Hemodialysis-Related Vision Loss from Anterior Ischemic Optic Neuropathy

Arshia Eshtiaghi\(^a\) Jonathan A. Micieli\(^b, c\)

\(^a\)Faculty of Medicine, University of Toronto, Toronto, ON, Canada; \(^b\)Department of Ophthalmology and Vision Sciences, University of Toronto, Toronto, ON, Canada; \(^c\)Kensington Vision and Research Centre, Toronto, ON, Canada

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Abstract
Vision loss from nonarteritic anterior ischemic optic neuropathy (NAION) is a rare complication of hemodialysis. Here, we present a case in a young woman and discuss the pathophysiology and implications for the nephrologist. A 24-year-old woman with end-stage renal disease developed unilateral, painless vision loss following treatment with hemodialysis. Fundoscopy revealed severe left inferior chalky-white optic disc edema, a presentation consistent with NAION. Her intradialytic blood pressure was reviewed and found to be significantly lower than her baseline, and a multidisciplinary meeting took place between her ophthalmologist and nephrologist to modify her dialysis sessions to minimize the chance of progression or involvement of her fellow eye. At the 2-month follow-up, the optic disc edema resolved, and her visual function remained stable. Overall, NAION is a rare complication of hemodialysis and may be a result of intradialytic hypotension, platelet and endothelial dysfunction, anemia, and accumulations of toxins such as urea. As there are no established treatments for NAION, management should focus on optimizing modifiable risk factors to prevent further vision loss in the other eye. These factors include increasing the number of dialysis sessions and duration of sessions, reducing the temperature of the dialysate, discouraging eating, and increasing the dialysate’s calcium concentration. Prompt recognition of NAION and multidisciplinary teamwork can minimize the risk of NAION progression and involvement of the contralateral eye.
Introduction

Nonanterior anterior ischemic optic neuropathy (NAION) is the most common acute optic neuropathy among individuals above the age of 50 years and has an annual incidence ranging between 2 and 10/100,000 [1]. It may also occur in younger individuals. NAION is characterized by sudden, typically painless vision loss with accompanying optic disc edema. The exact sequence of events leading to vision loss in NAION is still controversial. However, it is presumed that any systemic or local inciting factor that leads to transient hypoperfusion of the optic nerve head can cause NAION [2]. Flow to the optic nerve head is normally maintained at a constant level through autoregulatory mechanisms, even during fluctuations in intraocular pressure, mean arterial pressure, and changes in blood oxygen saturation. In NAION, the normal autoregulatory mechanisms that maintain perfusion to the optic nerve head are impaired, leading to ischemia, axonal swelling, and compartment syndrome [2].

Essentially every patient who develops NAION has a “disc-at-risk,” defined as an optic nerve with an absent or small physiologic cup [2]. Most patients will also have at least one other vascular risk factor, with the most common being hypertension, diabetes, and obstructive sleep apnea. The vision loss associated with NAION is usually permanent. Furthermore, approximately 15% of patients will develop NAION in the second eye over the next 5 years [3]. Since there are no proven effective treatments once NAION occurs, it is essential to monitor modifiable risk factors to prevent the subsequent development of NAION in the second eye. In patients with end-stage renal disease (ESRD) on hemodialysis, NAION may be an irreversible complication, and the etiology is multifactorial in nature including intradialytic hypotension (IDH).

Case Report/Case Presentation

A 24-year-old female developed sudden, painless vision loss in the top part of the visual field in her left eye just after completing hemodialysis. She had a past medical history of ESRD secondary to congenital nephrotic syndrome and was on hemodialysis 3 days per week since the age of 2 years. She had a living donor transplant at the age of 3 years from her mother but required hemodialysis again 3 years prior to presentation, which occurred 3 times per week. Her medications included pantoprazole, loperamide, calcium carbonate, and ferrous gluconate for anemia (Hb of 104). On examination, visual acuity was 20/20 in both eyes, and there was a left relative afferent pupillary defect. Fundoscopy revealed severe left inferior chalky-white optic disc edema with peripapillary wrinkling and hemorrhages (shown in Fig. 1). Confrontation visual fields revealed a left superior altitudinal defect, and this was confirmed on formal Humphrey 24-2 SITA-Fast visual field testing (shown in Fig. 2). The sudden and painless loss of vision in her left eye was most consistent with NAION in the setting of hemodialysis. Her intradialytic blood pressure was reviewed, and it had a nadir of 86/60 mm Hg, which is less than her baseline, with many fluctuations, supporting a diagnosis of NAION. A differential diagnosis of a vasculitis resulting in arteritic anterior ischemic optic neuropathy was also considered. However, she had no symptoms consistent with a systemic vasculitis, and a workup including a normal erythrocyte sedimentation rate and C-reactive protein and antineutrophil cytoplasmic antibody and antinuclear antibody was negative. She was 24 years old, and giant cell arteritis (GCA) was not considered since this is a condition that mainly occurs in individuals over 50 years of age. The chalky-white disc edema, the absence of pain, and sudden vision loss excluded the diagnosis of optic neuritis. Since there is no established treatment for NAION, a multidisciplinary meeting between ophthalmology, nephrology, and nursing teams took place to optimize her dialysis sessions to minimize the chance of progression or involvement of her fellow eye. These modifications included a change from three to five dialysis sessions of longer duration, a reduction in the temperature of the
dialysate, avoidance of eating during dialysis, and an increase in the dialysate’s calcium concentration. At the follow-up visit 2 months later, her vision remained stable, and the optic disc edema resolved. This confirmed the diagnosis of NAION since a systemic vasculitis would be expected to progress without treatment. Her visual function was also stable at the 1-year follow-up.

Discussion/Conclusion

The Relationship between Hemodialysis and NAION

IDH is thought to be a primary culprit in the development of NAION, but other factors may play a role [4]. Patients with ESRD are more likely to be in a hypercoagulable state secondary to platelet and endothelial dysfunction [5]. They are also more likely to have anemia secondary to endogenous erythropoietin deficiency and shortened red blood cell lifespan [4]. Finally, the accumulation of toxins in ESRD, especially urea, may contribute to toxic optic neuropathy [4].
Different guidelines use varying thresholds for defining IDH. The most commonly used definitions involve a drop in systolic blood pressure during hemodialysis ≥20 mm Hg, a drop in mean arterial pressure ≥10 mm Hg, or a nadir systolic blood pressure <90 mm Hg [6]. Regardless of its definition, IDH is a common complication of hemodialysis, with a prevalence ranging from 8% to 40% [7]. In the case we present, it is likely that the large fluctuations in blood pressure commonly seen with hemodialysis contributed to the patient’s development of NAION. A previous large cohort study found that patients with ESRD were 3.1 times more likely to develop NAION than matched controls. Our patient already had mild anemia, which coupled with IDH likely contributed to ischemia of her optic nerve head.

Uremic platelet and endothelial dysfunction may contribute to a hypercoagulable state. A literature review by Lutz et al. [5] found that there is both an increased risk of bleeding and increased risk of thrombi production in renal failure. The authors explored numerous mechanisms that could explain this hypercoagulability. In ESRD, platelets have increased surface concentrations of phosphatidylserine, a phospholipid that promotes the sequential binding of factor V and X, leading to thrombin formation. In ESRD, platelets also demonstrate increased expression of p-selectin, a platelet activation marker, which recruits leukocytes and promotes platelet aggregation. Homocysteine buildup in renal failure may also interfere with t-PA release by endothelial cells, resulting in the failure to break down formed blood clots.

The pallid or “chalky-white” optic disc edema seen in our patient’s left eye is actually not classic for NAION [8]. Pallid optic disc edema is often associated with vasculitis (e.g., GCA), whereas hyperemic optic disc edema is typically seen in NAION. However, pallid optic disc edema can sometimes be seen in NAION, especially in young individuals and in association with hemodialysis [9]. In this case, the chalky-white edema seen in her left eye is thought to represent a more severe degree of infarction. To differentiate between GCA and post-hemodialysis NAION, a vasculitis workup can be performed to look for elevated ESR and CRP, which is seen in GCA. However, these inflammatory markers can also be elevated in severe renal disease, making differentiation between GCA and post-hemodialysis NAION difficult. Therefore, to differentiate the two diseases, one should also search for clinical signs consistent with GCA (e.g., age >50 years, temporal headache, scalp tenderness, jaw claudication, history of polymyalgia rheumatica, etc.) versus those consistent with NAION (disc-at-risk, vasculopathic risk factors). A temporal artery biopsy is often needed. In this case, our patient was young and not in the age-group where GCA is considered, and the vasculitis workup was negative. Given her young age and a clear temporal relationship with the dialysis, vasculitis was considered unlikely, and the resolution of the optic disc edema in the expected time course and stability of her vision confirmed the diagnosis of NAION.

**Other Complications of IDH**

Although NAION is a rare complication of hemodialysis, IDH can also contribute to other forms of end-organ damage [7]. The most severe adverse outcomes associated with IDH are cardiovascular dysfunction and increased all-cause mortality. Patients who experience IDH are at an increased risk of myocardial infarction and myocardial stunning, which is the result of repeated episodes of ischemia that can eventually lead to permanent fibrosis and systolic heart failure. IDH has also been linked to frontal lobe atrophy and ischemic brain injury [7]. Less commonly, IDH can also result in mesenteric ischemia necessitating hospitalization [7]. Apart from end-organ damage, IDH is not a pleasant experience for patients and can contribute to symptoms such as nausea or vomiting, muscle cramps, dizziness, and syncope.

**How to Minimize the Risk of NAION with Dialysis**

Recent guidelines propose several standard modifications that may reduce the risk of IDH during dialysis [7]. These include evaluating patient volume status before each session...
to prevent hypovolemia, reducing the temperature of the dialysate (35–36°C) to stimulate vasoconstriction, increasing the dialysate’s calcium concentration to improve ventricular contractility, discouraging eating during or just before dialysis to prevent gastrointestinal shunting, increasing the duration of each dialysis session and the number of visits per week to reduce the ultrafiltration rate, administering fluids to reverse IDH when it occurs, intermittent pneumatic compression of the legs to increase venous return, high-flux hemofiltration, and switching from hemodialysis to peritoneal dialysis in refractory IDH. Other techniques to reduce IDH include sodium profiling and midodrine supplementation, although these should not be routinely used given conflicting evidence surrounding their safety. Outside of the context of hemodialysis, nephrologists can prevent end-organ ischemia in ESRD by correcting severe anemia with the use of erythropoiesis-stimulating agents, by carefully monitoring extremes in blood pressure and by working with primary care physicians to correct other modifiable risk factors.

**Conclusion**

In summary, we present a case of a 24-year-old female with congenital nephrotic syndrome who developed NAION in relation to hemodialysis, where IDH was likely a primary culprit. She presented with a unilateral visual field defect and was found to have chalky-white optic disc edema on fundoscopy. In patients with NAION, optimizing modifiable risk factors may prevent further vision loss in their other eye. For patients undergoing hemodialysis, this involves taking steps to prevent IDH and routinely monitoring for signs of end-organ damage.

**Statement of Ethics**

Written informed consent was obtained from the patient for publication of this case report and accompanying images. The study protocol was reviewed, and the need for approval was waived by the University of Toronto Research Ethics Board. The paper is exempt from Ethical Committee approval as it is a case report of a patient already previously seen. The case report adhered to the ethical standards of the Declaration of Helsinki.

**Conflict of Interest Statement**

The authors have no conflicts of interest to declare.

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**Author Contributions**

Jonathan A. Micieli developed the concept of the case report, and both Jonathan A. Micieli and Arshia Eshtiaghi were involved in interpreting the data and drafting and critically revising the manuscript.
Data Availability Statement

All data generated or analyzed during this study are included in this article.

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