Re: Intravenous tocilizumab in the treatment of resistant optic perineuritis: a case report

Dear Editor,

We read the report by Maleki et al.,1 and while we find it interesting, we believe that it contains significant errors that call into question the diagnosis optic perineuritis (OPN) and invalidate the conclusions made by the authors. The authors have failed to demonstrate that the patient truly had OPN, which relies mostly on neuroimaging for diagnosis. In Figure 1, the authors claimed to have shown enhancement of the optic nerve sheath near the right globe based on one unenhanced axial T2-weighted magnetic resonance imaging (MRI) image of the brain. It is not possible to assess enhancement on this MRI sequence (it can only be seen after gadolinium is administered). The authors needed to show the T1 postcontrast MRI image of the orbits with fat suppression, which should demonstrate optic nerve sheath enhancement. Likewise, the authors failed to provide objective evidence that the patient actually had a recurrence of OPN when his eye pain worsened because MRI of the orbits was reported as normal at that time. The work-up presented for OPN, which should include investigations for infectious (e.g., syphilis) and inflammatory (e.g., vasculitides such as granulomatosis with polyangiitis) causes, also was incomplete.2

From a neuro-ophthalmology perspective, we found it unusual that the patient was treated with only a single dose of intravenous methylprednisolone. The typical standard treatment for inflammatory optic neuropathies is 3–5 days of high-dose corticosteroids, which is often followed by a longer tapering dose of oral prednisone starting at 1 mg/kg of body weight.3 The authors also did not describe the timeline between the first dose of intravenous steroids and the first dose of tocilizumab. Based on our reading of the report, it is plausible that the intravenous methylprednisolone was the reason that the patient improved initially. The authors also made a statement at the end of their report documenting that the patient complained about returning pain at the visit for his second monthly tocilizumab infusion and that this “was confirmed with optic nerve head leakage on FA.” Pain is a subjective symptom and thus cannot be confirmed with fluorescein angiography. We would encourage the authors to collaborate with their neuro-ophthalmology and neuroradiology colleagues when treating patients with OPN, especially if reporting their results for publication, to avoid diagnostic and treatment errors.

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References


Footnotes and Disclosure

The authors have no proprietary or commercial interest in any materials discussed in this correspondence.

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Reply: Intravenous tocilizumab in the treatment of resistant optic perineuritis: a case report

Dear Editor,

We thank Micieli and Margolin for reading the correspondence about the case of resistant optic neuritis treated successfully with tocilizumab infusions; however, we were astonished at how confidently they criticized the diagnosis and treatment of a complicated case without asking for more evidence. First, we would like to mention that the word limit did not allow the authors to include all the history, laboratory tests, and paraclinical diagnostic tests in the correspondence. In addition, this patient presented to us with more than 300 pages of records of previous eye examinations, laboratory work-ups, and imaging reports done by a group of neuro-ophthalmologists and neuroradiologists in an academic centre.

For those who are not familiar with the field of ocular immunology and inflammation, we would like to clarify that it is necessary to rule out all infectious etiologies (e.g., tuberculosis, Lyme disease, syphilis, herpes family viruses, etc.) and noninfectious etiologies (e.g., arcoidosis, granulomatosis with polyangiitis, polyarteritis nodosa, systemic lupus erythematosus, etc.) in all ocular and orbital inflammatory diseases prior to any treatment. All possible infectious and noninfectious causes of optic

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perineuritis were ruled out in this patient prior to his presenting to us. He had only deferred cerebrospinal fluid tap. The patient had been followed for several months at an academic centre with a correct diagnosis but no successful treatment. There was no doubt about the correct diagnosis because 2 neuroradiologists had evaluated all images at 2 different academic centres prior to the patient’s initial visit with us.

We disagree with Micieli and Margolin’s comment on the T2-weighted magnetic resonance imaging (MRI) because enhancement of the optic nerve sheath in optic perineuritis with T2-weighted MRI has been reported before.1–3 The standard MRI protocol was followed for this case, and the diagnosis was confirmed. Additionally, we disagree with their comment on normal MRI in symptomatic patients. It is not uncommon to have symptoms prior to objective signs in ocular and orbital inflammatory diseases, such as posterior scleritis. We believe that the normal MRI at that point in a patient on 10 mg oral prednisone during tapering does not counteract the primary diagnosis of optic perineuritis.

Micieli and Margolin also did not pay attention to the term “resistant” in the title of the correspondence. This patient had a 3-day course of 1 g methylprednisolone pulse therapy before presenting to us without long-term relief. Moreover, he had failed multiple courses of high-dose oral steroid (60 mg/d) with slow tapering and 2 courses of treatment with 2 different nonsteroidal anti-inflammatory drugs (NSAIDs). In contrast, there is no consensus about the duration of intravenous steroid pulse therapy. It is important to note that the patient responded to 1 dose of 1 g intravenous methylprednisolone, but the problem returned. We gave 1 dose of intravenous methylprednisolone to protect the optic nerve against any damage until tocilizumab was approved. The patient’s response to that infusion means that the condition was inflammatory and that he required immunomodulatory therapy. Corticosteroids with different routes of administration are not considered a long-term treatment in the ocular and inflammatory eye and orbital diseases. The aim of treatment of these patients is steroid-free remission4 and eventually cure. Micieli and Margolin’s recommended treatment regimen had already failed several times prior to the patient presenting to us. Intravenous tocilizumab was started 1 month after the intravenous methylprednisolone infusion; however, it does not matter because fluorescein angiography showed more leakage from the optic nerve head at 1 month after intravenous methylprednisolone compared with 1 week after the intravenous methylprednisolone infusion.

We assume that Micieli and Margolin are familiar with the symptoms and signs of optic perineuritis.5 We also expect that they are familiar with fluorescein angiography to avoid such an unscientific and unwarranted comment about the relation between symptoms (retrobulbar pain) and inflammation in the optic nerve sheath (leakage on fluorescein angiography).

It is hard to believe that Micieli and Margolin are unaware that optic perineuritis is a variant of idiopathic orbital inflammatory syndrome6 and that neuro-ophthalmologic diagnostic and therapeutic protocols might not be applied to it. Furthermore, by searching the literature, we found that only oral corticosteroids and NSAIDs have been studied and employed extensively in patients with optic perineuritis.7 Only azathioprine as a conventional immunomodulatory agent has been employed and, even so, with insufficiently low doses and in a limited number of patients diagnosed with optic perineuritis.8 Our case had been diagnosed correctly with optic perineuritis by neuroradiologists. Yet, because of the same concept, the patient had been treated with systemic corticosteroids and NSAIDs unsuccesfully prior to presenting to us.

The patient has been symptom free for 18 months with a normal eye examination and normal fluorescein angiography, and he is currently on 12-week tocilizumab treatment during the tapering period. This implies that he was correctly diagnosed and treated successfully with a biologic response-modifier agent. Therefore, this treatment can be considered a novel treatment for such cases in the future.

We strongly advise Micieli and Margolin to be more conservative and cautious with their comments about the work of other scientists and researchers, especially in fields where that they lack familiarity, particularly when they decide to address their concerns as a letter to the editor. In addition, we suggest that they refer patients with optic perineuritis to ocular immunologists to avoid often severe ocular and systemic complications of long-term corticosteroids use.

We expect clinicians and scientists to be more open-minded, to be respectful of other scientists’ work, and to accept new ideas and concepts instead of sticking to traditional medications and old concepts.

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References

Mechanisms of post-radiation optic atrophy with neuroretinal rim thinning

Dear Editor,

We read with interest the article “Optic disc cupping after circumpapillary PD-103 slotted plaque radiation therapy.”1 Finger et al. examined a cohort of patients managed with slotted plaque radiotherapy for peripapillary, juxtapapillary, or circumpapillary choroidal melanoma and found that treatment was associated with subsequent increase in cup-to-disc ratio.

We recently published a series of patients managed with round Collaborative Ocular Melanoma Study plaques and found that of 78 patients, 41 developed post-radiation optic atrophy, and 15 had concomitant neuroretinal rim thinning,2 a phenotype matching that described by Finger et al. These findings are not unique to a slotted plaque design, but they could be more likely in the setting of greater radiation dose to the optic disc and posterior ciliary arteries. In our series, we found that all patients with neuroretinal rim thinning also developed some degree of optic disc pallor. Although Finger et al. found no significant increase in pallor after treatment, we suspect this may have been due to small sample size, especially given p = 0.051 and a change in both the median and minimum pallor grade from zero to one after treatment.

In our study, we found an additional association between higher baseline intraocular pressure (IOP) and development of post-radiation optic atrophy, with a further association of higher maximum IOP and the phenotype of neuroretinal rim thinning. Finger et al. emphasized that higher post-treatment IOP was likely not responsible for neuroretinal rim thinning in their series, but our data suggest that higher IOP, even if within the “normal” range, may increase susceptibility to post-radiation optic atrophy, perhaps due to connective tissue stress and strain.3

We applaud Finger et al. for their application of optical coherence tomography angiography. Optic disc cupping in their study correlated to changes in vessel length and density, leading to the hypothesis that radiation-induced ischemia could be responsible for the optic disc changes. Overall, we were excited to see validation of findings we have observed in our own practice, and we agree that prospective studies including correlation of visual field defects are necessary to better understand how post-radiation optic atrophy compares with glaucomatous optic neuropathy.

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References


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Reply: Mechanisms of post-radiation optic atrophy with neuroretinal rim thinning

Dear Editor,

Thank you for the opportunity to respond to Drs. Dalvin and Roddy’s letter to the editor regarding our recently published original observations describing “Optic disc cupping after circumpapillary Pd-103 slotted plaque radiation therapy.” They point out that their recently published article in the Journal of Neuroophthalmology noted, “Post radiation optic atrophy is associated with intraocular pressure and may manifest with neuroretinal rim thinning.” We read their article (which was published within 30 days of ours) with great interest. They reported that their posteriorly placed radiation plaques resulted in either no optic neuropathy, or optic neuropathy without neuroretinal thinning or...