Evidence of nocturnal hypotension in an inpatient prior to an episode of classic NAION

Nonarteritic anterior ischemic optic neuropathy (NAION) is a known cause of acute, painless, monocular vision loss in patients with small cup-to-disc ratios and at least 1 vascular risk factor.[1] The etiology has been debated, although Hayreh et al.[2] have hypothesized that nocturnal hypotension impairs perfusion to the optic disc causing ischemia to the optic nerve. Despite evidence supporting this via retrospective monitoring of diurnal changes in blood pressure (BP) with Holter monitoring in patients with prior outpatient episodes of NAION, this BP change has not been documented at the time of the event.[2] Additionally, some have argued that the diurnal variance in BP between those with NAION and those without NAION may be insignificant, and thus nocturnal BP levels may not play a causal role. We present an episode of classic NAION that transpired in the inpatient setting immediately following an episode of abnormally low BP. To our knowledge, this is the first reported case with a documented episode of nocturnal BP decrease preceding an episode of NAION.

A 28-year-old female with a history of uncontrolled type IIIc diabetes mellitus secondary to hereditary xerocytosis with transfusion dependence complicated by iron overload necessitating orthotopic cardiac transplant and chelation therapy was hospitalized after asymptomatic outpatient laboratory findings of hemoglobin 54 g/L and blood glucose 8.7 mmol/L. She was admitted and transfused 1 unit of packed red blood cells, and blood glucose was normalized. Given her complex medical history, the patient stayed in the inpatient setting for several days to be evaluated.

In the early hours of day 4 of her hospitalization, the patient reported acute, painless, unilateral, sectoral vision loss. Corrected visual acuity was 20/25 OU, and intraocular pressures via iCare measured 9 mm Hg OU. The pupil in her right eye was 6 mm and constricted to 4 mm and that in the left eye was 6 mm and constricted to 5 mm with a 3+ relative afferent pupillary defect. Her extraocular movements were intact, and Ishihara colour testing was 11/11 OU. Slit-lamp examination revealed 360° elevation and blurring of disc margins with superior pallor OS and an estimated cup-to-disc ratio of <0.1 OU.

Humphrey visual field testing showed an inferior altitudinal field defect with a mean deviation of −16.47 dB with some inferior temporal sparing OS. Optical coherence tomography yielded a retinal nerve fibre layer of 91 μm OD and 191 μm OS with a cup-to-disc ratio of 0.06 OD and 0.05 OS. Fundus photosgraph showed a crowded optic disc OD and a swollen optic nerve OS (Supplementary Fig. 1, available online; Fig. 1). No definite optic disc drusen was seen on fundus autofluorescence or optical coherence tomography.

Further work-up to rule out other causes of vision loss were negative, including serum anti- nuclear antibodies, anti-Sjogren's syndrome related antigen A autoantibodies, anti-proteinase 3, anti-neutrophil cytoplasmic antibody, anti-myelin oligodendrocyte glycoprotein, anti-neuromyelitis optica, angiotensin converting enzyme, QuantiFERON TB, syphilis IgG/IgM, rapid plasma reagin, Cytomegalovirus, Epstein- Barr virus, Herpes Simplex virus, Varicella Zoster virus, and cerebrospinal fluid serologies for Herpes Simplex virus, Bartonella, Lyme, and toxoplasmosis as well as cerebrospinal fluid culture. Given this constellation of findings, a diagnosis of NAION was made.

On further review, the patient's nocturnal BP several hours before symptoms was 97/65 mm Hg, around 10 mm Hg lower than her nocturnal systolic BP recordings in the preceding days of her hospitalization (Fig. 2). In this same interval, hemoglobin levels did not change more than 10 g/L, and no new transfusions or chelation therapies were administered.

Physiologic BP varies throughout the day and decreases during nighttime sleep. The typical optic nerve head

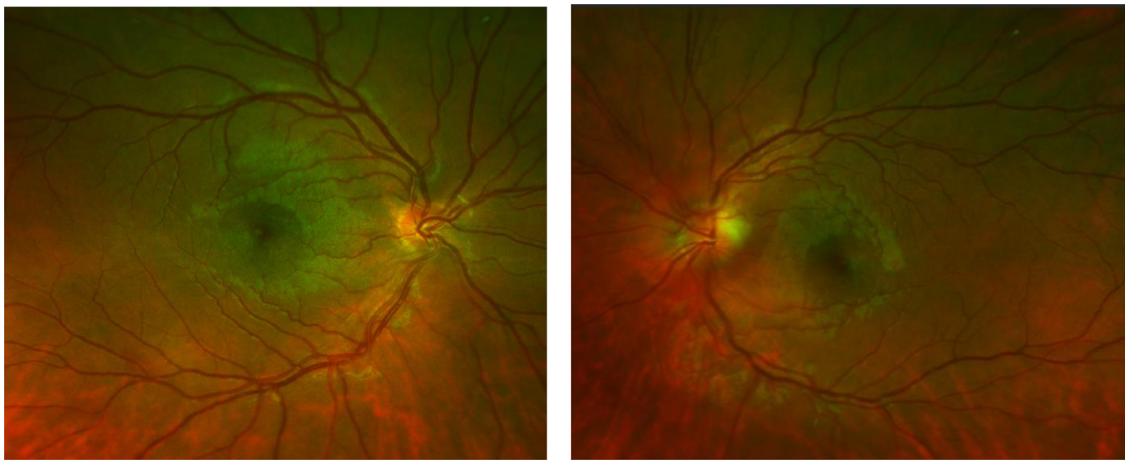

Fig. 1—Patient's fundus photographs.

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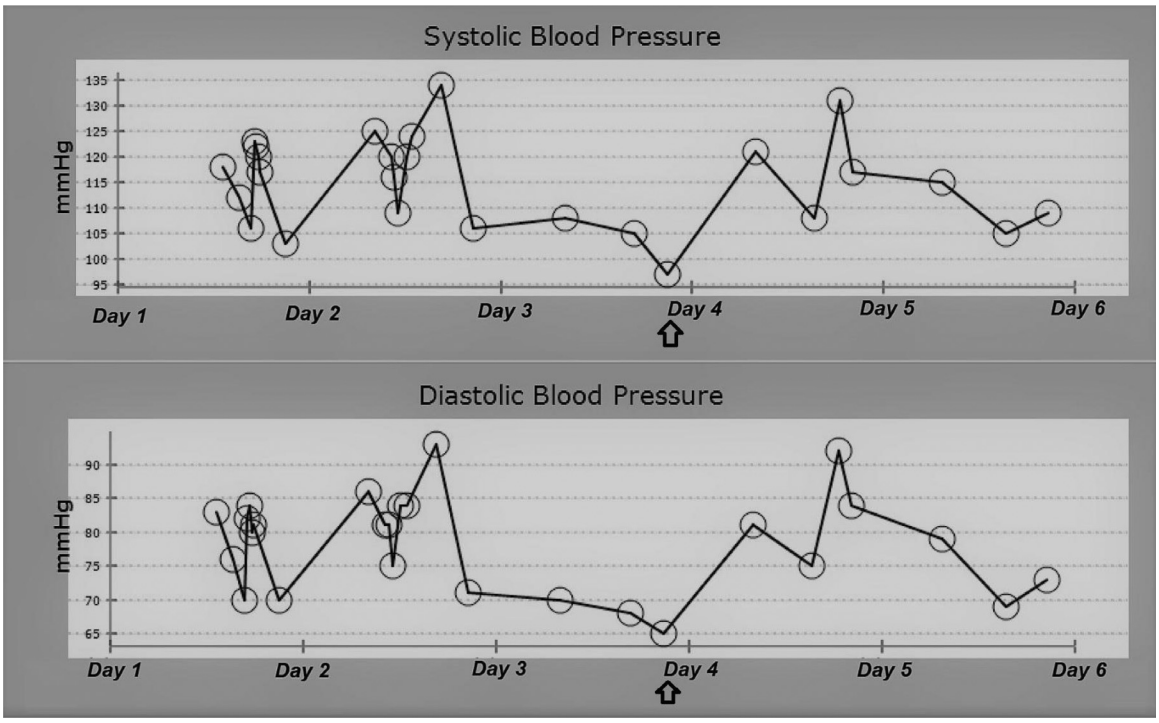

Fig. 2—Patient's nocturnal systolic blood pressure during hospitalization.

efficiently autoregulates blood flow, maintaining consistent perfusion despite physiologic variation in perfusion pressure and intraocular pressure. However, those with vascular risk factors, particularly hypertension and diabetes, have impaired autoregulation capabilities. Likewise, around 97% of patients with NAION have a small cup to-disc ratio. Although the association between this "disc at risk" and NAION is unknown, it is hypothesized that a crowded disc is prone to obstruction of axoplasmic flow, resulting in secondary compression, ischemia, and eventual ganglion cell death.[1] While the causal role of nocturnal BP decrease in the etiology of NAION is accepted by many, there is reasonable debate.

Of note, a 2016 article between Cestari and Arnold.[1] provided excellent insight into the challenges of this theory. Arnold argued that the diurnal variance in BP between those with NAION and those without may be insignificant, and thus nocturnal BP levels may not play a causal role in NAION. However, this difference between peak and trough BP levels does not account for a drop below the patient's perfusion threshold. The concluding analysis by Lee and Van Stavern contends that episodes of NAION represent the convergence of multiple factors (i.e., vasculopathic risk factors and small cup-to-disk ratios) that ultimately reach a tipping point. Our case suggests that this tipping point may indeed be an episode of below-threshold nocturnal BP decrease.[1]

Our vasculopathic patient was observed to have a diurnal systolic BP variation of around 25 mm Hg; however, in no preceding night of her hospitalization had her nocturnal systolic BP dipped below 104 mm Hg, and the patient first noticed symptoms of her classic NAION several hours after such a reading (97 mm Hg) was measured.

We describe an episode of nocturnal hypotension prior to the presentation of NAION. Although this patient is much younger than the usual population with NAION, she had multiple predisposing vasculopathic risk factors (i.e., type IIIc diabetes mellitus, cardiac transplantation secondary to autoimmune hemolytic anemia, iron overload, and chelation therapy), as with most patients with NAION. Although NAION remains multifactorial and nocturnal hypotension is not proven to cause NAION, our case provides evidence that considerable lowering of nocturnal BP may ultimately precipitate NAION.

Supplementary Materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.jcjo.2022.02.016.

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Footnotes and Disclosure

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