EJCRIM
European Journal
of Case Reports
in Internal Medicine

SUDDEN VISUAL LOSS DUE TO ARTERITIC ANTERIOR ISCHAEMIC OPTIC NEUROPATHY: A RARE MANIFESTATION OF EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS

Antonio Faraone[1], Alberto Fortini[1], Vanni Borgioli[2], Chiara Cappugi[1], Aldo Lo Forte[1], Valeria Maria Bottaro[1], Augusto Vaglio[3,4]

[1] Department of Multidimensional Medicine, Internal Medicine Unit, San Giovanni di Dio Hospital, Florence, Italy
[2] Department of Ophthalmology, San Jacopo Hospital, Pistoia, Italy
[3] Department of Biomedical, Experimental and Clinical Sciences "Mario Serio", University of Firenze, Florence, Italy
[4] Nephrology and Dialysis Unit, Meyer Children's Hospital IRCCS, Florence, Italy

Corresponding author: Antonio Faraone **e-mail:** antonio.faraone@uslcentro.toscana.it

Received: 31/01/2024 **Accepted:** 19/02/2024 **Published:** 21/03/2024

Conflicts of Interests: The Authors declare that there are no competing interests.
Patient Consent: Patient consent for publication was obtained.

How to cite this article: Faraone A, Fortini A, Borgioli V, Cappugi C, Lo Forte A, Bottaro VM, Vaglio A. Sudden visual loss due to arteritic anterior ischaemic optic neuropathy: A rare manifestation of eosinophilic granulomatosis with polyangiitis. *EJCRIM* 2024;**11**:doi:10.12890/2024_004345.

ABSTRACT

Background: eosinophilic granulomatosis with polyangiitis (EGPA) is a rare multisystem inflammatory disease characterized by asthma, eosinophilia and granulomatous or vasculitic involvement of various organs. While the eye is uncommonly affected in patients with EGPA, multiple ophthalmic manifestations have been reported, which can result in serious visual impairment without timely treatment.

Case report: we report the case of a 79-year-old woman with a history of asthma and nasal polyps who presented with low-grade fever, mild alteration of mental status, and fatigue. Chest X-ray revealed bilateral interstitial infiltrates. Lab tests showed elevated C-reactive protein level and eosinophilia (eosinophil count, 4.6 x10^9 cells/l); blood cultures and parasitological examination of stools tested negative. Four days after presentation, the patient reported sudden and severe blurring of vision in her left eye. Ophthalmological examination revealed bilateral swollen optic disc and visual field loss, more severe in the left eye. A diagnosis of EGPA complicated by arteritic anterior ischaemic optic neuropathy (A-AION) was proposed, while an alternative or concurrent diagnosis of giant cell arteritis was ruled out based on clinical picture. Immunosuppressive treatment with high-dose intravenous glucocorticoids was promptly started. The patient's visual defect did not improve; however, two months later, no worsening was registered on ophthalmic reassessment.

Conclusions: A-AION is an infrequent but severe manifestation of EGPA, requiring prompt diagnosis and emergency-level glucocorticoid therapy to prevent any further vision loss. Disease awareness and a multidisciplinary approach are crucial to expedite diagnostic work-up and effective management of EGPA-related ocular complications.

KEYWORDS

Anterior ischaemic optic neuropathy, eosinophilia, eosinophilic granulomatosis with polyangiitis, vasculitis, visual loss

EFIM
European Federation of Internal Medicine

Publisher
smc media srl

LEARNING POINTS

- Arteritic ischaemic optical neuropathy is a potential cause of sudden and severe visual loss in eosinophilic granulomatosis with polyangiitis (EGPA) patients.
- Visual loss due to arteritic ischaemic optical neuropathy is rarely reversible; however, a timely glucocorticoid treatment may prevent further progression of visual impairment.
- Multidisciplinary approach is crucial to expedite diagnostic work-up and effective management of EGPA patients with ocular complications.

INTRODUCTION

Eosinophilic granulomatosis with polyangiitis (EGPA) is a rare multisystem inflammatory disease characterized by asthma, eosinophilia and granulomatous or vasculitic involvement of various organs[1]. The eye and orbit are not typically involved; however, various ophthalmic manifestations have been described in EGPA patients[2]. We describe the case of an elderly woman who was admitted with classic manifestations of EGPA and developed sudden and severe vision loss, due to arteritic anterior ischaemic optic neuropathy (A-AION).

CASE DESCRIPTION

A 79-year-old woman presented to the emergency department with low-grade fever, mild alteration of mental status, and fatigue. Her past medical history was notable for asthma. She took no medications except for inhaled salbutamol. The patient's oxygen saturation on room air was 96%, body temperature was 37.7 °C. At physical examination, she was oriented but mildly lethargic; no headache or meningeal signs were present. Chest auscultation revealed expiratory wheezing in lung bases. The patient underwent head computed tomography (CT) scan, which was negative. Chest X-ray revealed bilateral interstitial infiltrates. Laboratory studies showed a high C-reactive protein level (CRP, 13 mg/dl, normal < 0.5 mg/dl), leukocytosis (total white blood cells, 22.7 x 10^9 cells/l) with eosinophilia (absolute eosinophil count, 4.6 x 10^9 cells/l), normal serum creatinine and unremarkable urinalysis. The patient was admitted to

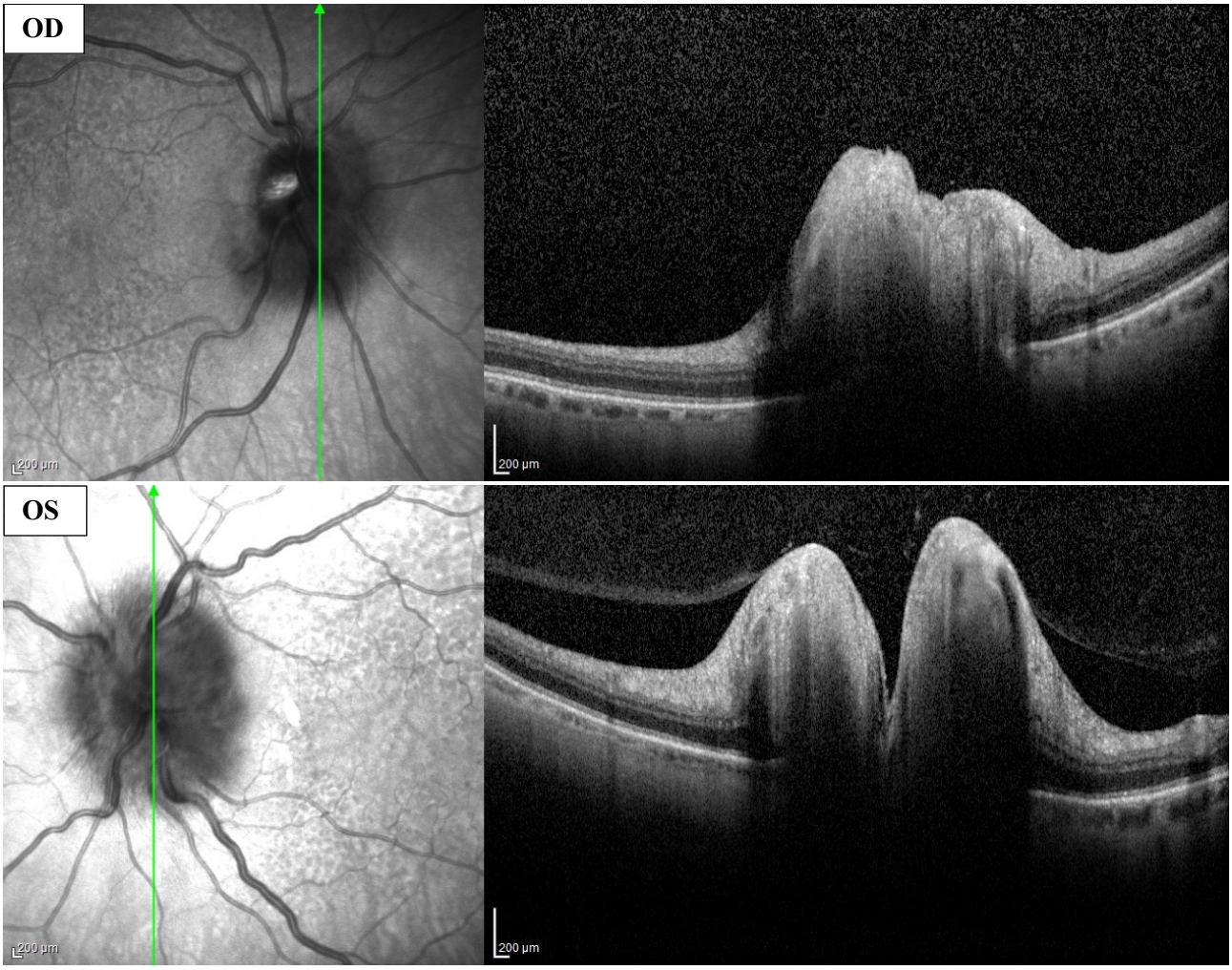

Figure 1. Fundus photograph and corresponding OCT of the right (OD) and left eye (OS), showing papilledema.

our internal medicine ward with a presumptive diagnosis of pneumonia and was started on ceftriaxone. Two days later, no clinical improvement was achieved. To rule out encephalitis, she underwent a cerebrospinal fluid test, which was unremarkable. The presence of eosinophilia led us to perform a stool parasitology test, which yielded negative results. Blood cultures were also negative. On the fourth day after admission, the patient reported sudden and severe vision loss in her left eye. Neurological examination did not reveal any focal signs. Magnetic resonance imaging of the head was negative. ECG showed sinus rhythm, and duplex carotid ultrasound revealed no significant atherosclerotic disease. An ocular vasculitis was postulated, and treatment with intravenous methylprednisolone 500 mg daily was promptly initiated. The day after, the patient underwent a complete ophthalmological examination. Visual acuity was "hand motion" in the left eye and 6/7.5 in the right; fundoscopy revealed oedema of both optic discs, more marked in the left eye, which was confirmed by the optical coherence tomography (OCT) *(Fig. 1)*. Humphrey visual field testing showed a predominantly superior altitudinal defect in the right eye, and widespread, severe field loss in the left eye *(Fig. 2)*. The ophthalmologist diagnosed the patient with arteritic anterior ischaemic optic neuropathy (A-AION) and expressed concern for giant cell arteritis (GCA). At this point, a thorough review of the patient's current manifestations and past medical background was conducted. She did not complain of temporal headache, scalp tenderness, jaw claudication, or shoulder or neck stiffness. No tenderness to palpation or decreased pulsation of the temporal arteries was found. Regarding past history, aside from adult-onset asthma, the patient reported surgery for recurrent nasal polyps. The search for serum ANCA yielded a negative result.

Based on the clinical picture including asthma, nasal polyps, eosinophilia, lung infiltrates and constitutional symptoms, a diagnosis of EGPA complicated by ocular vasculitis was made, while the hypothesis of a GCA was discarded. Four days after the start of steroid treatment, intravenous methylprednisolone was converted to oral prednisone (1 mg/kg) associated with mycophenolate mofetil 180 mg twice daily. In a few days, the patient's fever subsided and her eosinophilic count normalized, while no vision improvement was obtained. The patient was discharged and referred to the rheumatology and ophthalmology outpatient clinics. Two months later, no progression of visual field loss was detected.

DISCUSSION

Our case presented with ocular vasculitis in the background of eosinophilia, pulmonary infiltrates, constitutional symptoms, and history of asthma and nasal polyps. CRP was high, ANCA were negative. Based on clinical and laboratory criteria, a diagnosis of EGPA complicated by A-AION was made.

EGPA is a rare small-vessel ANCA-associated vasculitis, histologically characterized by tissue eosinophilia, necrotizing vasculitis and eosinophil-rich granulomatous inflammation[1]. Clinical manifestations are quite heterogeneous, although asthma, usually arising in adulthood, and eosinophilia are present in over 90% of cases. Despite its diverse clinical presentation, EGPA is traditionally described to evolve through three different phases: a prodromic 'allergic' phase, characterized by asthma and chronic rhinosinusitis; an eosinophilic phase, characterized by peripheral eosinophilia and eosinophilic infiltration of multiple organs, during which lung infiltrates,

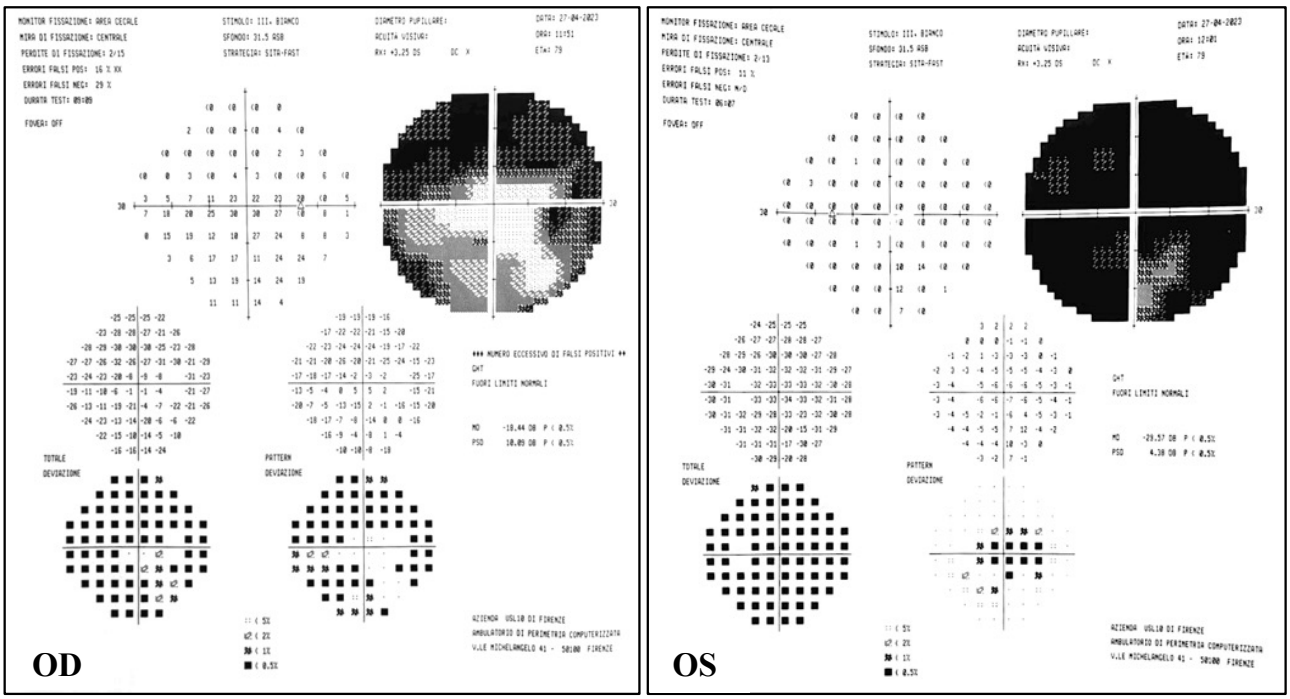

Figure 2. Humphrey visual field plot showing a mainly superior altitudinal visual field defect in the right eye (OD), and a severe and widespread visual field loss in the left eye (OS).

cardiomyopathy and gastroenteritis can be diagnosed; and a vasculitic phase, during which clinical manifestations of small-vessel vasculitis can appear, including peripheral neuropathy, skin lesions, and glomerulonephritis[1]. In this phase, constitutional symptoms such as fatigue, fever, myalgia, and weight loss are also frequently reported, as a consequence of generalized inflammation[3]. With regard to laboratory findings, active EGPA is characterized by high CRP and erythrocyte sedimentation rate. ANCA are detectable in 30-40% of cases and, in patients with a compatible clinical phenotype, they support the diagnosis of EGPA; the main subset of ANCA is anti-myeloperoxidase (MPO-ANCA)[1]. Given the absence of diagnostic criteria, EGPA should be diagnosed based on histopathological evidence of vasculitis on biopsy (rarely performed), and on highly suggestive clinical features[1]. The peculiarity of the present case is defined by its unusual ophthalmic involvement, in the form of A-AION, resulting in sudden and severe loss of vision mainly in the patient's left eye.

Ocular complications from EGPA have been rarely reported and can be categorized into two types: an orbital inflammation-like presentation (including conjunctival nodules, orbital myositis, orbital inflammatory syndrome, dacryoadenitis), and an ischaemic vasculitis presentation[2]. Akella et al. reviewed the literature on ophthalmic EGPA and found 25 patients with manifestations of vasculitis in the form of retinal artery or vein occlusion (48%), ischaemic optic neuropathy (ION) (32%), and retinal vasculitis or edema (8%). These patients presented most frequently with acute-onset loss of vision (88%), approximately 25% of them reported transient amaurosis prior to permanent vision loss, and most of them did not show improvement on therapy[2].

ION constitutes one of the major causes of blindness or seriously impaired vision among the middle-aged and elderly population[4]. The main cause of A-AION by far is GCA; however, other forms of systemic vasculitis, including EGPA, granulomatosis with polyangiitis and microscopic polyangiitis, can result in A-AION. Differential diagnosis is based on recognition of clinical and laboratory features associated with each disease[4]. In our case, the clinical and laboratory phenotype was highly suggestive for EGPA[5]. An alternative or concurrent diagnosis of GCA appeared improbable, since no clinical criteria were present, with the exception of sudden visual loss[6]. It is worth mentioning that, to confirm or rule out a suspected diagnosis of GCA, a biopsy and/or color Doppler ultrasound of temporal arteries are recommended[6,7]. Fluorodeoxyglucose positron emission tomography (FDG-PET) is another imaging modality that can assist the diagnosis of GCA in patients with a nondiagnostic initial workup, by showing abnormal aortic FDG uptake[6,7]. Since we did not perform these diagnostic exams in our patient, it should be recognized that we cannot reliably exclude the event of a GCA (responsible for A-AION) occurring fortuitously in the eosinophilic phase of an EGPA. Previous reports have described a limited number of patients with classical manifestations of EGPA and concurrent temporal arteritis, a condition that can result 1) from the overlapping occurrence of GCA and EGPA, or 2) from an unusual presentation of EGPA characterized by the involvement of a medium-size artery[8]. In all these patients fulfilling both the GCA and EGPA criteria, vision loss, when present, was associated with other typical clinical features of GCA, unlike our case[8].

Evidence regarding the treatment of severe ophthalmic complications of EGPA is scarce, but the clinical experience derived from the other ANCA-associated vasculitides and GCA suggests that these complications should be treated aggressively[1,7]. In general, A-AION requires an immediate glucocorticoid therapy to prevent any further vision loss in the affected eye or both eyes[9]. Unfortunately, even a prompt initiation of glucocorticoids is rarely associated with a significant recovery of the visual disturbance already occurred[2,10].

In our patient, as expected, no improvement of vision was observed despite timely treatment with high-dose immunosuppressive treatment. However, we can hypothesize that it prevented further progression of A-AION, especially in the less involved right eye.

CONCLUSION

A-AION is an uncommon but serious manifestation of EGPA, which can result in severe vision loss if left untreated. Awareness of EGPA ophthalmic complications along with a multidisciplinary approach are crucial to timely diagnose and effectively treat this uncommon disease. A concomitant GCA should be excluded in EGPA patients with A-AION by means of clinical, laboratory, imaging and biopsy criteria. A comprehensive ophthalmological evaluation in patients with suspected or confirmed active EGPA, aimed at detecting early signs of ocular involvement and guiding the choice of immunosuppressive therapy, might be advisable.

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