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

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 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 T_2-weighted magnetic resonance imaging (MRI) because enhancement of the optic nerve sheath in optic perineuritis with T_2-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 remission[4] 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 syndrome[6] 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.[5] 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.[5] 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 unsuccessfully 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

DOI of original article: http://dx.doi.org/10.1016/j.jcjo.2021.11.008

https://doi.org/10.1016/j.jcjo.2022.02.013
ISSN 0008-4182

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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Footnotes and Disclosure

We thank Andrew M. Philip for his help with editing this correspondence.

None of the authors have any conflict of interest with the content of this correspondence.