CASE REPORT

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Optic Perineuritis: How Does it Differ from Optic Neuritis?

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ABSTRACT Sometimes, a diagnostic error between optic neuritis (ON) and optic perineuritis (OPN) can occur. The differential diagnosis of these two entities is very important because the prognosis and response to treatment are different from each other. We describe here three unusual OPN cases that presented with the symptom of sudden onset blurred vision and are associated with different etiologies (Familial Mediterranean fever, Lyme disease and possible Behcet's disease). Ophthalmological examination and optical coherence tomography can not clearly discriminate ON from OPN, however, magnetic resonance imaging of the optic nerve can help form a diagnosis through the typical appearance of optic nerve enhancement and myeline sheath detachment. These cases are discussed in detail in this article.

Keywords: Optic perineuritis; familial mediterranean fever; lyme disease; possible Behcet's disease

Optic perineuritis (OPN) and acute optic neuritis (ON) are clinically similar disorders. Sometimes, ocular motility disturbances, ptosis, and chemosis can accompany OPN. While ON is common in multiple sclerosis, OPN can be related to vascular, toxic, infectious, metabolic, neoplastic and inflammatory etiologic factors. Unlike demyelinating ON, central vision is spared in OPN, and it responds well to corticosteroids but recurrence is more likely to occur. Differential diagnosis of these disorders is usually dependent on radiologic features.[1,2] Fat-suppressed, contrasted magnetic resonance imaging (MRI) sequences can aid in recognizing the distinction between the two disorders.[3] The differential diagnosis is very important because the prognosis and the response to treatment are different.[1,2] In this article, we report three rare cases with clinical, ophthalmologic and radiologic findings.

CASE REPORTS

CASE 1

A seventy-five-year-old man was referred to our outpatient clinic complaining of the sudden onset of blurring, redness, and pain in the left eye for two days. Neurologic examination showed restricted abduction of the left eye in a conjugate horizontal gaze with a mildly dilated left pupil. Edema of

the left optic disc was determined by fundoscopic examination. The best corrected visual acuity was 20/30 in both eyes. Computerized visual field (VF) analysis demonstrated peripheral defect in right eye and almost total defect in left eye. The retinal nerve fiber layer (RNFL) analysis made by optic coherence tomography (OCT) was normal in the right eye, and borderline segment reduction was detected in the left eye (Figure 1). T1 fat-supressed axial image and post-contrast MRI images showed tram-track appearance and enhancement around the left optic nerve. Four months before the current status, the patient had an acute febrile episode, arthralgia with an elevated level of acute phase reactants (erythrocyte sedimentation rate (ESR) 60 mm/h, C-reactive protein (CRP) 14 mg/L). Repeated laboratory testing included determination of hemoglobin (HGB), glucose, CRP, ESR were normal. He has a family history of Familial Mediterranean Fever (FMF). The gene analysis for mutations in the MEFV gene was made by polymerase chain reaction (PCR). It was analyzed by direct sequencing of exons 2, 3, 5, 10 of the MEFV gene. The gene analysis revealed a heterozygosis of R202Q. The patient received high dose (1000 mg/per day) intravenous methylprednisolone (IV MPZ) for 7 days. MPZ was continued orally at 1 mg/kg/day for 1 month and terminated through gradual reduction. Colchicine was started at a dosage of 0.6 mg twice per day and gradually increased. He recovered his vision almost completely after 3 months.

CASE 2

A forty-year-old woman was referred to our outpatient clinic with a progressive visual loss in her right eye over a period of one month. Neuro-ophthalmologic examination revealed only light perception in the right eye and 20/20 in the left eye. The ocular motility was normal. Fundoscopic examination demonstrated paleness and papilledema of the right optic disc and normal appearance of the left optic disc. Computerized VF analysis demonstrated complete VF loss in the right eye and normal VF in left eye. A T1 fat-suppressed axial image showed significant enhancement around the right optic nerve and normal parenchyma of the brain (Figure 2). Routine laboratory investigations including blood cell count with the exception of high leukocyte count (12.600/mm^3), transaminase, CRP, ESR, blood creatinine and electrolytes, thyroid stimulating hormone and uric acid were normal. Extractable nuclear antigen (ENA) profile was negative. The Rose Bengal plate test, the Brucella standard agglutination test, human immunodeficiency virus (HIV) antibodies, venereal disease research laboratory (VDRL) test, Treponema pallidum hemagglutination (TPHA) and HLA–B51 tests were also negative. Lyme IgM antibody ELISA was positive at 1.2 (≥1.10 was positive) and IgG antibody was negative at 0.24. The blood sample has been verified by Western blot test that was found positive, and patient was examined by infectious diseases specialist. The patient was treated with oral doxycycline (100 mg twice per day) for 6

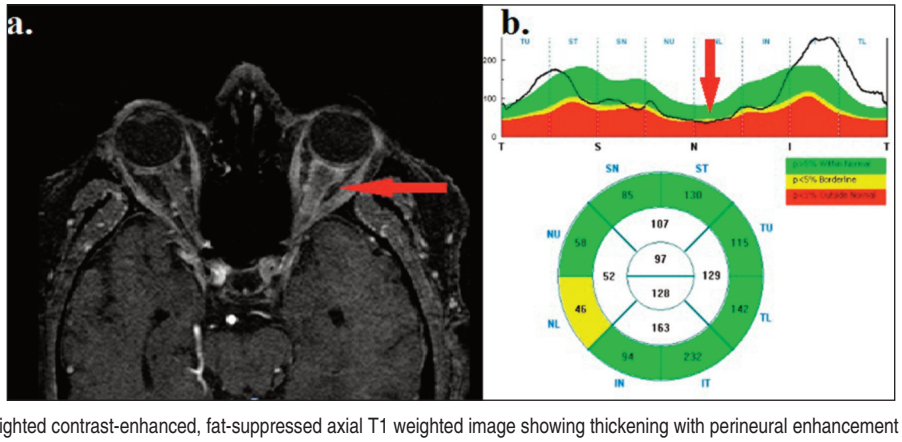

FIGURE 1: a) T1-weighted contrast-enhanced, fat-suppressed axial T1 weighted image showing thickening with perineural enhancement of left optic nerve; **b)** Optical coherence tomography showing mild reduction in retinal nerve fiber layer thickness in left eye affected by optic perineuritis.

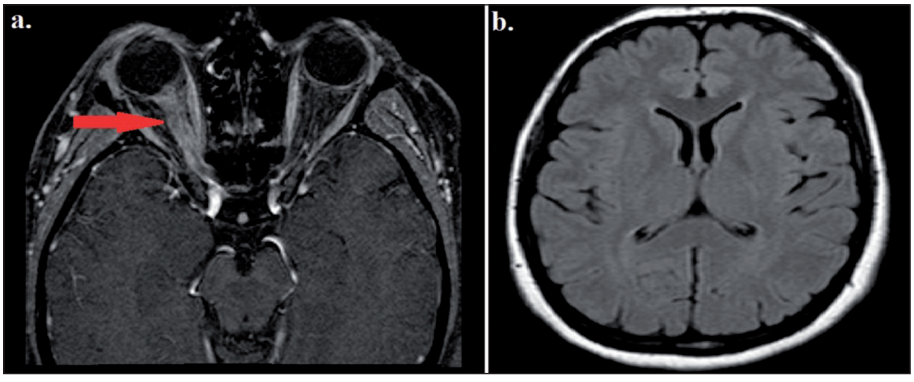

FIGURE 2: a) Fat-suppressed magnetic resonance imaging scan of the orbita with contrast enhancement in an axial image; **b)** Axial T1 weighted image of brain shows normal parenchyma.

months. After six months, Lyme IgM antibody was negative and the drug was discontinued. Her ophthalmologic examination showed that visual acuity was 10/20 in the right eye.

CASE 3

A forty-six-year-old woman was referred to our outpatient clinic due to visual loss in the left eye for five days. In her eye examination, best corrected visual acuity was 20/20 in the right eye and counting fingers at 1 meter in the left eye. On fundoscopic examination, temporal paleness on the left optic disc was determined, while fundoscopy of the right eye was normal. Inferior altitudinal VF defect in the left eye was detected by computerized VF test. However, the retinal nerve fiber layer at OCT was normal. A neurologic examination was normal except for blurred vision in the left eye. T1 fat-suppressed MRI images showed detachment of the optic sheath and enhancement around the left optic nerve (Figure 3). There were no other pathological finding in the brain or cervical spine.

Routine laboratory investigations transaminase, ESR, CRP, blood creatinine and electrolytes, TSH, and uric acid were normal. Anti-nuclear antibody and ENA profile were also negative. Rose Bengal Plate Test, the Brucella Standard Agglutination Test, HIV antibodies, TPHA, and VDRL tests were negative. The HLA-B51 test was found positive. The patient received high dose (1000 mg/per day) IV MPZ for 7 days, and treatment was continued with oral dexamethasone (5 mg/day) and azathioprine (100 mg/day). Her vision recovered almost completely 6 months later.

Written informed consent was obtained from all the patients for publishing this case reports.

DISCUSSION

Optic perineuritis (OPN) is an inflammatory disorder of the optic nerve sheath characterized by visual disturbance.[2] OPN has a different etiology and treatment than ON. Clinical findings, VF test, OCT and MRI take an important role in differential diagnosis.[1,2] The diagnosis of OPN is based on clinical and radiological findings. Patients symptoms may consist of sudden or progressive visual loss in one eye accompanied or not by eye pain. Orbital MRI demonstrated contrast enhancement around the optic nerve on fat-suppressed, contrasted sequences.[3] "Tramtrack" sign on axial views and "doughnut" sign on coronal views are caracterstic for OPN.

Age may be an important factor that differentiate OPN from ON.[2] ON is common in young individuals, especially if it is associated with multiple sclerosis. OPN is seen in older individuals. The age of our three patients are above 40 years old and supports this data.

It has been reported that syphilis, tuberculosis, sarcoidosis, giant cell arteritis, Crohn disease, herpes zoster, Wegener granulomatosis are specific causes of OPN.[1,2,4]

Familial Mediterranean fever (FMF) is an auto-inflammatory disease which starts during childhood or adolescence with recurrent poly-

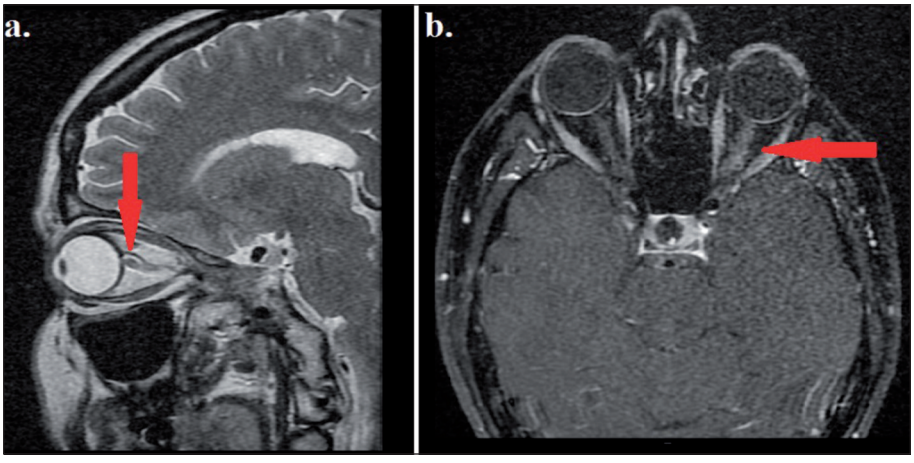

FIGURE 3: a)T2-weighted sagittal image and, **b)** T1 weighted fat-suppressed contrast-enhanced axial images show thickening with perineural enhancement of left optic nerve.

serositis attacks. Although it has been reported that uveitis, retinal ischemia, cataract, glaucoma and retinal detachment are related to FMF, optic nerve involvement has been rarely reported in the literature.[5] Alim et al. evaluated the thickness of the peripapillary retinal nerve fiber layer (RNFL) and retinal ganglion cell-inner plexiform layer (GCIPL) in 42 adult-onset FMF patients by OCT but no relation was detected.[6] The inflammatory process mediated by IL-1β can be responsible for FMF-related optic nerve involvement.[5] The diagnosis of case 1 was established as OPN related to adult-onset FMF. To the best of our knowledge this is the first case of OPN in medical literature associated with FMF.

Lyme related ON (LRON) is a very rare ocular manifestation of Lyme disease. It has been reported that Lyme seropositivity and isolated ON can be controversial. Sibony et al. examined 440 patients with ON and they have found that Lyme enzyme-linked immunosorbent assay (ELISA) was positive in 6.4% of the patients. They reported that asymptomatic cases, false-positive results, cross-reactive reaction, and non-specific humoral reactions can be high.[7] Kubova et al. examined 81 patients with neuro brucellosis and LRON was found in 27% of the patients.[8] In Case 2, despite the positive detection of Lyme antibodies, the insufficient response to treatment may be associated with false positives.

Behcet's disease can cause both ON and OPN.[9] Our third patient does not fit the International Criteria for Behcet's Disease.[10] She had no recurrent mouth ulcers, genital ulcers, uveitis, skin lesions and/or arthralgias. Only HLA-B5 was positively detected. It may be the first presenting symptom of Behcet's disease or a false positive response.

Investigation of the etiological factors and differential diagnosis for ON and OPN cases take a critical role in treatment. The initial symptoms may vary and many infectious, inflammatory and autoimmune disorders may be the reason for ON or OPN in most of the cases. Physicians must keep in mind that MRI and accompaing clinical findings can help to discriminate OPN from ON. Further research is needed.

Informed Consent

Informed consent was obtained from the patients. Consents were obtained from the patients and their legal guardian to publish the case reports, and information was de-identified to protect anonymity.

Authorship Contributions

Idea/Concept: *Sibel Karşıdağ;* ***Design:*** *Sevki Şahin;* ***Control/Supervision:*** *Nilgün Çınar;* ***Data Collection and/or Processing:*** *Miruna Florentina Ateş;* ***Analysis and/or Interpretation:*** *Ziya Akingöl;* ***Literature Review:*** *Sibel Karşıdağ;* ***Writing the Article:*** *Sevki Şahin;* ***Critical Review:*** *Miruna Florentina Ateş;* ***References and Fundings:*** *Miruna Florentina Ateş.*

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

REFERENCES

1. Takemaru M, Tachiyama K, Shiga Y, Kanaya Y, Shimoe Y, Kuriyama M. [A case of optic perineuritis-a literature review of Japanese cases and clinical problems]. Rinsho Shinkeigaku. 2017;57(11):716-22. [Crossref] [PubMed]
2. Bergman O, Andersson T, Zetterberg M. Optic perineuritis: a retrospective case series. Int Med Case Rep J. 2017;10:181-8. [Crossref] [PubMed] [PMC]
3. Tien RD, Hesselink JR, Szumowski J. MR fat suppression combined with Gd-DTPA enhancement in optic neuritis and perineuritis. J Comput Assist Tomogr. 1991;15(2):223-7. [Crossref] [PubMed]
4. Bansal R, Singh R, Takkar A, Lal V. Combined central retinal artery and vein occlusion with optic perineuritis following herpes zoster dermatitis in an immunocompetent child. Indian J Ophthalmol. 2017;65(11):1233-5. [Crossref] [PubMed] [PMC]
5. Başaran Ö, Kavuncu S, Güven A, Uncu N, Acar-Çelikel B, Çakar N. Familial Mediterranean fever associated with optic neuritis, successfully treated with anti-interleukin 1 agents. Turk J Pediatr. 2016;58(3):327-30. [Crossref] [PubMed]
6. Alim S, Esen M, Demir AK, Demir S, Ortak H, Güneş A, et al. Peripapillary retinal nerve fiber layer and ganglion cell-inner plexiform layer thickness in adult-onset familial Mediterranean fever. Int Ophthalmol. 2018;38(1):183-90. [Crossref] [PubMed]
7. Sibony P, Halperin J, Coyle PK, Patel K. Reactive Lyme serology in optic neuritis. J Neuroophthalmol. 2005;25(2):71-82. [Crossref] [PubMed]
8. Kubová Z, Szanyi J, Langrová J, Kremlácek J, Kuba M, Honegr K. Motion-onset and pattern-reversal visual evoked potentials in diagnostics of neuroborreliosis. J Clin Neurophysiol. 2006;23(5):416-20. [Crossref] [PubMed]
9. Erdoğan S, Sorgun MH, Yalçındağ N, Atilla H, Yücesan C. Bilateral optic neuritis in a patient with Behçet's disease who respond to therapeutic plasma exchange. J Neuroophthalmol. 2015;35(4):342-7. [Crossref] [PubMed] [PMC]
10. International Study Group for Behcet's Disease. Criteria for diagnosis of Behçet's disease. International Study Group for Behcet's Disease. Lancet. 1990;335(8697): 1078-80.