Granulomatosis with polyangiitis-associated ischemic optic neuropathy in a previously healthy 50-year-old female

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ABSTRACT

Purpose: To describe a case of anterior ischemic optic neuropathy as a presenting sign of granulomatosis with polyangiitis.

Observations: A previously healthy 50-year-old female developed right eye, then left eye, redness and pruritis and was diagnosed with allergic versus viral conjunctivitis. Five days later, she noted an acute decline in vision in the right eye, corresponding with a decrease on Snellen testing from 20/30 to 20/100 with correction. She was noted to have a right relative afferent pupillary defect, 2+ pallid disc edema, and OCT (Spectralis, Heidelberg Engineering, Carlsbad, CA) findings of significant retinal nerve fiber thickening. Review of systems revealed a three-month history fatigue, right-sided headaches, jaw claudication, bronchitis, cough without hemoptysis, and epistaxis, as well as interval development of a petechial rash across her body, migratory polyarthralgias, fevers, and tachycardia. ESR and CRP were markedly elevated, and the patient was admitted to the hospital for a systemic vasculitis workup. She was started on IV methylprednisolone. Her vision improved dramatically with steroids, measuring 20/50 with correction in the right eye after 24 hours and returning to baseline after five days. An extensive workup including imaging, bloodwork, and biopsies led to a diagnosis of granulomatosis with polyangiitis, with PR3-positive ANCA.

Conclusions: Ocular findings, including anterior ischemic optic neuropathy, may be the presenting signs for patients with granulomatosis with polyangiitis. Prompt recognition and treatment with high-dose steroids and immunomodulatory therapy is important for visual recovery.

Importance: Prompt recognition of potential vasculitis-related vision loss can lead to timely initiation of vision-saving treatment.

1. Introduction

Granulomatosis with polyangiitis (GPA) is a systemic necrotizing vasculitis of small arteries and veins. Vision loss or total blindness from GPA has been reported in up to 37% of patients with this disease, and is more common in cases where there is a delay in diagnosis or treatment. The age of GPA symptom onset can vary greatly, with cases being described as early as 6 years of age and a peak incidence between ages 64 and 75 years. We describe a case of a 50-year-old patient diagnosed with GPA whose presenting symptom was vision loss.

2. Case

A 50-year-old female with three months of bronchitis refractory to medical therapy presented with intermittent blurry vision, photophobia, and a throbbing right-sided headache. The patient reported right eye redness and pruritis over the past month and similar symptoms in the left eye over the past two weeks. Best-corrected Snellen visual acuity was 20/30 in the right eye and 20/25 in the left eye. Slit lamp exam was remarkable for bilateral 4+ conjunctival injection with follicular eruption involving the upper eyelids and multiple small, white stromal opacities in periphery of the cornea. She was diagnosed with allergic versus viral conjunctivitis and started on fluorometholone 0.1% twice daily and preservative-free artificial tears as needed.
She returned five days later with a complaint of worsening vision. Her Snellen visual acuity in the right eye had declined to 20/100, and there was a new right relative afferent pupillary defect. Intraocular pressure, confrontation visual field testing, and extraocular movements were within normal limits. Ishihara color plate testing showed 2/10 correct responses in the right eye and 10/10 correct responses in the left eye. Slit lamp exam was similar to examination five days prior. Dilated fundus exam showed 2+ pallid disc edema of the right optic nerve head. OCT (Spectralis, Heidelberg Engineering, Carlsbad, CA) was remarkable for significant swelling of the inferior retinal nerve fiber layer (Fig. 1). Positive findings on review of systems included the following: interval development of petechial-like blisters on her fingers, toes, and bilateral inner thighs; fevers; tachycardia; migratory polyarthralgia with her hands, wrists, elbows, knees, and hips; and fatigue. In the past three

Fig. 1. OCT retinal nerve fiber layer thickness at the time of initial presentation.
months, the patient had developed bronchitis and wheezing as well as other assorted symptoms: phlegm, jaw claudication, cough without hemoptysis, epistaxis, nausea/vomiting, severe abdominal pain, and fatigue. Labwork obtained was notable for leukocytosis with WBC count of 15.0 × 10^9/L (reference range 3.2–9.8 × 10^9/L), 2+ blood in the urine, CRP 153.1 (reference range 0–4.9 mg/L), rheumatoid arthritis latex turbid 126.5 (reference range 0–13.9 IU/mL), and ESR 72 (reference range 0–40 mm/hr). Given concern for a systemic vasculitis, the patient was referred to the emergency room for further evaluation. An MRI orbits with and without contrast was obtained and unremarkable.

Fig. 2. Humphrey Visual Field 24-2 and OCT macula one day after treatment with IV steroids.
The patient was admitted and started on methylprednisolone 1g IV daily.

By the following day, her right eye vision had improved to 20/50 with correction by near card. Humphrey Visual Field testing (Zeiss, Oberkochen, Germany) showed generalized depression of the right eye and nonspecific changes of the left eye (Fig. 2a). OCT (Spectralis, Heidelberg Engineering, Carlsbad, CA) of the right eye showed a swollen optic nerve head, and OCT of the left eye showed a hyper-reflective band in the middle layers of the retina, suspicious for paracentral acute middle maculopathy (Fig. 2b). Fluorescein angiography (Spectralis, Heidelberg Engineering, Carlsbad, CA) showed delayed choroidal filling and areas of choroidal nonperfusion in the right eye, as well as late peripheral capillary leakage. By five days after steroid initiation, patient’s visual acuity had improved to 20/20 with correction in both eyes by near card.

Labwork returned positive for anti-neutrophil cytoplasmic antibody, with a 1:640 anti-neutrophil cytoplasmic antibody titer. Anti-proteinase 3 (PR3) antibody was also elevated >100 (reference range ≤20 Units). Lyme testing, antinuclear antibody panel, CCP antibody testing, RPR testing, Rocky Mountain Spotted Fever IgM, hepatitis panel, C3 and C4 levels, blood cultures, anti-streptolysin O, IgG subclasses, cryoglobulin, respiratory virus panel, anti-myeloperoxidase antibody, glomerular basement membrane antibody, and PT/INR were within normal limits. Quantiferon gold was tested twice and returned indeterminate. A 4-mm punch biopsy of a skin lesion of the left thigh showed IgG diffuse granular deposits in broad bands at the basement membrane with no

Fig. 3. Optos and OCT from the time of diagnosis versus three weeks after treatment.
distinct perivascular deposits, consistent with a small vessel vasculitis. Core needle biopsy of the patient’s kidney showed focal necrotizing glomerulonephritis, pauci-immune type, and extensive thinning of glomerular basement membranes.

The patient was diagnosed with GPA, with PR3-positive ANCA. She improved systemically and was discharged on oral prednisone.

At ophthalmic follow-up two weeks later, the patient reported improvement in her vision. Her best-corrected Snellen visual acuity was 20/25 in the right eye and 20/20 in the left eye. Her right relative afferent pupillary defect persisted. The right optic nerve was noted to be pale with a 1+ cuff of fluid. OCT (Spectralis, Heidelberg Engineering, Carlsbad, CA) (Fig. 3a) and wide-field fundus photography (Optos, Dunfermline, United Kingdom) (Fig. 3b) showed interval improvement in optic nerve head swelling. The patient was started on azathioprine 100mg daily, and she began a multi-month prednisone taper, per rheumatology.

At her most recent follow-up, 3.5-month after her hospitalization, her best corrected Snellen visual acuity was 20/25 in the right eye and 20/20 in the left eye, and the right optic nerve was noted to have 4+ pallor. Her right relative afferent pupillary defect persisted. Humphrey Visual Field testing (Zeiss, Oberkochen, Germany) (Fig. 4a) and OCT (Spectralis, Heidelberg Engineering, Carlsbad, CA) (Fig. 4b) showed...
interval improvement in the patient’s visual field and resolution of optic nerve head swelling, respectively.

3. Discussion

Ocular manifestations are common in cases of GPA, typically seen in the form of orbital mass, scleritis, or episcleritis; however, ocular involvement manifesting as anterior ischemic optic neuropathy is rare. The classic teaching in ophthalmology is to presume a diagnosis of giant cell arteritis, given its life-threatening consequences, if history and exam suggest arteritic anterior ischemic optic neuropathy (AAION). While we agree with this practice, our case highlights the importance of considering additional forms of vasculitis in the differential, while employing prompt therapy.

If suspicion for GPA or other vasculitis is high based on history and review of systems, immediate laboratory testing should be pursued. This includes CBC, BMP, ESR, CRP, ANCA, antinuclear antibodies, anti-glomerular basement membrane antibodies, C3 C4, and cryoglobulins. Radiographic tests, including chest CT and/or X-ray to assess for pulmonary involvement (pulmonary infiltrates, nodules, or hilar adenopathy), and MRI orbits with and without contrast, if ocular involvement is suspected, should also be considered. Biopsy of any involved sites, e.g., skin, conjunctiva, or kidney, may also be attempted.

If suspicion is reasonably high given initial history, exam, and laboratory testing, high dose glucocorticoids (IV methylprednisolone initially followed by prednisone 1 mg/kg/day) should be initiated, followed by consideration of immunomodulating therapies such as cyclophosphamide or rituximab. Without prompt treatment of GPA, survival rates are as low as 20% at one year.

In summary, underlying systemic vasculitides, including GPA, should be considered in cases of anterior ischemic optic neuropathy. A careful exam and thorough review of systems, focusing on the presence of other vascular skin lesions or organ involvement, can provide valuable information in yielding an ultimate diagnosis of systemic vasculitis. Immediate workup and treatment can significantly improve prognosis and reduce morbidity.

4. Conclusions

Vision loss may be a presenting symptom of GPA. It is important to keep GPA and other vasculitides on the differential in cases of anterior ischemic optic neuropathy, especially in the setting of review of systems suggestive of the disease. Prompt recognition and treatment of GPA is important for visual recovery.

Patient consent

Consent to publish the case report was not obtained, as this report does not contain any personal information that could lead to the identification of the patient.

Ethics committee approval

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OCT retinal nerve fiber layer (RNFL) thickness report from OCT (Spectralis, Heidelberg Engineering, Carlsbad, CA) showing thickening of the RNFL of the right eye.
Humphrey Visual Field (Zeiss, Oberkochen, Germany) testing with mild improvement in generalized depression of the right eye and possible emerging superior arcuate defect of the left eye (a).
OCT (Spectralis, Heidelberg Engineering, Carlsbad, CA) cross sectional b-scans of the right eye, from the time of diagnosis (top) to the time of follow up (bottom) showing reduction in nerve swelling over time (b).

Interactive questions

1. Which of the following is false regarding granulomatosis with polyangiitis?
   a. It is a systemic necrotizing vasculitis of small arteries and veins
   b. It has been associated with vision loss, including blindness
   c. It is almost exclusively seen in patients over the age of 55 years
   d. It should be on the differential for patients with epistaxis, hemoptysis, and/or petechial rashes

   Answer: c. The age of granulomatosis with polyangiitis symptom onset can vary greatly, with cases being described as early as 6 years of age and a peak incidence between ages 64–75 years.

Arteritic anterior ischemic optic neuropathy

a. Should raise concern for giant cell arteritis
b. Can rarely be seen with granulomatosis with polyangiitis
c. Should be treated promptly with high dose steroids
d. All of the above
e. A & C

Answer: d.

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