A review of optic perineuritis

Evelyn Tai Li Min1,2, Jessica Mani Penny Tevaraj1,2, Lakana Kumar Thavaratnam1,2, Raja Azmi Mohd Noor1,2, Win Mar Salmah2,3, Wan Hazabbah Wan Hitam1,2

1Department of Ophthalmology, School of Medical Sciences, Health Campus, Universiti Sains Malaysia, Kubang Kerian, Kelantan 16150, Malaysia
2Hospital Universiti Sains Malaysia, Kubang Kerian, Kelantan 16150, Malaysia
3Department of Radiology, School of Medical Sciences, Health Campus, Universiti Sains Malaysia, Kubang Kerian, Kelantan 16150, Malaysia

Correspondence to: Evelyn Tai Li Min. Department of Ophthalmology, School of Medical Sciences, Health Campus, Universiti Sains Malaysia, Kubang Kerian, Kelantan 16150, Malaysia. daileid@yahoo.com

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Abstract

Optic perineuritis (OPN) refers to a spectrum of conditions involving pathologic inflammation of the optic nerve sheath. The classic triad of OPN consists of unilateral optic neuropathy associated with pain and/or disc oedema, but the condition often mimics other optic neuropathies, resulting in delayed diagnosis and suboptimal treatment.

We performed a database search of Medline and Ovid in January 2016 for articles published in any language with the keywords ‘optic perineuritis’. Sixty articles were found, published from 1956 to 2015. Two reviewers (Tai ELM and Tevaraj JMP) performed an independent screening of abstracts. Articles of interest were subsequently examined for the clinical presentation, etiology, natural history and outcome of this condition. In cases where references to previous publications were made, we screened those references for potentially relevant studies, and where applicable, the original publication is cited.

CLINICAL FEATURES

Clinically, OPN usually presents with an optic neuropathy accompanied by pain and disc edema11. Involvement tends to be unilateral, with pain exacerbated by eye movements11. As most patients with OPN tend to be female, as occurs in ON, it is difficult to distinguish these two on the basis of clinical presentation alone, especially as its unilateral presentation tends to mimic optic neuritis11,14-15. Bilateral OPN is rare, and often attributed to underlying systemic disease12,16-19.

INTRODUCTION

Orbital inflammatory disease (OID) may involve multiple tissues, such as in diffuse anterior OID, or be restricted to specific structures, as occurs in orbital pseudotumour, myositis, periscleritis and perineuritis1-5. Optic perineuritis (OPN) is a rare presentation within the spectrum of conditions classified as OID, in which optic nerve sheath is the predominant tissue involved1,6-7.

First described in 1883, OPN encompasses a range of disorders characterized by pathologic inflammation of the optic nerve sheath, resulting in marked thickening due to nonspecific fibrosis1. It is usually unilateral and idiopathic, although infectious8 and autoimmune9-11 causes have been reported. Clinically, this disease may mimic retrobulbar optic neuritis (ON), or cause optic disc swelling that may simulate an optic nerve sheath meningioma (Figure 1)12-13.

METHODS

We performed a database search of Medline and Ovid in January 2016 for articles published in any language with the keywords ‘optic perineuritis’. Sixty articles were found, published from 1956 to 2015. Two reviewers (Tai ELM and Tevaraj JMP) performed an independent screening of abstracts. Articles of interest were subsequently examined for the clinical presentation, etiology, natural history and outcome of this condition. In cases where references to previous publications were made, we screened these references for potentially relevant studies, and where applicable, the original publication is cited.


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Clues to the diagnosis of OPN may be derived from minor differences between the presentation and course of OPN and ON. Firstly, the age distribution of patients with OPN is broader, and the average age of patients older than in ON, with the mean being in middle age \[1,20-21\]. Secondly, patients with OPN tend to have a paracentral or arcuate scotoma, rather than the central scotoma commonly associated with ON \[1\]. Thirdly, subacute onset of the disease (over weeks), with progressive visual loss without treatment, is typical of OPN \[1\].

The key features differentiating optic perineuritis from optic neuritis are outlined in the following table (Table 1).

Although the majority of cases of OPN are idiopathic, physical examination should be performed to look for signs of specific infectious and inflammatory causes, such as syphilis \[12,16,18\], tuberculosis \[8\], sarcoidosis \[9\], giant cell arteritis \[19\] and Wegener’s granulomatosis \[10,22\]. Previous literature has attributed most cases of bilateral OPN to systemic conditions, especially syphilis \[12,16,18\]. Autoimmune causes are emerging as another significant risk factor \[23-24\], with a recent review observing that almost 50% of patients diagnosed with OPN over a 7y period had associated Behcet’s disease \[25\]. The majority of patients in that study were only diagnosed with Behcet’s disease after the diagnosis of OPN was made, which suggests that OPN may be a precursor to other autoimmune conditions \[25\].

### INVESTIGATIONS

The diagnosis of OPN itself can be confirmed by histopathologic or radiographic demonstration of peri-neurial inflammation. The histological feature is inflammation of the optic nerve sheath, evidenced by a predominantly lymphocytic infiltrate and/or peri-neural fibrous tissue \[1,13,26\]. However, an optic nerve biopsy is not routinely indicated, as the diagnosis may be readily made based on the clinical and radiographic findings \[1\].

Radiological imaging is indispensable in making a diagnosis of OPN. The characteristic finding in OPN is contrast enhancement of the intra-orbital optic nerve sheath with sparing of the optic nerve, seen as a ‘tram track sign’ on axial view and a ‘doughnut sign’ on coronal view (Figure 2) \[1\]. Although these abnormalities may be detected on computed tomography (CT) scanning, the spatial resolution of CT is insufficient to distinguish peri-neural enhancement from the intra-neural enhancement seen in demyelinating ON \[1\].

Ideally, a fat-suppressed, post-gadolinium contrast magnetic resonance imaging (MRI) of the orbit should be performed to look for the classic perineural contrast enhancement of OPN \[1,21,27\]. The optic nerve itself may occasionally also show enhancement, due to contiguous inflammation of the intra-neural pial septa. Other radiographic findings include streaky

### Table 1 Key differences between optic perineuritis and optic neuritis

<table>
<thead>
<tr>
<th>Features</th>
<th>Optic perineuritis</th>
<th>Optic neuritis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pathology</td>
<td>Optic sheath inflammation</td>
<td>Optic nerve inflammation</td>
</tr>
<tr>
<td>Age distribution</td>
<td>Older</td>
<td>Younger</td>
</tr>
<tr>
<td>Onset of visual loss</td>
<td>Subacute</td>
<td>Acute</td>
</tr>
<tr>
<td>Scotoma</td>
<td>Paracentral/arcuate</td>
<td>Central</td>
</tr>
<tr>
<td>MRI findings</td>
<td>Peri-neural enhancement (‘tram track sign’ on axial view and ‘doughnut sign’ on coronal view). Fat streakiness may also be present.</td>
<td>Intra-neural enhancement</td>
</tr>
<tr>
<td>Response to corticosteroids</td>
<td>Visual function often improves dramatically with corticosteroid treatment.</td>
<td>Intravenous methylprednisolone followed by oral prednisolone may speed recovery, but does not affect final visual outcome.</td>
</tr>
<tr>
<td>Relapse in relation to corticosteroid therapy</td>
<td>Risk of relapse if duration of corticosteroid therapy is inadequate.</td>
<td>Higher risk of recurrence with use of oral prednisolone alone (without a preceding course of intravenous methylprednisolone)</td>
</tr>
<tr>
<td>Natural history</td>
<td>Progressive deterioration without treatment</td>
<td>Recovers spontaneously</td>
</tr>
</tbody>
</table>

![Figure 1 Fundus photos of various presentations of OPN](image)

A: Normal optic disc; B: Bilateral generalised optic disc swelling with splinter haemorrhages.
enhancement of orbital fat and subtle enhancement of extraocular muscles and/or sclera\textsuperscript{[1]}. These findings are in contrast to the radiological appearance of optic neuritis, in which the mean cross-sectional area of the optic nerve is initially increased, due to oedema; subsequently, optic atrophy usually develops\textsuperscript{[28]}. Other investigations which may be useful to rule out infectious, inflammatory or autoimmune diseases include serological tests for syphilis\textsuperscript{[18]}, a Mantoux test and chest radiograph for tuberculosis\textsuperscript{[8]}, serum angiotensin converting enzyme for sarcoidosis\textsuperscript{[9]}, as well as erythrocyte sedimentation rate, which is usually raised in giant cell arteritis\textsuperscript{[19]}, Wegener’s granulomatosis\textsuperscript{[10,22]}, and Behcet’s disease\textsuperscript{[25]}.

**MANAGEMENT**

Corticosteroid therapy in OPN is known to cause dramatic and rapid reversal of the signs and symptoms, but relapse commonly occurs with a short course of treatment\textsuperscript{[1,6,29]}. The myriad potential adverse effects of chronic use of corticosteroids have been well reported\textsuperscript{[30-33]}, and may complicate the management of this condition. In some cases, vision may fail to improve despite corticosteroid therapy\textsuperscript{[25]}. The cause of the poor visual outcome has been attributed to chronic inflammatory infiltration with concentric deposition of fibro-connective tissue in the dural sheath, causing compressive optic neuropathy with ischemic infarction\textsuperscript{[34]}. It is difficult to give a conclusive statement regarding the prognosis of OPN, as the rarity of this condition precludes the availability of large, long-term studies, and most of our knowledge has been pieced together from isolated case reports or small case series\textsuperscript{[19,21,27,35-38]}. The largest case series of OPN up to date, which included 14 patients seen in 2 neuro-ophthalmology clinics, concluded that patients with OPN respond more dramatically to corticosteroids than their counterparts do in optic neuritis, but that they are more prone to recurrences after discontinuation of treatment\textsuperscript{[1,39]}. Spontaneous resolution of this condition is rarely documented\textsuperscript{[35,40]}. In our setting, we usually treat our OPN patients with an extended course of oral corticosteroids, gradually tapering the dose to a maintenance level which is continued for a period of months.

**CONCLUSION**

OPN is a rare condition. Although the classic triad of pain, optic neuropathy, and optic disc swelling is usually present, its clinical presentation may easily mimic other optic neuropathies. MRI is thus an invaluable component of the diagnostic workup of this condition. It is pertinent to keep in mind, too, that despite the dramatic response to corticosteroids, prolonged therapy, with slow tapering of the dose, may be necessary to reduce the risk of relapses.

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