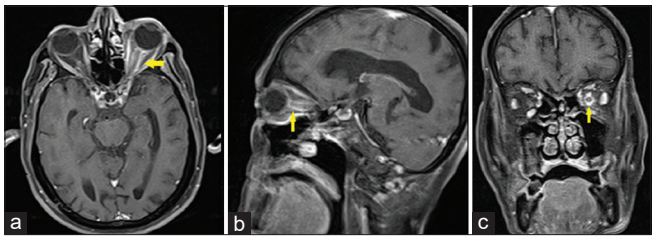

Figure 3: (a) T1, axial, fat suppressed, post contrast MRI image showing enhancement of left optic nerve sheath and mild surrounding fat tissue stranding. (b) T1 sagittal oblique, fat suppressed, post gadolinium contrast MRI image showing left optic nerve sheath enhancement (tram track sign). (c) T1, coronal, fat suppressed, post contrast MRI image showing left optic nerve sheath enhancement and mild surrounding fat tissue stranding (doughnut sign)

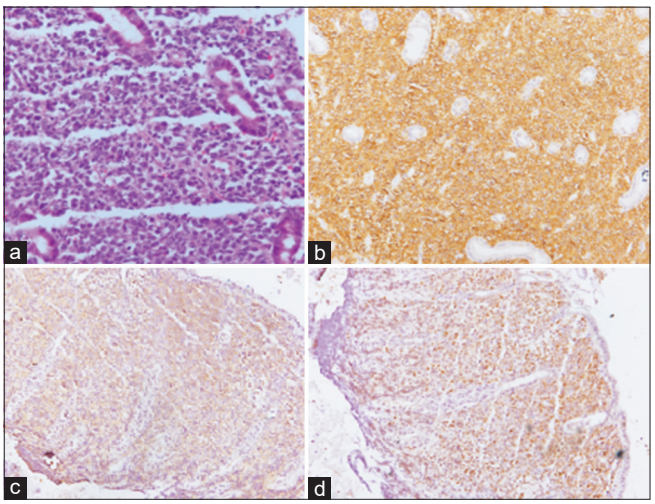

Figure 4: (a) Histopathological report of the gastric biopsy showing infiltration of lamina propria by large atypical lymphoid cells. There is destruction of most of the crypts with only few preserved crypts (Hematoxyline And Eosin stain, 200×). Result of Immune markers which were applied for tissue characterization were: (b) CD 20 positive (100×), (c) CD 10 positive (100×), (d) BCL6 positive (100×)

presentation led to the diagnosis of ischemic mononeuropathy which does not require immediate neuroimaging.[2] The risk factor in form of hyperhomocystenemia was identified and treated accordingly.[3] Hyperhomocystenemia has been found to be an independent risk factor for CRVO as well.[4] Nevertheless the rapid progression of the oculomotor nerve palsy, signs of inflammation warranted a neuro-imaging. The imaging showed enhancement of ONS and involvement of orbital tissue at orbital apex. Thus, the diagnosis of OPN along with oculomotor nerve palsy and CRVO was made. However, the possibility of ophthalmoplegia from extraocular muscle involvement cannot be ruled out.

OPN is inflammation of the ONS *per se*. The characteristic radiological feature is described as a "tram track appearance" due to enhancement of the sheath without nerve enhancement. The other radiological findings include involvement of extraocular muscles and surrounding orbital tissue. It may be a manifestation of idiopathic OID or systemic granulomatous diseases like sarcoidosis, tuberculosis, and vasculitis.

In the largest case series of 14 patients with OPN reported by Purvin *et al*.,[1] 4 had ocular motility defects which were either coexistent at the time of presentation or developed later. However, it is remarkable to note that in our patient, the nerve palsy preceded the perineuritis. Incidentally, oculomotor dysfunction is a common manifestation of lesions at orbital apex and there is a possibility that nerve itself may have got involved due to its proximity to the optic nerve. It may be difficult to isolate whether it was extraocular muscles involvement or compression of nerve that led to ophthalmoplegia. However, since the abduction was not severely involved, it makes us inclined towards the compression of nerve as the probable cause. Vascular occlusions have also been reported infrequently and may occur due to compression of the vessels within the inflamed ONS, rather than due to inflammation.[5,6]

Interestingly, tram track appearance can also be seen in meningioma, lymphoma, or metastasis. A systemic evaluation was necessary to find out any primary site of inflammation or neoplasm. Hence, a PET scan was ordered which revealed the presence of gastric lesion which was proven as B cell lymphoma on biopsy.

Lymphoma in optic nerve or sheath has been classified as: primary optic nerve involvement, optic nerve involvement with CNS disease, optic nerve involvement with systemic disease, and optic nerve involvement with primary intraocular lymphoma.

There are total five cases of optic nerve involvement with Large B cell lymphoma described in literature [Table 1].[7-10] Four

Table 1: Cases of diffuse large B cell Lymphoma associated with optic nerve involvement

Author (year)	Age/ sex	Vision	Fundus findings	Imaging (Brain, Orbit)	Primary locus	CSF analysis
Saatci (1999)[6]	14 yr/M	No light perception	CRAO & CRVO	MRI-periventricular involvement	CNS	High protein
Lee (2002)[7]	56 yr/M	20/400	Optic disc head swelling with retinal haemorrhage	MRI-Paraventricular nodules with optic nerve and sheath enhancement	CNS	WNL
El Kettani (2006)[8]	75 yr/F	No light perception	Optic disc edema	CT- bilateral optic nerve involvement	CNS	Atypical lymphocytes
Matsuyama (2013)[9]	84 yr/F	No light perception	Not Available (NA)	MRI- Suprasellar tumour	CNS	NA
Kim (2010)[10]	2 yr/F		Optic disc edema	CT Abdomen- lesion involving both kidneys, inguinal lymph nodes, subcutaneous suprapubic lesion	Kidneys, inguinal nodes, subcutaneous suprapubic lesion	No malignant cells seen

of these cases had associated CNS involvement while one had systemic disease. Since our patient did not give consent for CSF cytology, we can never be sure if this was metastasis to CNS primarily involving optic nerve or was it simply inflammation of the optic nerve? Absence of uptake in the brain may rule out any other site of CNS metastasis. Moreover, normal CSF analysis in presence of isolated optic nerve involvement in cases of systemic lymphomas has been reported.[11] There is also a theoretical possibility that this may be an inflammatory manifestation of the lymphoma which cannot be proven without extensive immune-histopathological investigations.

Conclusion

This case emphasizes that even though optic perineuritis falls under spectrum of idiopathic orbital inflammatory disease, a meticulous systemic work up should be done to rule out not only infective, inflammatory causes but also neoplastic aetiology.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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