

LESSON OF THE MONTH

Ophthalmic manifestations of dermatomyositis

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Case report

A 25 year old woman presented to her general practitioner with an urticarial rash on her chest. Three weeks later it had spread to her cheeks and forehead, but sparing the eyelids, to the shoulders and dorsum of the hands. This was associated with increasing fatigue, mouth ulceration, peri-ungual erythema, and arthralgia of the wrists and ankles. She had been previously healthy, was taking no medication and the family history was unremarkable. A diagnosis of systemic lupus erythematosus (SLE) was made by a dermatologist and oral prednisolone was started at 40 mg/day.

Investigations were as follows: haemoglobin 14.2 g/dl, leucocytes $6.4 \times 10^9/l$, platelets $100 \times 10^9/l$, erythrocyte sedimentation rate (ESR) 7 mm 1st h, antinuclear antibody (ANA), deoxyribonucleic acid (DNA), anti-cardiolipin antibodies, rheumatoid factor (RF), and extractable nuclear antigens (ENA), including Jo-1, were all negative. Immunoglobulin concentrations were normal. One week later, because of worsening myalgia, the creatine kinase (CK) was measured and found to be increased at 2999 iu/l (normal < 160 iu/l). The revised diagnosis was dermatomyositis.

The patient was admitted to hospital for observation and the dose of oral prednisolone increased to 60 mg/day. Azathioprine was started at 50 mg/day. On the second day of admission, four weeks after the onset of her systemic symptoms, she complained of visual blurring. The Snellen visual acuity was 6/24 in both eyes. Scattered posterior pole cotton wool spots and haemorrhages with macular oedema were reported by an ophthalmologist. The CK had risen to 6650 iu/l. Chest radiograph, electrocardiogram, and renal function were normal. Pulsed intravenous methylprednisolone at a dose of 500 mg for three days was given at this stage, in view of the acute general deterioration. Within a week of admission, she was transferred to Leeds General Infirmary. Her clinical condition continued to deteriorate. The CK rose to 18000 iu/l, CRP increased to 64 mg/l but the plasma viscosity remained normal at 1.66 mPa. A muscle biopsy specimen showed limited necrosis, regeneration, and inflammation consistent with dermatomyositis. She had marked global weakness with particularly profound axial weakness, she was unable to lift her head off the pillow and had difficulty swallowing saliva. Intravenous immunoglobulin at 1 g/kg for two

days was given (patient weighed 56 kg). She was moved to the intensive care unit for fear of sudden respiratory failure, although she had not complained of any respiratory symptoms and her tidal volumes were satisfactory. A tracheostomy was inserted and nasogastric feeding started. Plasma exchange was also performed three times on alternate days, followed by a pulse of cyclophosphamide at 10 mg/kg; a lower dose being chosen in view of her persistent thrombocytopenia. A dramatic improvement was seen over the ensuing week in her global weakness and CK but the most significant remaining problem was her persistent reduced visual acuity. Renal and cardiac function remained normal throughout this acute illness. High dose oral prednisolone was continued.

Ophthalmological examination, six weeks from onset, revealed near visual acuity reduction, equivalent to Snellen 6/24, extensive cotton wool spots, and intra-retinal haemorrhages with macular oedema. Both optic discs and large retinal vessels appeared normal. The findings were compatible with an occlusive vasculitic process and not an infective aetiology such as cytomegalovirus (CMV) retinitis. CMV serology was negative. There was no evidence of ophthalmoplegia.

Over the next few weeks her vision deteriorated in the right eye because of worsening macular oedema from the damaged retinal vasculature. Fundal appearance showed new and resolved areas of retinal haemorrhage and cotton wool spots (fig 1). Forty days after admission she was discharged with all investigations for malignancy negative and vision reduced to "hand movements" in her right eye and 6/36 in the left. One year later, fundoscopy shows optic atrophy in the right eye and a chronic maculopathy more obvious in the left eye (fig 1). The Snellen visual acuity in the right eye is reduced to 2/60 and the left eye has improved to 6/18. She received six intravenous pulses of cyclophosphamide (10 mg/kg) and methylprednisolone (6.6 mg/kg), three pulses at three weekly intervals followed by three pulses at four weekly intervals. She was then switched to methotrexate 20 mg weekly and the dose of oral prednisolone continued to be reduced slowly to 10 mg daily. Unfortunately eight months later she experienced a flare of vasculitis (fig 2), although her CK remained normal. Her treatment was therefore escalated and she received a further six pulses of

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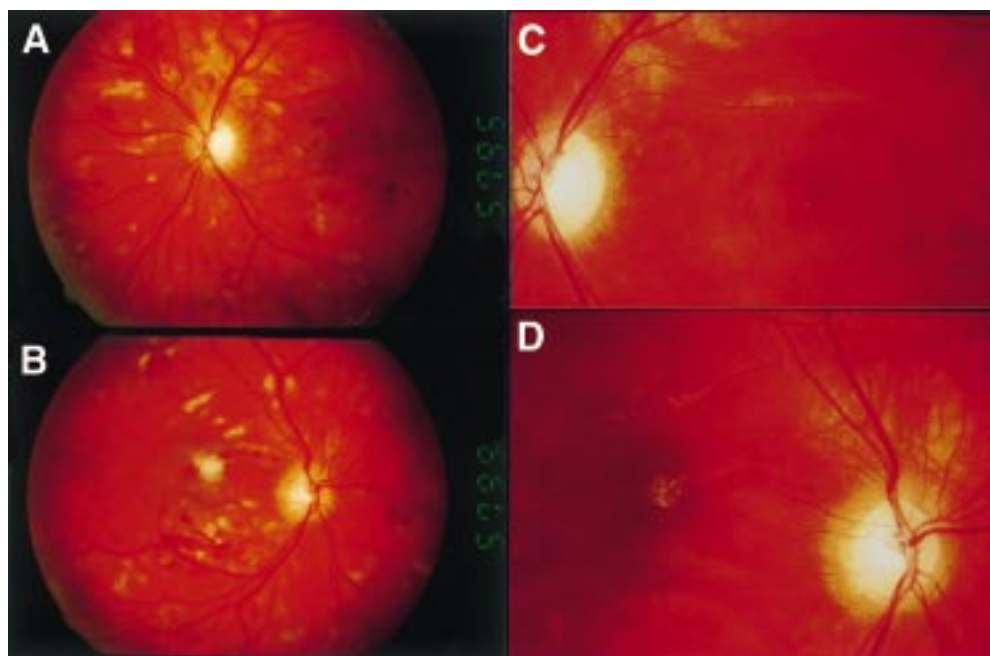


Figure 1 Seven weeks after presentation: scattered posterior pole intra-retinal haemorrhages and cotton wool spots; right eye (A) and left eye (B). One year after initial presentation: the right eye shows optic atrophy and a maculopathy (C) and left eye shows a more obvious maculopathy (D).



Figure 2 Vasculitis of the hands.

intravenous methylprednisolone and cyclophosphamide, as per original regimen. Five months later she switched back to methotrexate 20 mg weekly and cyclosporin A was also added, starting at 1.5 mg/kg/day and increasing to 3 mg/kg/day over six weeks. She is currently taking prednisolone 7.5 mg daily, methotrexate 20 mg weekly, and cyclosporin A 200 mg daily. Her autoantibodies remain negative.

Discussion

Retinopathy associated with dermatomyositis is rare and was first described by Bruce in 1938.¹ Since then a few case studies have reported it in both adults and children.²⁻⁶

The retinopathy of our patient, leading to persistent and profound visual loss, has only been reported four times before.^{3,4,7,8} More commonly, retinopathy associated with dermatomyositis completely resolves without lasting complications. The last reported case had some visual improvement subsequent to publication to Snellen right eye 6/60 and left eye 6/36 (from right eye 1/60 and left eye 2/60), over a year after the initial presentation (personal contact with P Murray). The cotton wool spot is non-specific and indicates arteriolar obstruction or capillary damage, mediated by nerve fibre layer infarction, which produces axonal swelling and rupture. Profound visual loss in dermatomyositis is caused by macular haemorrhage or macular oedema, which produces central scotomas. Visual recovery is usually complete. Over subsequent months the haemorrhages and cotton wool spots will be expected to resolve completely. Rarely, areas of pigment clumping are left, some surrounded with lighter halos (Elschnig's spots), indicating choriocapillary infarction.³ Later still there may be diffuse pallor of the optic disc resulting from retinal neuronal atrophy producing irreversible visual impairment, which is very rare.³ It has been postulated that children are more likely to have associated retinopathy because of the increased systemic vasculitis seen in the juvenile form of dermatomyositis.^{9,10}

The heliotrope eyelid eruption is considered a hallmark of the disease. Involvement of the extraocular muscles is extremely rare and can cause pain and ophthalmoplegia.^{11,12} The associated peri-orbital redness and oedema

producing ptosis, chemosis, and exophthalmos may initially be mistaken for infective orbital cellulitis. Additional features seen are conjunctivitis and iritis,¹³ episcleritis¹⁴ and uveitis with glaucoma.¹⁵

The causes of retinal vasculitis are multiple and may be broadly split into systemic inflammatory disease (for example, Behçet's disease, SLE, Wegener's granulomatosis, sarcoidosis, multiple sclerosis), ocular inflammatory disease (for example, pars planitis, Birdshot chorioretinopathy), infectious disease (for example, toxoplasmosis, tuberculosis, CMV, herpes, HIV, lyme disease, cat scratch disease) or malignancy (for example, lymphoma, cancer associated retinopathy). Fundus fluorescein angiography may show more vascular involvement than is clinically obvious.

The probable diagnosis can be made after a complete medical history and systemic review. Further subdivision is made on the ocular findings and depends upon which retinal vessels are predominantly involved, distribution of the inflammation, the degree of vitritis or the presence of retinal infiltrate, which is more likely to be related to neoplasia. All the special investigations are tailored according to the degree of aetiological suspicion.

The level of immunosuppression and agent used depends upon the cause and clinical significance of the ocular inflammatory manifestation balanced against systemic symptoms. Close liaison with the ophthalmic department is therefore warranted.

The underlying aetiology of dermatomyositis is still unknown. Intravenous immunoglobulin may modulate the complement attack complex on the muscle cell.¹⁶ Other mechanisms of immune dysregulation, viral insult, and malignancy have all been implicated.¹⁷ Auto-reactive T cell mechanisms are thought to be the main component of human idiopathic inflammatory myopathies though the antigen is still unknown.¹⁸ There may be some genetic predisposition.¹⁹ The retinal infarctive events are felt to be similar to the arteriolar endothelial damage and platelet thrombi seen in muscle biopsy specimens.²⁰

The profound axial weakness compared with the milder proximal weakness, the thrombocytopenia and severe irreversible retinopathy made this patient unusual.

The lesson

- Retinopathy in dermatomyositis is rare and usually recovers fully. Visual and systemic deterioration may be rapid. Visual complaint requires a prompt ophthalmological opinion to confirm a vasculitic retinopathy picture so that high dose immunosuppression can be started immediately.

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