Rare disease

Initial neuro-ophthalmological manifestations in Churg–Strauss syndrome

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Summary

Churg–Strauss syndrome (CSS) is a systemic vasculitis with frequent respiratory tract involvement. It can also affect the nervous system, notably the optic tract. The present work reports the case of a 65-year-old man diagnosed as having CSS in the context of several acute onset neurological symptoms including muscle weakness and signs of temporal arteritis, including bilateral anterior ischaemic optic neuropathy (ON). Electroretinograms (ERGs) and visual evoked potentials (VEPs) were performed. Flash ERGs were normal whereas VEPs were highly abnormal, showing a dramatic voltage reduction, thus confirming the ON. The vision outcome was poor. Ophthalmological presentations of CSS have rarely been reported, but no previous case of sudden blindness documented by combined ERG and VEP investigations were found in the literature. The present case strongly suggests that the occurrence of visual loss in the context of systemic inflammation with hypereosinophilia should lead to considering the diagnosis of CSS.

BACKGROUND

Churg–Strauss syndrome (CSS), or allergic granulomatous angiitis, is a rare disease affecting small-sized to medium-sized vessels.^{1 2} The most frequent clinical manifestations are respiratory tract involvement (75%) such as asthma, which is an almost universal feature, pulmonary infiltrates and allergic rhinitis, followed by mononeuritis multiplex (65% to 75%), gastrointestinal, cardiac, dermatological and renal involvement.¹ Neurological manifestations other than mononeuritis multiplex are uncommon.² Ocular manifestations are rarely reported.³ We report the case of a patient diagnosed as having CSS after a series of neurological symptoms and signs including muscle weakness and temporal arteritis. He experienced sudden blindness caused by bilateral ischaemic optic neuropathy (ON) documented by electroretinographic (ERG) recordings and visual evoked potentials (VEPs).

Only a few cases of ischaemic ON in this context have been reported in the literature.^{4–10} To date no case documented by combined ERGs and VEPs has been published.

CASE PRESENTATION

During a trip to Kenya, a 65-year-old man experienced unusually profuse rhinorrhoea, then, a few days later, a fever with intense proximal myalgia. He also described an episode of mandibular claudication followed by left periorbital pain, diplopia and blurred vision. These symptoms spontaneously resolved but the patient consulted a week after his return to France because of a global motor weakness predominating on his right side, in the context of recurring proximal myalgia, cephalalgia, fever and asthenia.

He had a history of late-onset asthma since the age of 50. This was responsive to inhaled corticosteroid treatment and associated with an asymptomatic and moderate

hypereosinophilia (1 g/litre) that had been discovered during a routine check-up 2 years before admission. He had travelled many times to Kenya since his retirement at the age of 60.

Following his consultation, routine blood tests showed marked hypereosinophilia (6.7 g/litre) associated with a systemic inflammatory response, and in September 2007 the patient was admitted to the Department of Infectious Diseases on suspicion of tropical parasitic disease. At 2 days after admission, the patient suddenly developed blurred vision, initially on the right and then bilaterally, and became blind within 24 h.

The patient was then transferred to the Neurology department. On admission he presented with a global muscle weakness clearly lateralised on his right side and predominant on the proximal muscle groups associated with diffuse myalgia, normal tendon reflexes and plantar reflexes flexor on both sides. The patient had recent paraesthesiae in the left median nerve territory without somatosensory deficit on clinical examination. He was hyperthermic (40°C) but showed no signs of meningitis. The vision loss was complete, and pupils were dilated bilaterally without reaction to light.

INVESTIGATIONS

A whole body CT scan in search of deep parasitic disease or infections revealed bilateral pulmonary infiltrations. Cerebrospinal fluid cytology and chemistry were normal including protein immunoelectrophoresis. Elevated blood creatine kinase levels (2900 UI/litre) suggested rhabdomyolysis, which was thought to explain the motor deficit. A complete screening for tropical parasites and bacterial or viral infections was negative. Echocardiography was

Figure 1 Fluorescein angiography of the right eye (left) and left eye (right) before injection (upper left), and 1 min (upper right), 3 min (lower left) and 6 min (lower right) after injection of fluorescein. Retinal vessels are of normal calibre and aspect. A moderate bilateral papillary oedema (empty arrow) can be seen, with minor haemorrhage in the right eye (solid arrows).

Figure 2 Flash visual evoked potentials (VEPs) and electroretinogram (ERG): ERG responses recorded with an active electrode placed on the inferior eyelid of the stimulated eye and bilateral earlobe reference electrodes are shown in the top and bottom traces. VEPs recorded at the O1 (left) and O2 (right) occipital positions of the 10/20 international electroencephalography (EEG) system, recorded against a mediofrontal reference electrode (Fz) are shown in the two intermediate traces for each eye. ERG and VEPs were recorded simultaneously by averaging monocular responses to 100 full-field white flashes delivered at 1 Hz. Stimulation runs were repeated three times for each eye and responses to each of these runs are superimposed in all traces. Negativity at the active recording electrode is represented by upward deflection. The vertical dotted line represents the upper normal limit (134 ms) of peak III latency in our normative database. Left eye stimulations: the ERG is of normal latency and amplitude showing a and b waves (upper trace), but no reproducible cortical VEPs could be obtained. This is consistent with preserved retinal function and a severe conduction block in the left optical nerve. Right eye stimulations: the ERG is of normal latency and amplitude showing a and b waves (bottom trace). Delayed VEP peaks III and IV can be identified on superimposed traces with an amplitude that is slightly above noise level. Calibration: 2.5 μ V for ERG, 5 μ V for VEPs.

normal. Electroneuromyography data, obtained 10 days after disappearance of muscle weakness under corticosteroid treatment disclosed a left median nerve axonal neuropathy by showing a reduction of 50% for muscle action potentials voltages in abductor pollicis brevis and of 68% for sensory fibres action potentials voltages in the left median nerve, as compared to values measured in the right median nerve, with no proximal or distal motor conduction slowing and no abnormality of muscle action potentials

outside the left median nerve territory. A nasal mucosa biopsy showed an inflammatory mucosa with non-specific polymorphic infiltrates. An early MRI of the brain was normal, including sequences focused on the optic nerves, aside from a bilateral frontal sinusitis. Spinal MRI was also normal. Serum antibodies to neutrophilic cytoplasmic antigens were present with an elevated titre of anti-myeloperoxidase antibodies (181, normal <20) and an increased level of IgE (238 KU/litre, normal <150).

Table 1 Published cases of ischaemic optic neuropathy in Churg–Strauss syndrome (CSS)

Reference	Gender	Age at ischaemic neuropathy	Delay after CSS diagnosis	One/both eyes	Fundus examination	Fluorescein angiography	Electrophysiological examinations	Anti-neutrophil cytoplasmic antibody test	Other systemic involvement	Visual prognosis	General prognosis
Acheson et al ⁷	M	44	0	Bilateral, delay 3 months (L then R)	Pale optic discs	Late hyperfluorescence from the right disc	None	Not performed	Pulmonary involvement, fever	No visual recovery	Improvement pulmonary symptoms
Partial et al ⁴	F	10	0	Bilateral over 2 days	Massive renal opacities, macular oedema, extensive haemorrhages, sludging in venous system	Extensive macular non-perfusion and blocking defect from retinal opacification and haemorrhage. Vasculitis-type leakage from the posterior pole retinal vessels. Optic discs stained with fluorescein.	None	Negative	Pulmonary, gastrointestinal, muscular and renal involvement	No visual recovery	
Alberts et al ⁸	F	76	0	Unilateral	Pale optic nerve with perineural retinal haemorrhages	Not described	None	Positive	Inferior vena cava thrombus, asthma, peripheral neuropathy, jaw claudication and visual loss	Good	Good
Kattah et al ¹⁰	M	55	0	Unilateral	Pale optic disc (R) + ciliary artery occlusion	Delayed choroidal perfusion in both eyes, predominantly R	None	Positive	Sensory motor neuropathy	Poor	Good
Vitali et al ⁵	F	56	0	Bilateral (symptomatic L, not asymptomatic R)	Optic nerve atrophy (L), pale, non-excavated optic disc (R)	Decreased number of capillaries in the right optic nerve head, non-perfused atrophic left disc, bilateral chorioretinal lesions; bilateral anterior ischaemic optic neuropathy + retinal infarction	None	Positive	Myocarditis, mononeuritis multiplex, asthma, muscle involvement	Poor (L)	
Weinstein et al ⁶	M	61	0	Bilateral, delay 5 weeks (R definite then L, not lasting)	Pale right optic disc with decreased number of capillaries, single retinal haemorrhage. Left optic disc normal but retinal infarcts.	Not performed	Electroretinogram; normal a and b waves in both waves	Not performed	Mononeuritis multiplex	Poor right eye	Good (6 months)
Giorgi et al ⁹	M	46	0	Unilateral	Pale right optic disc	Marked hypofluorescence of the disc at early phase of angiogram			Asthma, peripheral neuropathy		
Hayakawa et al ¹²	F	66	After CSS diagnosis	Unilateral					Bronchial asthma, eosinophilic pneumonia, mononeuritis multiplex, fever, skin rashes		

Initial ophthalmological findings before the occurrence of blindness were paleness of the optic discs and arterial thinning of the retina with arteriovenous crossing signs. At 1 week after onset of blindness, ophthalmological examination was suggestive of acute bilateral ischaemic anterior ON. His retinal vessels looked normal and, apart from paleness of the optic discs, the only abnormality was a minor retinal haemorrhage in the right eye. Fluorescein angiography showed preserved retinal vessels (figure 1). Pattern ERGs and VEPs could not be obtained because the patient was unable to maintain fixation on the centre of the screen. Flash ERGs showed normal retinal responses. White flash VEPs showed low amplitude peaks III and IV that were reproducible on three consecutive runs of right eye stimulations. Virtually no cortical response was obtained to left eye stimulation (figure 2).

TREATMENT

Faced with this highly probable CSS vasculitis, we treated the patient with 1 g/day of methylprednisolone on admission in our department, 2 days after onset of blindness. The effect was initially spectacular on fever, myalgia and muscle weakness, blood eosinophilic count and systemic inflammatory response, but vision did not improve. This treatment was subsequently changed to cyclophosphamide and oral prednisone (1 mg/kg) with prophylactic antibiotherapy (ivermectine and trimethoprim sulfamethoxazole).

OUTCOME AND FOLLOW-UP

At 2.5 months after blindness onset, exposure to bright light evoked phosphenes, but without useful vision for daily activities. No visual improvement has occurred over a follow-up period of 18 months.

DISCUSSION

This case illustrates the fact that acute neurological and neuro-ophthalmological symptoms can be the first manifestations of CSS. Muscle involvement mimicking myositis is rare.¹¹ The transient muscle weakness and pains that were reversible in 24 h under corticosteroid treatment in our patient and associated to elevated blood creatine kinase were considered likely to reflect such a process. However

this interpretation does not fully explain the right predominance of the motor deficit in upper and lower limbs, for which brain and spinal MRI provided no further explanation. There were no clinical signs of rhabdomyolysis (no dark urines) and no factors predisposing to rhabdomyolysis. Because of the complete reversibility of muscle symptoms no further investigations were undertaken, in particular muscle biopsy was not carried out.

Sudden blindness due to bilateral ischaemic ON can be dramatic. Only a few cases of ischaemic ON in this context have been reported in the literature^{4–10} and are reviewed in table 1.

Ischaemic ON usually occurs early in the course of the disease, as in our patient; in a few case reports it was the first manifestation of the disease.^{4–10} However, simultaneous bilateral onset is exceptional⁴; most often the eyes are successively affected over a time course of a few weeks or a few months.^{6–7} Sometimes ON can be asymptomatic and discovered fortuitously.⁵

To date only a few cases documented by electrophysiological investigations have been published. In one 61-year-old man with bilateral but not simultaneous ischaemic ON, flash ERG was performed showing preserved a and b waves but VEPs were not recorded.⁶ In our patient, the association of preserved ERGs and markedly abnormal VEPs, together with the eye fundus examination and fluorescein angiography results, is highly suggestive of retrolubar ON caused by acute anterior optic nerve ischaemia.

The prognosis for vision recovery after anterior ischaemic ON in CSS is usually poor with no or little visual recovery.^{4–10} Our patient also had poor visual outcome. The delay of 72 h between visual loss and intravenous corticosteroid treatment occurred due to the initial diagnostic difficulties.

Our case as well as the few others reported in the literature strongly suggests that the occurrence of visual loss in the context of systemic inflammation with hypereosinophilia should lead to considering the diagnosis of CSS and to prompt corticosteroid treatment, even if there is no certitude whether prompt treatment would help to achieve functional recovery.

Learning points

- ▶ Churg–Strauss syndrome (CSS) is a rare cause of sudden blindness.
- ▶ Electrophysiological explorations are useful to identify the precise mechanism of blindness.
- ▶ Visual loss in the context of systemic inflammation should lead to considering the diagnosis of CSS and to prompt corticosteroid treatment.

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Competing interests None.

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