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Footnotes and Disclosure

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

Intravenous tocilizumab in the treatment of resistant optic perineuritis

Optic perineuritis (OPN) is a rare orbital inflammatory disease that mainly involves the optic nerve sheath and surrounding tissues. It is accompanied by eye pain and various levels of optic nerve dysfunction, such as decreased vision, visual field defect, and positive afferent pupillary defect. In contrast to optic neuritis, OPN is not a self-limited disease and always requires treatment.[1]

The main treatment for OPN is systemic corticosteroid therapy, which causes rapid and dramatic improvement, but recurrence is common and requires a longer course of treatment.[1] Nonsteroidal anti-inflammatory drugs (NSAIDs) and azathioprine, along with oral corticosteroids, have also been employed in the treatment of patients with OPN, but their effectiveness has not been consistent. The most resistant cases require radiation therapy.[1]

To the best of our knowledge, a steroid-free immunomodulatory therapy regimen has not been employed in the treatment of primary OPN. In the case reported here, for the first time we successfully employed tocilizumab for a patient with resistant primary OPN.

This study was approved by the New England Institutional Review Board, which has issued a waiver of informed consent for the retrospective chart review analysis. This study was performed in accordance with the Helsinki Declaration of 1964 and its later amendments. The participant provided consent for any identifying information for publication.

A 21-year-old man was referred to our centre for a second opinion on retrobulbar pain in his right eye that had started 1 year before presentation to us. The pain had been progressively worsening since it first started. Initial blood work-up for inflammatory diseases had been negative. Brain and orbital magnetic resonance imaging (MRI) with contrast medium early in the course of the disease had revealed enhancement of the optic nerve sheath in the right eye compatible with the diagnosis of OPN (Fig. 1). Extensive blood work-up such as aquaporin-4 antibody, myelin oligodendrocyte glycoprotein antibody, and plasmablast panel also was negative or normal. Chest computed tomography scan was normal. Visual acuity, B-scan ultrasound, and visual fields of both eyes had been reported normal. The patient had deferred lumbar puncture.

The patient had been started on prednisone 20 mg/day with significant improvement in his symptoms. Five

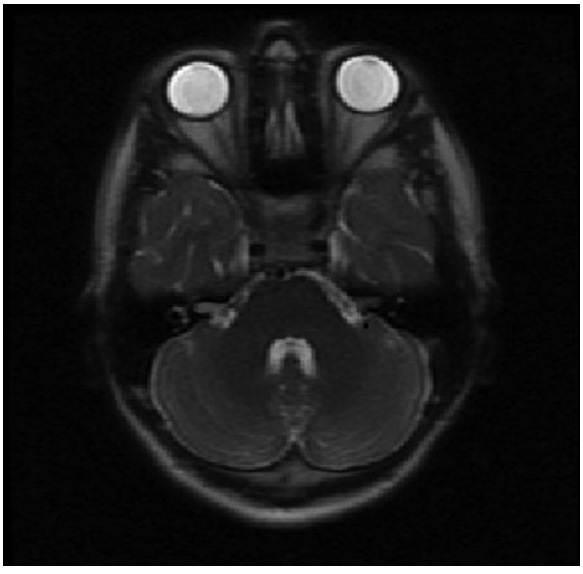

Fig. 1—T_2-weighted magnetic resonance image that demonstrates the enhancement of optic nerve sheath near the right globe.

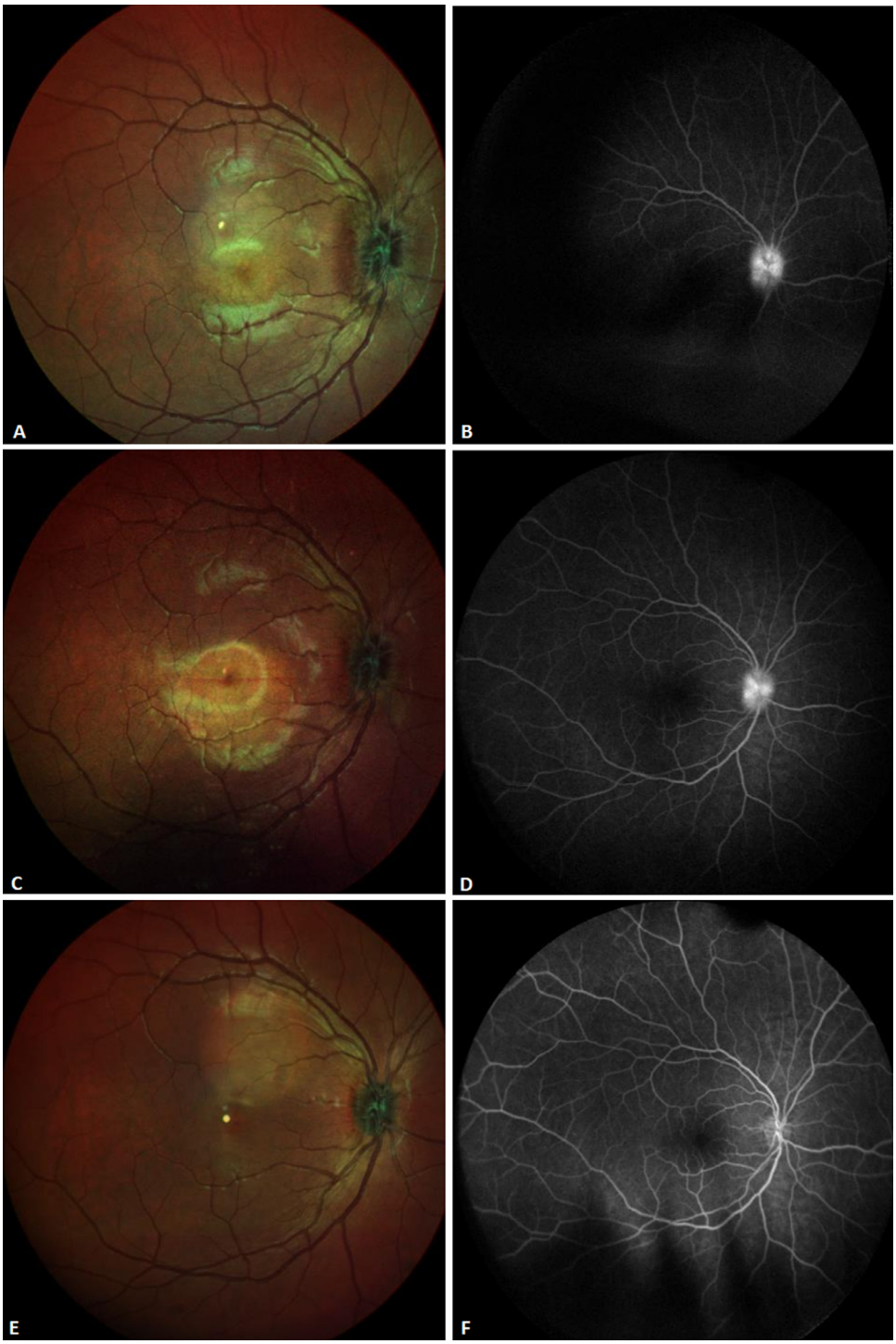

Fig. 2—(A) Multicolour image of the right eye at the initial visit that shows impressive swelling of the optic nerve head. There is no change in the macula, periphery of the retina, or retinal vasculature. (B) Fluorescein angiography of the same eye at the late venous phase with significant dye leakage from the optic nerve head. (C, D) Multicolour image and fluorescein angiography of the same eye, respectively, after the second tocilizumab infusion at a dose of 8 mg/kg. Optic nerve head swelling and leakage are better, but the patient is more symptomatic at this time. (E, F) The same eye after the third infusion of the higher dose of tocilizumab (10 mg/kg). Nerve head swelling has been resolved, and there is no leakage of the fluorescein dye on or around the optic nerve head. The patient was completely asymptomatic at this visit.

months later, he developed systemic side effects of prednisone, and prednisone was reduced to 10 mg/day. A month later, his eye pain became worse, but brain and orbital MRI did not reveal enhancement or other abnormalities. Ibuprofen 400 mg twice daily was added, and the prednisone was tapered and stopped. Ibuprofen was replaced by indomethacin 75 mg three times a day with no improvement.

At presentation to us, the patient had been on indomethacin for his pain as needed, but he was concerned about the constant pain and side effects of NSAIDs. His vision was 20/20 in both eyes. An eye motility test and an anterior segment examination were completely normal. Afferent pupillary defect was negative. Colour vision was normal in both eyes. Dilated fundoscopy revealed optic nerve head swelling in the right eye. The left eye was completely normal. B-scan ultrasound showed enlargement of the optic nerve head in the right eye without any signs of posterior scleritis. The visual fields were normal in both eyes. Fluorescein angiography (FA) demonstrated extensive leakage from the optic nerve head in the right eye (Fig. 2A, 2B).

Because the optic nerve damage was the major concern, the patient received 1 dose of methylprednisolone 1 g intravenously. The different options for long-term treatment, including oral prednisone, off-label conventional immunomodulatory therapy, and off-label intravenous tocilizumab therapy,[5] were discussed along with the pros and cons of each. The patient decided to proceed with intravenous tocilizumab therapy with a dose of 8 mg/kg every 4 weeks.

After the first infusion, the retrobulbar pain completely resolved, but FA was still showing leakage on and around the optic nerve head. During the second visit for his second monthly infusion, the patient complained about returning pain. This was confirmed with optic nerve head leakage on FA (Fig. 2C, 2D). Tocilizumab was boosted to 10 mg/kg monthly based on our experience with other resistant inflammatory diseases of the eye. This change was successful in terms of resolving the pain. Additionally, serial monthly FA demonstrated improvement of the optic nerve head leakage over time, and the leakage stopped after the third infusion with the higher dose (Fig. 2E, 2F). At that time, the tocilizumab was tapered with an increase in the interval between infusions.

Up to the present, the patient has received 2 infusions at 6-week intervals and 1 infusion at an 8-week interval. The plan is for another infusion at 8 weeks, 2 infusions at 10-week intervals, 2 infusions at 12-week intervals, and then cessation of therapy. Serial FA every 3–6 months and yearly brain and orbital MRI with and without contrast medium will be continued to make sure that recurrence will not happen. To avoid any medication toxicity, a medication toxicity questionnaire was completed, and a complete blood count, liver function tests, and kidney function tests will be evaluated at each visit.

Most cases of OPN are primary, but secondary cases of OPN have been reported in sarcoidosis,[2] Beçhet disease,[3] and vasculitis.[4] Systemic corticosteroid therapy is the mainstay of treatment for patients with primary OPN, thus requiring a longer course of treatment with very slow tapering.

Pathologic findings in OPN are perivascular lymphocyte infiltration of the optic nerve sheath with secondary fibrotic thickening. Granulomatous inflammation, focal necrosis, and infarction secondary to vasculitis also have been reported in patients with OPN.[1] These findings make immunomodulatory therapy a reasonable treatment for primary OPN.

Tocilizumab has been employed in the treatment of a wide range of eye inflammatory diseases.[5] This case report is the first in which tocilizumab was employed successfully in the treatment of resistant primary OPN.

In this case, the patient had tried oral corticosteroid and had a relapse when it was tapered. Additionally, 2 different NSAIDs were unsuccessful in controlling the inflammation and inducing remission. The patient was started on tocilizumab based on our successful experience with tocilizumab in controlling various types of eye inflammation.[5] Interestingly, the patient did not reach complete remission with a regular dose, and tocilizumab was boosted based on our experience with tocilizumab in other resistant inflammatory eye conditions. A higher dose of tocilizumab induced and maintained remission in our patient.

Tocilizumab monotherapy may be a good option for the treatment of patients with resistant primary OPN, but more potent studies are recommended to examine this hypothesis.

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Footnotes and Disclosure

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Wellness among Canadian ophthalmology resident physicians: a national survey

Residency is a particularly stressful and dynamic period during which learners must balance the demands of patient care, education, and personal responsibilities. Evidence of high levels of burnout among resident physicians has driven the development of initiatives and programs to help address this negative consequence of residency training. As a novel topic in the realm of medical education, more information is required to further characterize the sources of burnout and depression and the nuances of various specialities. Although surveys have been completed among resident physicians in Canada,[1–3] to the best of our knowledge, there have not been any ophthalmology-specific residency wellness surveys conducted on a national level.

Our study aimed to explore causes of stress and reduced wellness, incidences of depression and burnout, and resources available to Canadian ophthalmology residents through an online anonymous survey.

A 24-question survey was developed based on a similar U.S. national ophthalmology resident survey[4] as well as previous medical education studies on residency wellness.[1–3] Themes of the survey included causes of stress and reduced wellness, incidence of depression and burnout, and resources available. Definitions of both depression and burnout were presented to the respondent prior to the corresponding question. The survey was reviewed, modified, and validated by 2 ophthalmologists, 2 senior ophthalmology residents, and 1 senior psychiatry resident.

All ophthalmology residents in Canada (N = 217) were emailed a short anonymous survey (Google Forms) from May 6 to June 13, 2020. The survey was distributed via a resident physician mailing list of the Canadian Ophthalmological Society—Société canadienne d'ophtalmologie (COS-SCO) that included all 15 Canadian programs. Programs with a high resident response rate (>70.0%) were entered in a draw for a $500 prize as an incentive to boost participation. The funding for this prize was provided by the COS-SCO. The survey was originally distributed on May 11, 2020, with biweekly reminder emails. The survey closed on June 13, 2020. This survey was the second part of a two-part survey; the first part investigated the impact of COVID-19 on residency training.[5] Survey data were exported to Microsoft Excel 2013 (Redmond, Wash). All descriptive statistics were performed using Microsoft Excel.

Of 217 residents across Canada, 102 completed the survey (47.0%), representing all 15 residency programs. Table 1 summarizes the survey questions and results. Respondents encompassed all years of residency similarly, and there was equal representation of male and female respondents. Participation in the survey was higher in the larger residency programs (>20 residents [37.3%]).

In total, 64.7% of respondents answered that they had access to free counselling services as part of their program. Of those who did have access, 73.2% of respondents knew how to access these services. In regard to emphasis placed on a culture of resident wellness, 35.3% of respondents believed there was minimal emphasis, whereas 4.9% stated that there was no emphasis at all. Obstacles to addressing residency wellness included lack of wellness programming (33.3%) and lack of time to attend such programming (48.4%). The top 3 scenarios that led to or caused stress and decreased wellness in residency programs included academic stressors (e.g., examinations, rounds, 17.6%), call-related stress (16.9%), and stress in finding postresidency fellowships and jobs (11.0%).

In the 12 months prior to completing the survey, 38.2% of respondents answered that they met the criteria for depression or burnout. Of those, 7.0% had to take time off clinical duties. Based on those who reported the emphasis placed on resident wellness as minimal or none, 51.2% met the criteria for burnout or depression. Conversely, 29.5% of those who reported moderate or extensive emphasis on resident wellness met the criteria for burnout or depression; 36.3% of respondents answered that their program did not have access to a formal wellness program intended to reduce resident stress, burnout, and depression, and 38.2% of respondents were unaware of whether such a program existed. Of the respondents who had formal wellness programs, the main components were a mentorship program (28.1%); debriefing or support-group sessions (15.7%); self-care, mindfulness, or meditation training (15.7%); and education in fatigue and stress management (12.4%). Current methods that residency programs use to promote wellbeing include social wellness (e.g., casual gatherings) (33.5%),