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COMMENTARY

Vision Loss from Atypical Optic Neuritis: Patient and Physician Perspectives

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ABSTRACT

This article, co-authored by a patient affected by bilateral, recurrent, atypical optic neuritis, and clinicians, discusses the mental burden of living with uncertainty and the possibility of further sight loss, along with the side effects of treatment. The patient shares some of the challenges, coping strategies, and the value they found in creating and participating in a patient support group. The physicians consider whether current clinical measures adequately capture the outcomes that matter to patients and discuss the role for patient-reported outcome measures (PROMs). We identify technological advances that are lowering traditional barriers to the use of PROMs in research and routine clinical care and look towards new PROM instruments enhancing shared patient-physician care in the future.

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PLAIN LANGUAGE SUMMARY

In this patient-physician perspective article, we share the story of a patient affected by an autoimmune disease that attacks the nerves connecting the eyes and the brain and reflect back physicians' perspectives on the disease and the patient's experience of it. In a compelling account, we gain some understanding of what it might be like to live with the fear of unpredictable episodes of sudden, recurrent sight loss and the important impacts that this has on a patient's life and mental wellbeing. We recognize that the outcome metrics that physicians

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usually focus on, such as measurement of vision and imaging of the optic nerve, do not fully capture the outcomes that most matter to the patient. We explore patient-reported outcome measures that go some way towards bridging this gap. Finally, we consider the technological advances that will make more comprehensive capture of the patient experience a reality in future clinical practice and research, supporting both patients and physicians to optimize shared care.

Keywords: Chronic relapsing inflammatory optic neuropathy (CRION); Optic neuritis; Patient-reported outcome measure (PROM); Quality of life

Key Summary Points
Patient perspectives on the impact of optic neuritis have been seldom reported in the medical literature.
There is growing recognition of the importance of the 'patient voice' in ophthalmology research and clinical practice.
Patient accounts provide valuable insights into the outcomes and metrics that matter most to patients.
A few patient-reported outcome measures have been developed in neuro-ophthalmology, and in multiple sclerosis and neuromyelitis optica spectrum disorder specifically. In our view, these are not yet psychometrically optimized for use in optic neuritis patients in routine clinical practice or clinical trials.
Technological developments are overcoming traditional barriers to the routine use of comprehensive patient-reported outcome measures.

PATIENT PERSPECTIVE

I was 28 when, 12 years ago, I felt a twinge in my right eye after a mild flu. Not thinking anything of it, I gave it little thought until, after 2 weeks, the pain had become constant. After ineffective antibiotic treatment, I was referred to the hospital, where they established I had optic nerve inflammation and only 40% of the vision in my right eye remained. With intravenous prednisone therapy my eyesight improved up to 80%, but after 2 weeks it dropped again, this time to no perception of light in just 36 h. Subsequent intravenous prednisone did not help. An MRI (magnetic resonance imaging scan) ruled out multiple sclerosis and I was told this was an episode of bad luck: My immune system had probably confused my eye nerve with a virus and attacked it. Living with only one seeing eye is actually not a big change (unless you have an aspiring squash career, which I did not), and I got used to it in a matter of weeks. But 7 years after this episode, I felt the same tingling sensation in my left eye. Losing one eye is fine, but going blind in both is a completely different matter. I was diagnosed with a chronic relapsing inflammatory optic neuropathy (CRION). Intravenous prednisone when attacks flare up and daily prednisone tablets have since helped to retain the eyesight in my left eye. In spite of this treatment, I get two or three attacks per year, and although repeat OCT (optical coherence tomography) scans show that the nerve damage hasn't deteriorated much, so far I've been lucky.

The above is roughly what I tell people when they ask me about it. The current medical world is mostly focused on traditional measurable metrics. For me, the key metrics my doctors use include visual acuity, OCT scans, and intraocular pressure. But there are other unquantifiable factors, such as mental aspects, convenience of treatment, and quality of life, that in the current medical climate get less attention. In my experience this can leave important patient questions unaddressed, in turn missing an opportunity to do better in helping patients deal with their disease and its treatment.

Take mental stress for instance. In my case, losing sight in one eye was not a big deal. But losing sight in my other eye would drastically change my life. I have a 16-month-old son at home, and I want to see him growing up. So naturally, I want to do all I can to keep my eyesight, and my independence. I'm convinced human beings in general aren't good at dealing with the unknown. We have a natural tendency to look for (a sense of) control. We want to eliminate the distress of the unknown, so we're always looking for cognitive closure. And when the medical world cannot help you in achieving this sense of control, you start to venture out by yourself to see what you can do. The overarching question for me is, "what is causing this, and what can I do to limit the attacks and keep my eyesight?" Given the rising incidence of autoimmune diseases in the population, it seems to point at environmental factors (vs. genetic factors), so I wonder what I can do to change my environment, to balance my immune system again. I've looked in various directions: Are autoimmune disorders related to stress? If so, how can I minimize stress? What role does diet play? What is the relationship between gut health and the immune system? Can more physical activity and more sleep have a positive effect?

To find answers to these questions I started to read up online. But as most doctors have probably experienced with patients, Google will find any correlation you want. Confirmation bias thrives online. And it's very easy to get down a rabbit hole or into an echo chamber on topics that might lack a scientific evidence base. I started changing my routines. What I eat, when I eat, when and how much I work out, and my sleeping patterns. With each change I felt hopeful about finding the holy grail, but then the next attack would come, prompting me to re-evaluate and correct course.

For most patients I'm convinced the mental burden is the most difficult part of their disease. Regardless if it's autoimmune disease, cancer, or even a complicated fracture. Variations on "What will happen to me in the future?" For me the constant question is, "Will I go blind", and the underlying question is, "How is my eyesight right now? Am I seeing less or more?" When I have an attack, I'm re-evaluating my eyesight up to 1000 times a day: "Should I be able to read that sign across the road? Is it the lighting in the room or is it my vision?" And so on. This "Am I going blind" Sword of Damocles completely occupies me. I'm afraid my body will not respond quickly enough to treatment of an attack, which will further damage my optic nerve. But at the same time, I do not want to increase the dose of my medication unnecessarily, as this could cause more side effects. When I go to clinic for a check-up, the visual acuity and OCT results do not always match up with my experience of the quality of my eyesight. All the while, I try not to let it occupy me too much, as it puts more mental stress on my body, and it feels like this might further create a negative spiral. But it's like the pink elephant in the room: impossible not to think about it when someone tells you not to! I'm confronted with the quality of my eyesight every waking moment, so it's more difficult to shut down that thought process. These mental struggles are inherent to all diseases—my situation is far from unique. And I understand that some doctors might think it's futile to discuss this aspect with the patient as there are often no clear answers or solutions to give. My point is that patients will venture out themselves if not discussed. Our natural tendency is to want to fill the void of not knowing, and putting this mental aspect more central in the treatment/communication with the patient can help patients, even if the answers are not there.

I feel lucky to have a great relationship with my neuro-ophthalmologist, and this has helped me a lot. Through discussing the mental aspects, my doctor floated the idea of creating a patient group to create a space where similar patients can find information and share experiences. Experiences of what has helped them personally, and what hasn't. We share thought processes around dealing with the disease and keep each other informed of developments in treatments. The patient group helps to sift through the forest of articles, theories, and possible solutions and helps us to better avoid the confirmation bias when venturing out to find answers alone. It has helped us share best practices. One example, for instance, is how to

lose water retained by your body due to the prednisone. I experimented with a cleanse diet of 1 week where I only ate greens, nuts, and apples. No caffeine, carbs, alcohol, salt, sugar, and fats. I lost nearly a kilo a day throughout the cleanse, and repeat it every so often. It helps me to lower my internal pressure and avoids me looking bloated. Though small, these are important victories in dealing with this disease and having a patient group is a great way to be able to share and discuss.

PHYSICIAN PERSPECTIVE

> "…and now come and sit beside me for a little while, and touch me with your hand. For I cannot see you, Charley; I am blind."

These are the words of a young woman to her child, after discovering that she had lost her vision. The quote is taken from the novel Bleak House by Charles Dickens (1812–1870) [1]. In this novel, the time course and clinical signs of a disease process, which could have resulted from simultaneous bilateral optic neuritis or chiasmitis, are carefully married up chronologically with the emotions and social interactions of the main character, Esther Summerville. This story predates discovery of the ophthalmoscope, the clinical definition of optic neuritis, and any form of treatment. Yet the human thoughts and emotions are little different today: "I have a 16-month-old child"; "I want to see him grow up"; "Will I go blind?" The last question is difficult to answer, for whilst we now have treatment options, they may fail in some individuals and in differing types of optic neuritis.

Optic neuritis is an important cause of potentially irreversible vision impairment [2]. The most typical cause is a demyelinating inflammatory lesion, which can be isolated or associated with multiple sclerosis. Patients with typical optic neuritis usually experience good recovery of their visual acuity in the first month after the vision loss, without any treatment, although the quality of the recovered vision, and especially the contrast sensitivity or colour perception, may be worse than before. In contrast, 'atypical' causes of optic neuritis may present with more severe vision loss (e.g. visual acuity worse than 6/60 at onset), bilateral involvement, and/or no pain on eye movement. These cases usually require urgent high-dose corticosteroid therapy, and some, including CRION, are 'steroid dependent', meaning that the disease often relapses when the steroid dose is weaned or discontinued. Therefore, second-line steroid-sparing agents (e.g. azathioprine) are required in these patients, aiming to reduce the risk of steroid side effects and further vision loss or neurological morbidity resulting from relapses [3]. Plasma exchange, intravenous immunoglobulin, and biological therapies are also used.

The patient outlines how the impacts of optic neuritis and its treatment extend far beyond the limited visual function measures and OCT imaging parameters monitored in clinic to encroach upon many different domains of quality of life. There is growing recognition of the value of, and need for, patient-reported outcome measures in medicine and ophthalmology [4, 5]. Few tools have been developed to date for neuro-ophthalmology, and optic neuritis specifically. For example, the neuro-ophthalmic supplement to the National Eye Institute Visual Functioning Questionnaire (NEI-VFQ) includes ten questions [6]. These include questions on visual symptoms, performance in vision-related daily activities, and appearance. This tool has been used in optic neuritis clinical trials [7]. However, it covers only three domains of quality of life, and the composite summary score lacks psychometric validity, and is not amenable to parametric statistical analysis [8, 9]. More recently, a 46-item instrument was developed for neuromyelitis optica spectrum disorder, one rare cause of optic neuritis [10]. This includes questions on a large number of quality of life domains, including vision and vision-related functioning, impacts on life goals and roles, general health-related functioning, mobility, bladder function, bowel function, sexual function, mood, pain, general fatigue, and cognition. A systematic review of PROM instruments applicable in optic neuritis is underway and will

report on the psychometric properties and quality of available instruments [11].

To overcome some of the psychometric limitations of PROMs assessing quality of life in other ophthalmic diseases (e.g. diabetic retinopathy and hereditary retinal disease), comprehensive, Rasch-validated multi-dimensional instruments with interval scoring are being developed [12, 13]. These capture over ten quality of life domains that matter to patients, have interval scale properties, and yield parametrically distributed continuous outcome measures. These 'third-generation' PROM tools have the potential to transform clinical trial outcome measures and routine patient care [5].

Technological advances are rapidly addressing the traditional barriers to the integration of PROMs in clinical medicine. PROMs can now be administered on phones, tablets, and computers, with software to overcome low vision, literacy, and language barriers to completion, with computer-adaptive testing to reduce time response burden, and utilizing cloud-based data storage and integration platforms to link PROM outcomes into the electronic medical record for virtual review by physicians [14]. Iterative, patient-involved development of such PROM tools has the potential to transform both patient and physician experience, enhancing the potential for truly shared care. This article is based on previously conducted studies and does not contain any studies with human participants or animals performed by any of the authors.

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