Clinical Case Report

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Anomalous coagulation factors in non-arteritic anterior ischemic optic neuropathy with central retinal vein occlusion

A case report

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Abstract

Rationale: Non-arteritic anterior ischemic optic neuropathy (NAION) is characterized by sudden, painless visual loss and optic disc edema. NAION occurs mainly in the presence of cardiovascular disease and hypercoagulability, mainly in patients over 50 years of age. We experienced a case of NAION associated with central retinal vein occlusion (CRVO) in a young man with no underlying disease.

Patient concerns: A 46-year-old man was referred to our clinic following a sudden loss of vision in his right eye. The patient exhibited no underlying disease and reported no ongoing medication. Significant visual loss and visual disturbance of the right eye were observed. The pupil of the right eye was enlarged and an afferent pupillary defect was observed. On fundus examination, retinal hemorrhage was observed in the peripheral retina; macular edema was observed in optical coherence tomography analysis. However, optic disc edema was not evident. No abnormal findings were found in routine blood tests for hypercoagulability. After 3 days of steroid intravenous injection, macular edema disappeared and visual acuity was improved, but optic disc edema began to appear. One week later, optic disc edema was evident and visual acuity was significantly reduced; thus, the patient was diagnosed with NAION. In fluorescein angiography, peripheral retinal ischemia was observed, suggesting that CRVO was complicated. Blood tests, including analysis of coagulation factors, were performed again, showing that coagulation factors IX and XI were increased.

Diagnoses: Anomalous coagulation factors in non-arteritic anterior ischemic optic neuropathy with central retinal vein occlusion.

Interventions: Systemic steroids were administered.

Outcomes: One month later, optic disc edema and retinal hemorrhage gradually diminished and eventually disappeared; however, visual acuity did not recover.

Conclusion: In young patients without underlying disease, cases of NAION require careful screening for coagulation disorders. Even if there is no abnormality in the test for routine coagulation status, it may be necessary to confirm a coagulation defect through an additional coagulation factor assay.

Abbreviations: CRVO = central retinal vein occlusion, NAION = Non-arteritic anterior ischemic optic neuropathy, OCT = optical coherence tomography, RAPD = relative afferent pupillary defect.

Keywords: central retinal vein occlusion, factor 9, factor 11, non-arteritic anterior ischemic optic neuropathy

1. Introduction

Non-arteritic anterior ischemic optic neuropathy (NAION) is characterized by sudden, painless loss of visual acuity and visual field, associated with optic disc swelling.[1] Although the precise mechanism of NAION has not yet been elucidated, vascular risk factors, such as hypertension,[2,3] hyperlipidemia,[4,5] diabetes,[2,3] and smoking,[6] have been associated with an increased risk of NAION. Because such risk factors increase with age, NAION often occurs at relatively older ages and is known as the most common acute optic neuropathy in patients over 50 years of age.[7] As another potential risk factor for NAION, hypercoagulable states have been postulated in several case reports.[8–10]

Rarely, NAION also occurs in young patients. In such cases, it is important to distinguish between diseases that cause optic disc swelling in a young age, such as optic neuritis, optic disc drusen, optic nerve glioma, and pseudotumor cerebri. Because NAION demonstrates poor visual prognosis and can also occur in the fellow eye, it is important to diagnose NAION in young patients and to identify risk factors for NAION in the younger population. Notably, if NAION occurs in a young patient, a

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detailed examination of the hypercoagulable state should be performed. We have experienced a case of NAION with central retinal vein occlusion (CRVO) in a young patient, associated with elevated coagulation factors IX and XI. To our knowledge, this is the first report to observe an increase in coagulation factors IX and XI in a case of NAION.

2. Case report

A 46-year-old man was referred to our clinic because of a sudden onset of painless visual loss in his right eye. No history of medical conditions, such as hypertension, diabetes, or hyperlipidemia, was found, and he reported no ongoing medication. The best corrected visual acuities of the right and left eyes were 20/500 and 20/20, respectively. In the Ishihara color vision test, the right eye could not identify any of the 15 plates, whereas the left eye correctly recognized all 15 plates. The pupil of the right eye was dilated and a grade 3 relative afferent pupillary defect (RAPD) was observed in the right eye. Dot hemorrhages were observed in the peripheral retina during fundus examination of the right eye (Fig. 1A). The optic disc shape was nearly normal (Fig. 1B). The fundus of the left eye was normal. Optical coherence tomography (OCT) showed significant macular edema of the right eye (Fig. 1C). No optic disc edema was observed. In visual field tests, a significantly constricted visual field was observed in the right eye. Fluorescein angiography showed a generalized leakage of the right eye, and the optic nerve head was strongly stained in the late phase of angiography (Fig. 1D). A blood test was performed, including complete blood count, erythrocyte sedimentation rate, prothrombin time, activated partial thromboplastin time, kidney and liver function test, lipid profiles, tests for syphilis (rapid plasma reagin, fluorescent treponemal antibody absorption), tests for antiphospholipid antibody syndrome (lupus anticoagulant, anti-cardiolipin antibodies), antithrombin III, protein C and protein S, and homocysteine.

Our first diagnosis was optic neuritis; therefore, the patient was hospitalized and received high-dose intravenous steroid therapy (1 g/day). After 3 days of treatment, the best corrected visual acuity of the right eye had improved to 20/60. Ishihara color vision test had also improved to recognize 11 plates, and visual field test showed a significant improvement. No abnormal findings were observed in blood tests. No brain lesions were observed in the brain magnetic resonance imaging scan. During fundus examination, peripheral retinal hemorrhages were stationary, but an edematous optic nerve head was observed (Fig. 1E). Macular edema resolved in the OCT, but optic disc edema was noted (Fig. 1F).

The patient was discharged from hospital with slowly tapered oral steroid medication. One week after discharge, he returned to our clinic because of poor visual acuity in the right eye. Visual acuity had reduced to 20/1000, and color vision was also significantly impacted. Fundus examination showed an increase in peripheral retinal hemorrhages and very severe optic disc edema (Fig. 2A–C). Fluorescein angiography showed a non-perfusion area of the peripheral retina that was not previously observed (Fig. 2D). Blood tests were performed again; in this instance, we also assessed coagulation factors. Importantly, coagulation factors IX and XI were found to be increased. The patient was referred to a hematologist for systemic evaluation for thrombotic diseases. However, no abnormalities were observed in other organs.

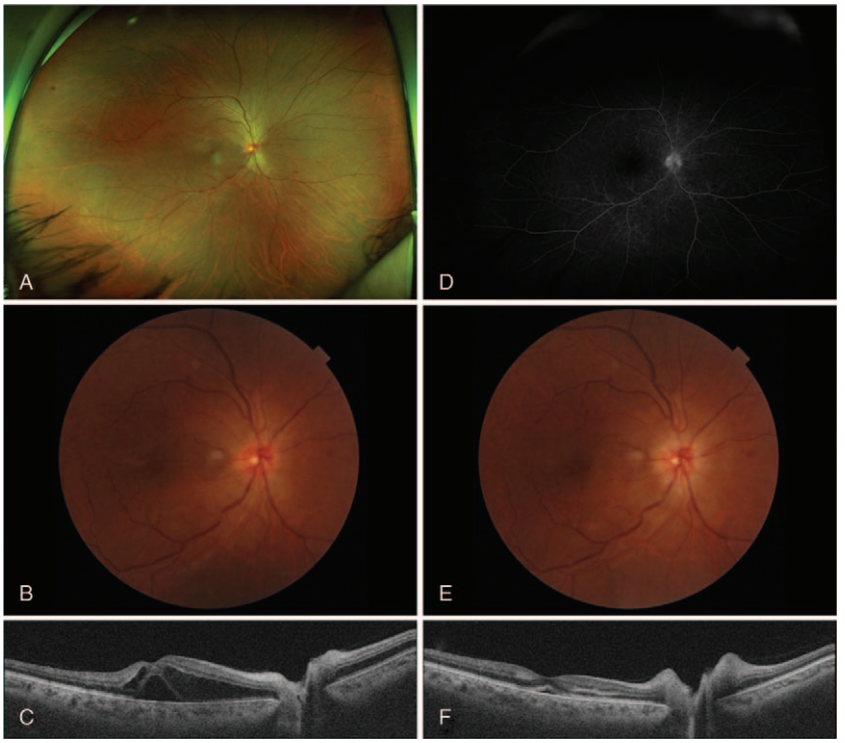

Figure 1. Ophthalmologic examination at initial visit (A–D) and after high-dose intravenous steroid therapy (E, F). (A) Peripheral retinal hemorrhage is observed in a wide fundus photograph. (B) The shape of the optic nerve is nearly normal. (C) Macular edema is observed in optical coherence tomography (OCT). (D) Mild optic nerve staining is observed in fluorescein angiography. (E) After steroid pulse therapy, the optic disc edema begins to appear. (F) Resolution of macular edema and the development of optic disc edema are observed in OCT.

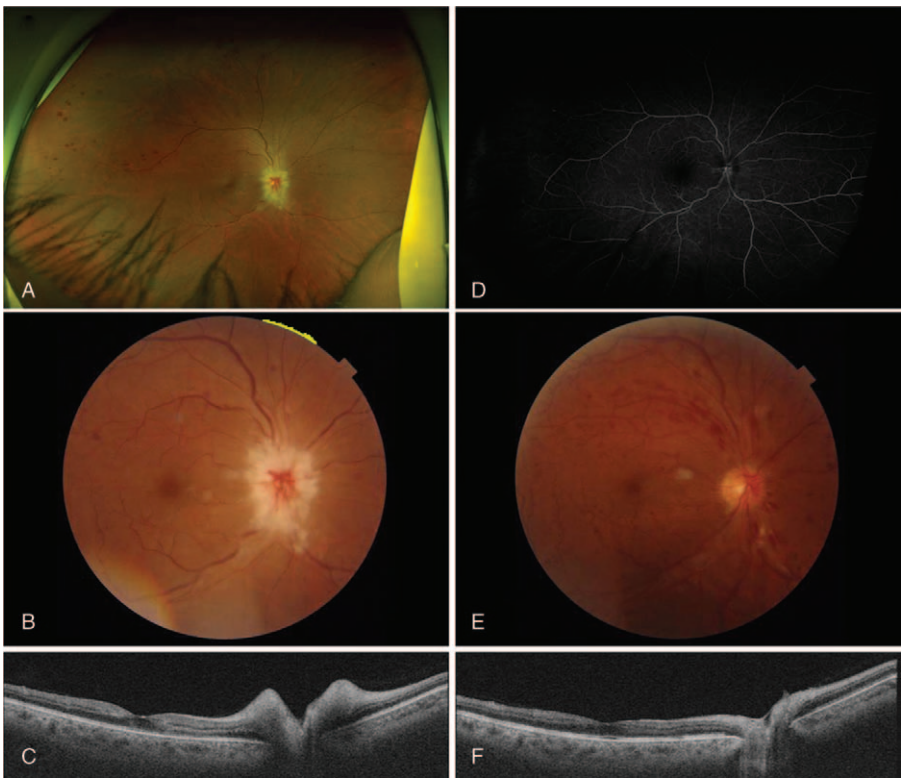

Figure 2. Ophthalmologic examination after 1 week (A–D) and 1 month (E, F) of treatment. (A, B) Marked optic disc edema is observed. A wide fundus photograph shows increased peripheral retinal hemorrhage. (C) Marked optic disc edema is observed in optical coherence tomography (OCT). (D) Non-perfusion of the peripheral retina is observed in fluorescein angiography. (E) No optic nerve edema is observed. (F) OCT demonstrates the disappearance of optic disc edema.

Optic nerve head swelling began to decrease gradually and completely disappeared after 1 month. At this time, laser photocoagulation was applied to the non-perfusion area of the peripheral retina. Two months later, optic disc edema was not observed, but flame-shaped hemorrhages around the optic nerve were observed more prominently (Fig. 2E, F). The patient's visual acuity remained very low (counting finger).

3. Discussion

This case exhibited 4 changes in clinical features during the follow-up period. Initial clinical manifestations were macular edema, subtle peripheral retinal hemorrhage, and positive RAPD suggestive of optic neuropathy; therefore, we performed steroid pulse therapy. After treatment, macular edema decreased and visual acuity was temporarily restored. However, worsened optic disc edema and increased peripheral retinal hemorrhage were observed; moreover, visual acuity decreased again. Finally, disc edema and retinal hemorrhage resolved without any treatment, but low vision remained as a sequelae. The atypical progression of disease and the patient's young age made it difficult to diagnose NAION and CRVO.

We presumed that subclinical NAION, without prominent disc swelling, had appeared initially, and that CRVO occurred secondarily due to venous compression caused by acute swelling of the optic disc. Although macular edema is more commonly associated with CRVO, initial macular edema appeared to be secondary to NAION itself, as peripheral retinal hemorrhage was very subtle at the initial visit.[11] However, we cannot exclude CRVO as a cause of macular edema. Steroid pulse therapy improved the macular edema in this case and resulted in temporary visual improvement. The effect of systemic steroids in NAION remains controversial. Hayreh and Zimmerman reported that systemic steroids in NAION patients resulted in a rapid reduction of optic disc edema, leading to positive visual outcomes.[12] In contrast, Rebolleda et al reported that the same dose of systemic steroids did not improve the visual acuity or visual field of NAION patients.[13] In our case, systemic steroids improved the macular edema that was induced by NAION, mild CRVO, or (possibly) both factors; however, the optic disc edema was further aggravated after intravenous steroid use. This aggravated disc swelling may be a result of disease progression or a procoagulant effect of systemic steroid therapy.[14]

There have been previous reports of NAION associated with CRVO. Abu el-Asrar et al reported 2 cases, one with impaired fibrinolytic function and another with positive antiphospholipid antibodies.[15] In both cases, the patient was under 50 years of age. In a study that revealed factors associated with NAION in >1 million subjects, hypercoagulable states displayed a 146% increased hazard of being diagnosed with NAION. In addition, retinal venous occlusive disease itself has been shown to increase the risk of NAION fourfold.[16] Therefore, it is important to identify the hypercoagulable state through blood testing in cases where NAION, associated with CRVO, is present in young patients.

In our case, the coagulation factors IX and XI were elevated in blood tests. The test for the coagulation factor is not routinely performed as part of thrombophilia evaluations in our clinic; thus, it was not performed as part of the initial blood test. Hypercoagulable states associated with elevated coagulation factors are less well-known than other risk factors, such as hyperhomocysteinemia, deficiencies of protein C, protein S, and

antithrombin. Factor IX is a vitamin-K-dependent clotting factor and an important component of the intrinsic pathway of the coagulation process. A congenital deficiency of factor IX is known to cause hemophilia B leading to bleeding tendency. van Hylckama Vlieg et al reported that high levels of factor IX increased the risk of deep vein thrombosis.[17] Heikal et al reported that elevated factor IX activity also increased the risk of arterial transient ischemic attack and stroke, as well as venous thromboembolism.[18] Factor XI is a component of the intrinsic pathway, contributing to the formation of thrombin, which is involved in the generation of fibrin. Deficiency of factor XI is known to cause mild-to-moderate hemorrhagic disease.[19] Further, an increase in factor XI has been reported to increase venous thrombosis.[20] Increased factors IX and XI in this patient may have contributed to the occurrence of NAION with CRVO by promoting the coagulation process in both arterial and venous circulation.

4. Conclusion

We experienced a rare case of NAION with CRVO, which occurred in a young patient. This is the first report to identify elevated coagulation factors IX and XI in a patient with NAION, accompanied by CRVO. If NAION with CRVO occurs in younger patients, detailed examinations of hypercoagulable states, including coagulation factors, may be needed.

Author contributions

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