Case report

Anterior ischaemic optic neuropathy in eosinophilic granulomatosis with polyangiitis (Churg-Strauss syndrome): a case report and review of the literature

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ABSTRACT

We report a 62-year-old man with mild fever, headache and acute visual loss in his right eye due to anterior ischaemic optic neuropathy (AION), followed a few days later by pain in the legs and left arm associated with numbness and weakness.

Giant cell arteritis complicated by AION was suspected at the beginning and high-dose oral glucocorticoids were started. However, on the basis of the past medical history of nasal polyposis, asthma, and hypereosynophilia as well as of further investigations (biopsy of the nasal mucosa showing granulomatous inflammation with a rich eosinophilic infiltrate, electromyography demonstrating, mononeuritis multiplex and positive p-ANCA), eosinophilic granulomatosis with polyangiitis (EGPA), previously known as Churg-Strauss syndrome, was diagnosed.

Because visual acuity in the right eye deteriorated despite glucocorticoid therapy, pulse intravenous cyclophosphamide was started, subsequently replaced by oral azathioprine, while prednisone was slowly tapered. This treatment led to gradual improvement of the neurological symptoms, whereas the right visual impairment remained unchanged.

EGPA-related AION is an uncommon lesion that is probably due to vasculitic involvement of posterior ciliary and/or chorioretinal arteries. The prognosis of established AION is poor for the affected eye, even when glucocorticoid treatment is started immediately. However, early recognition of AION and prompt aggressive treatment with high-dose glucocorticoids plus cyclophosphamide can prevent visual loss in the unaffected eye.

Introduction

Giant cell arteritis (GCA) is the most common large-vessel vasculitis. GCA is typically characterised by headache and a variety of other cranial and systemic manifestations. Visual loss, usually due to anterior ischaemic optic neuropathy (AION), occurs in about one-sixth of patients with GCA (1). Therefore, GCA ranks high in the differential diagnosis of patients presenting with headache and AION.

Eosinophilic granulomatosis with polyangiitis (EGPA) or Churg-Strauss syndrome (CSS) is an anti-neutrophil cytoplasmic antibodies (ANCA)-associated vasculitis whose hallmark features are asthma, extravascular eosinophilic granulomas, and peripheral eosinophilia (2). Ocular involvement is rare in EGPA. Herein, we describe a patient with EGPA that developed headache and sudden-onset monocular blindness due to AION, thus mimicking GCA. We also searched the literature for other cases of EGPA complicated by AION.

Case report

A 62-year-old man was admitted in July 2011 to the Emergency Room because of sudden onset of pain and pins and needles' sensation in the left arm and the first four left fingers. Past medical history disclosed chronic obstructive pulmonary disease (COPD), bronchial asthma and relapsing nasal polyposis of several years' duration.

Computerised tomography (CT) scan of the brain and a carotid duplex ultrasound were requested, both of which were unremarkable. The patient was discharged home without specific treatment. Five days later, he developed headache and abrupt-onset visual loss in his right eye followed by mild

Table I. Summary of the cases of EGPA complicated by anterior ischaemic optic neuropathy reported in the literature.

Ref.	ANCA status	Criteria used for diagnosis	n. of cases	Age of patient	Gender of pt.	Symptoms	Therapy	Time from first manifestation of CSS to development of AION	Outcome
7	NR	Churg and Stauss (1951)	1	61	M	Sudden visual loss in the right eye and episodes of amaurosis fugax in the left eye	PDN 20 mg/day tapering	One year	Visual deficit unchanged; no new visual symptoms
14	Negative	ACR (1990)	1	44	M	Bilateral sequential sudden visual loss (painless)	PDN 40 mg/day tapering plus CYC 750 mg/sett for 4 weeks	Five years	No visual recovery; no new visual symptoms
15	Positive (MPO-ANCA)	Churg and Strauss (1951)	1	55	M	Sudden visual loss in the right eye (painful)	Pulsed iv MP 1 gr daily for 5 days followed by oral CYC 150 mg/day plus oral MP 80 mg/day tapering	Several years	No visual recovery, but improvement of the choroidal circulation in both eyes.
18	Negative	Churg and Strauss (1951)	1	46	M	Visual loss in the right eye	NR	NR (diagnosis of CSS made previously)	NR
19	Positive (MPO-ANCA)	ACR (1990)	1	39	M	Blurring of vision in the right eye and centrocecal scotoma	PDN 60 mg/day tapering plus CYC 100 mg/day	More than ten years	Rapid recovery from visual impairement
20	Positive (MPO-ANCA)	ACR (1990)	1	56	W	Sudden visual loss tin he left eye followed by dipolopia; no symptoms in the right eye	MP 40 mg/day tapering plus CYC 750 mg/sett for 4 weeks	Twenty-six	Gradual improvement of ocular symptoms
21	Positive (MPO-ANCA)	ACR (1990)	1	76	W	Visual loss in the left eye; diplopia 2 months before	MP 60 mg/day tapering	One year	Improvement of visual acuity
22	NR	ACR (1990)	1	49	W	Ocular irritation but no visual disturbance	80 mg PDN 80 mg/day tapering	NR	Visual deficit unchanged

#NR: Not reported; MP: methylprednisolone; PDN: prednisone; CYC: cyclophosphamide.

fever (up to 38°C). He was referred to the department of Neurology of his local hospital. Physical examination revealed pulsating and non-tender temporal arteries, while mild basal inspiratory and expiratory rales were heard on chest auscultation. GCA complicated by AION was suspected and oral prednisone 75 mg/day was started. Laboratory tests performed four days after initiation of prednisone therapy showed normal complete blood count except for hypereosinophilia (>10%), and normal ESR and C-reactive protein (CRP).

Fundoscopy showed oedema of the right optic disk and flame haemorrhages, consistent with AION. Chest x-rays demonstrated signs consistent with COPD, while brain and head magnetic resonance (MR) imaging and MR angiography showed no abnormal findings in the brain parenchyma or vessels. However, inflammatory lesions of paranasal sinuses were noted. EGPA was suspected on the basis of the history of nasal polyposis, asthma, and hypereosynophilia.

Further investigations were arranged. Biopsy of the nasal mucosa demonstrated granulomatous inflammation and a rich eosinophilic infiltrate, in keeping with EGPA, while visual evoked potentials showed increased latencies in both eyes (right>left). The patient was diagnosed as having EGPA complicated by AION and discharged with prednisone 75 mg/day. However, despite glucocorticoid therapy, he went on to develop pain in the legs and left arm associated with numbness and weakness, while visual loss acuity in the right eye deteriorated further.

At the end of August, the patient was referred to our Department.

On admission acute-phase reactants were normal with ESR 20 mm/1st hour (normal values 2-37 mm/1st hour) and C-reactive protein 0.57 mg/dl (normal values <0.5 mg/dl). Eosinophil count was also normal with absolute values of 0.16x1000/mmc (normal values 0.04–0.60) and percentage values of 1.3% (normal values 1.00–6.00%); p-ANCA were slightly positive with MPO 4.3 (normal values 0–3.5 UI/ml).

Physical examination revealed reduced light-touch sensation in both legs and left arm.

Fundoscopy showed a pale optic disk

with partial resorption of flame haemorrhages on the right eye and normal findings on the left. Visual acuity was 0.5 decimal on the right and 1.00 decimal on the left.

An electromyography (EMG) of 4 limbs revealed diffuse bilateral sensory-motor axonal involvement in both legs and left arm, consistent with mononeuritis multiplex.

We confirmed the diagnosis of EGPA complicated by AION and started the patient on pulse intravenous cyclophosphamide (3 pulses of 15 g/kg every 2 weeks followed by 3 pulses every 3 weeks), while slowly tapering the prednisone. Cyclophosphamide was subsequently replaced by oral azathioprine 2 mg/kg/day. The patient described gradual improvement of his neurological symptoms with resolution of the leg pain and minimal residual paresthesia. In contrast, right visual impairment remained unchanged.

At the last follow-up in May 2012 the patient remained free of relapses on his maintenance therapy of prednisone 5 mg/day and azathioprine 150 mg/day.

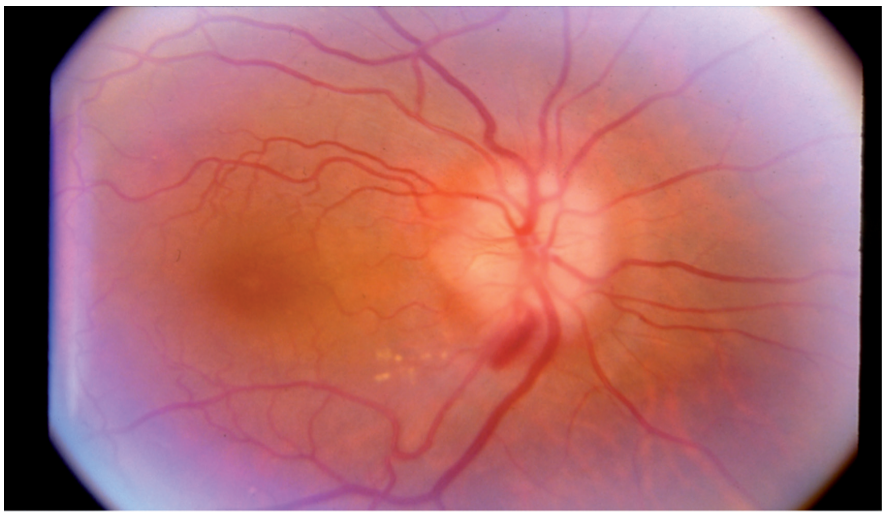

Fig.1. AION on acute phase.

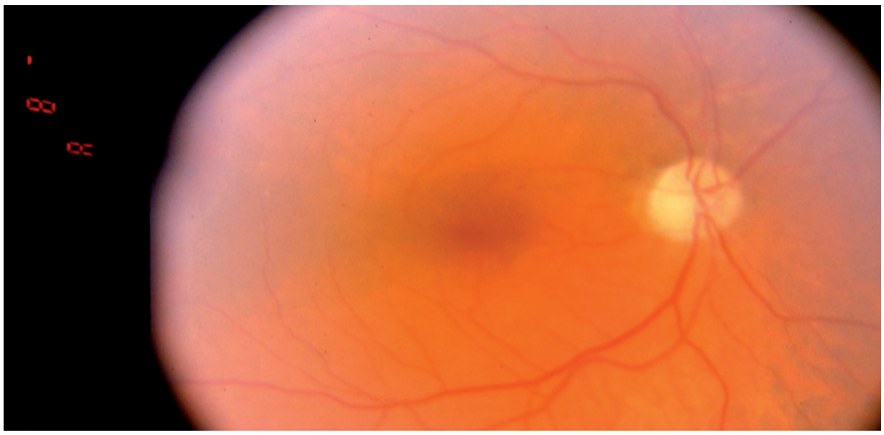

Fig. 2. Optic nerve atrophy post-AION.

Discussion

EGPA is a rare ANCA-associated vasculitis characterised by extravascular eosinophilic granulomata, peripheral eosinophilia, and asthma. EGPA may affect multiple organs, especially including the lungs, the upper respiratory tract, the peripheral nervous system, the kidneys, the gastrointestinal tract, and the skin (2). Ocular and neuro-ophtalmological manifestations are rare and include eosinophilic granulomata in the eyelids and conjunctiva, corneal ulcerations, scleritis, episcleritis, and uveitis (3-6); mononeuritis multiplex leading to extraocular muscle palsies (7); retinal ischaemic infiltrates and branch arterial occlusions (8-13); and AION (14-16). EGPA-related AION is an uncommon lesion that is probably due to vasculitic involvement of posterior ciliary and/or chorioretinal arteries vasculitis (8). To our knowledge, there are only nine published cases of AION associated with EGPA, eight of which are summarised in the Table I. One case was written in Japanese and has been excluded (17). In the majority of these reports, asthma was the first manifestation of EGPA, while AION developed subsequently. Interestingly, in every case, including our patient, the onset of AION was concomitant with the onset of peripheral neuropathic involvement, suggesting that vaculitis might be responsible for both types of manifestations. The prognosis of established AION is poor for the affected eye, even when glucocorticoid treatment is started immediately (20). In contrast, glucocorticoids may prevent the progression of amaurosis fugax to irreversible visual loss (7). In addition, clinicians must be aware that AION may be a manifestation of EGPA, because its early recognition and prompt treatment can prevent the development of visual loss in the other eye, similarly to GCA (15). In conclusion, we suggest that in patients with AION the differential diagnosis should be broadened beyond GCA, considering also other types of vasculitis such as EGPA. Patient with EGPA and AION should receive aggressive treatment with high-dose glucocorticoids plus cyclophosphamide to prevent visual loss in the unaffected eye.

References

1. SALVARANI C, CANTINI F, HUNDER GG: Polymyalgia rheumatica and giant-cell arteritis. *Lancet* 2008; 372: 234-45.
2. NOTH I, STREK ME, LEFF AR: Churg-Strauss syndrome. *Lancet* 2003; 361: 587-94.
3. SHIELDS CL, SHIELDS JA, ROZANSKI TI: Conjunctival involvement in Churg-Strauss syndrome. *Am J Ophthalmol* 1986; 102: 601-5.
4. NISSIM F, VON DER VALDE J, CZERNOBILISKY B: A limited form of Churg-Strauss syndrome. *Acta Pathol Lab Med* 1982; 106: 305-7.
5. CURY B, BREAKEY AS, PAYNE BF: Allergic granulomatous angiitis associated with uveoscleritis and papilledema. *Arch Ophthalmol* 1966; 55: 261-6.

6. ROTHSCHILD PR, PAGNOUX C, SEROR R *et al*.: Ophtalmologic manifestations of systemic necrotizing vasculitides at diagnosis: a retrospective study of 1286 patients and review of the literature. *Semin Arthritis Rheum* 2013; 42: 507-14.
7. WEINSTEIN JM, CHUI H, LANE S *et al*.: Churg-Strauss syndrome (allergic granulomatous angiitis). Neuro-ophthalmologic manifestations. *Arch Ophthalmol* 1983; 101: 1217-20.
8. DAGI LR, CURRIE J: Branch retinal artery occlusion in Churg-Strauss syndrome. *J Clin Neuro Ophthalmol* 1985; 5: 229-37.
9. CHUMBLEY LC, HARRISON EG, DEREMEE RA: Allergic granulomatosis and angiitis (Churg-Strauss syndrome). Report and analysis of 30 cases. *Mayo Clin Proc* 1977; 52: 477-84.
10. DAGI LR, CURRIE J: Branch retinal artery occlusion in the Churg-Strauss syndrome. *J Clin Neuroophthalmol* 1985; 5: 229-37.
11. ASAKO K, TAKAYAMA M, KONO H *et al*.: Churg-Strauss syndrome complicated by central retinal artery occlusion: case report and a review of the literature. *Mod Rheumatol* 2011; 21: 519-23.
12. TÜRKÇÜOĞLU P, ISIK A, DENIZ N *et al*.: Central retinal artery occlusion in an ANCA negative Churg-Strauss syndrome patient. *Int Ophthalmol* 2007; 27: 369-71.
13. MAN BL, FU YP, SHUM KS, MOC CC: Bilateral central retinal artery occlusionin a patient with Churg-Strauss vasculitis. *Clin Exp Rheumatol* 2011; 29 (Suppl. 64): S137.
14. ACHESON JF, COCKERELL OC, BENTLEY CR, SANDERS MD: Churg- Strauss vasculitis presenting with severe visual loss due to bilateral sequential optic neuropathy. *Br J Ophthalmol* 1993; 77: 118-9.
15. KATTAH JC, CHROUSOS GA, KATZ PA *et al*.: Anterior ischemic optic neuropathy in Churg-Strauss syndrome. *Neurology* 1994; 44: 2200-2.
16. CARMICHAEL J, CONRON M, BEYNON H *et al*.: Churg-Strauss Syndrome presenting with visual loss. *Rheumatology* (Oxford) 2000; 39: 1433-4.
17. HAYAKAWA K, AKATSUKA I, MATSUKURA S *et al*.: Case of anterior ischemic optic neuropathy accompanied by Churg-Strauss syndrome. *Nihon Ganka Gakkai Zasshi* 2004; 108: 612-7.
18. GIORGI D, LAGANÀ B, GIORGI A *et al*.: Ischemic optic neuritis in Churg-Strauss syndrome. *Recenti Prog Med* 1997; 88: 273-5.
19. LIOU H-H, YIP P-K, CHANG Y-C, LIU H-M: Allergic granulomatosis and angiitis (CSS) presenting as prominent neurologic lesions and optic neuritis. *J Rheumatol* 1994; 21: 2380-4.
20. VITALI C, GENOVESI-EBERT F, ROMANI A *et al*.: Ophthalmological and neuro-ophthalmological involvement in Churg-Strauss syndrome: a case report. *Graefes Arch Clin Exp Ophthalmol* 1996; 234: 404-8.
21. ALBERTS AR, LASONDE R, ACKERMANN KR *et al*.: Reversible monocular blindness complicating Churg-Strauss syndrome. *J Rheumatol* 1994; 21: 363-5.
22. ROSENBLATT BJ, FOROOZAN R, SAVINO PJ *et al*.: Asymptomatic optic neuropathy associated with Churg-Strauss syndrome. *Ophtalmology* 2003; 110: 1650-2.