diagnosis in recent years, and recognition of examples in the orbit in only the past 2 years.

We thank Professor J. Rosai at Memorial Sloan-Kettering Cancer Centre, New York, for confirming the diagnosis, Mr B. Eyden, Christie Hospital NHS Trust, Manchester, for advice on the electron microscopy, and Mrs P. Tarpey, Department of Histopathology, Manchester Royal Infirmary, for technical assistance.

A. M. McElvanney
J. L. Noble
Manchester Royal Eye Hospital
Oxford Road
Manchester M13 9WH
UK

D. G. O'Donovan
R. E. Bonshek
Department of Pathological Sciences
University of Manchester
Manchester M13 9PT
UK

S. S. Banerjee
Department of Histopathology
Christie Hospital NHS Trust
Manchester M20 9BX
UK

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Sir,

Cryoglobulinaemia Masquerading as Rheumatoid Vasculitis: The Retina Provides the Clue

We present a case of a severe systemic illness in which retinal observation helped prompt further investigations leading to the diagnosis of cryoglobulinaemia. The ocular complications of cryoglobulinaemia have rarely been documented.

Case Report

A 72-year-old Caucasian man with severe erosive rheumatoid arthritis presented with painful and swollen lower legs, with necrotic ulcers on three of his toes and over both medial malleoli. Both feet were warm and his peripheral pulses were evident. An erythematous petechial rash with macules and telangiectasia was noted below the knees; this later spread to his forearms and face (Figs. 1, 2). Skin biopsy showed IgM and C3 deposits with occasional IgG consistent with an immune complex vasculitis. A diagnosis of rheumatoid vasculitis was made and he was admitted for systemic immunosuppression with intravenous pulses of cyclophosphamide and methylprednisolone.

He then complained of a severe reduction in vision. Visual acuities were 6/36 in the right and 6/60 in the left. There was no relative afferent pupillary defect. Anterior segment and vitreal examination of

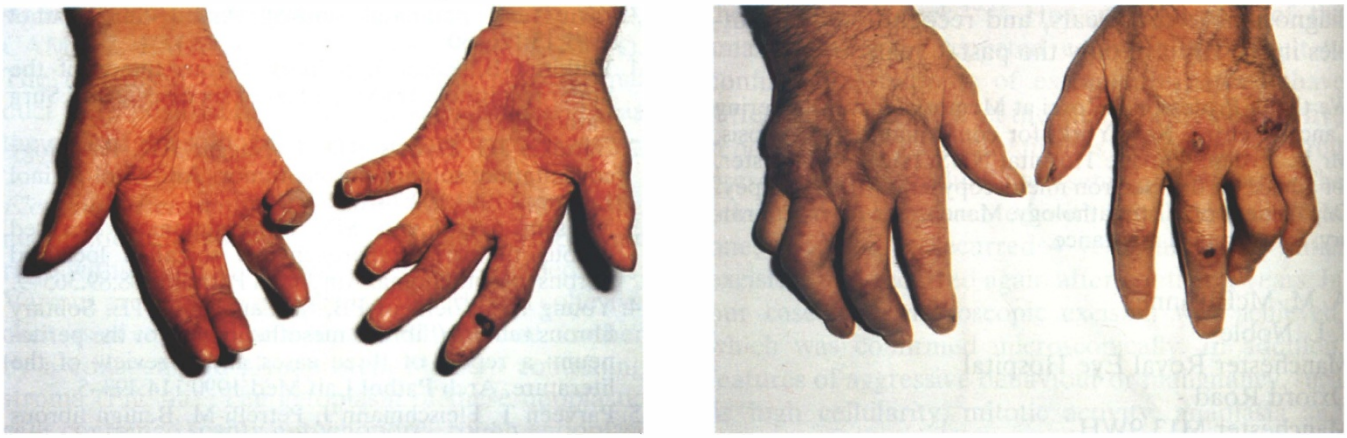


Fig. 1. *The hands showing a vasculitic rash and necrotic ulcers as well as evidence of rheumatoid arthritis, including joint deformities and rheumatoid nodules.*

both eyes was normal. Fundal examination revealed bilateral posterior pole cotton wool spots and retinal haemorrhages. The cotton wool spots were mainly distributed in a peripapillary pattern. Both maculae appeared oedematous (Fig. 3). There was retinal arteriolar narrowing but no venous dilatation or tortuosity. This retinal appearance would be most unusual in rheumatoid vasculitis and so prompted further investigation.

Fluorescein angiography showed no evidence of retinal vasculitis and a B-mode ultrasound scan was normal. His blood pressure was normal at 160/90 mmHg. A full haematological and biochemical work-up was performed with the following results: mild normocytic, normochromic, anaemia, haemoglobin 11.3 g/dl; erythrocyte sedimentation rate 113 mm/s; plasma viscosity 1.85 mPa/s (normal 1.50–1.72 at 25°C); serum electrophoresis, monoclonal IgG, IgG 54.4 g/l (normal 6–16 g/l), with immunoparesis of IgA, 0.6 g/l (normal 0.75–4 g/l) and IgM, <0.22 g/l (normal 0.25–2.4 g/l); β_2 microglobulin 12.4 g/l (normal <4.0 g/l); Bence Jones proteins detected in the urine. These results are consistent with a diagnosis of multiple myeloma. However, a skeletal survey for lytic lesions and a bone marrow aspirate were normal. Antibodies to double-stranded DNA were not detected. Further investigation revealed evidence of serum cryoglobulins. Renal function was impaired; urea 27.1 mmol/l, creatinine 384 μmol/l. A renal biopsy showed a glomerulonephritic picture with segmental vasculitic lesions and arterial thrombosis consistent with the renal effects of cryoglobulinaemia.

The working diagnosis was of a systemic vasculitis secondary to cryoglobulinaemia, in association with multiple myeloma, in addition to rheumatoid arthritis. As his condition was deteriorating, despite the use of cyclophosphamide and methylprednisolone, the patient was treated with plasma exchange, and chemotherapy with melphalan. This stabilised his condition and his renal function improved. However, he remained in hospital for 6 months for rehabilitation having had all his toes amputated for digital ischaemia. Also he had become rather confused, possibly secondarily to the cerebral effects of the cryoglobulinaemia. Unfortunately his vision stabilised at 6/60 in both eyes. The acute retinal changes

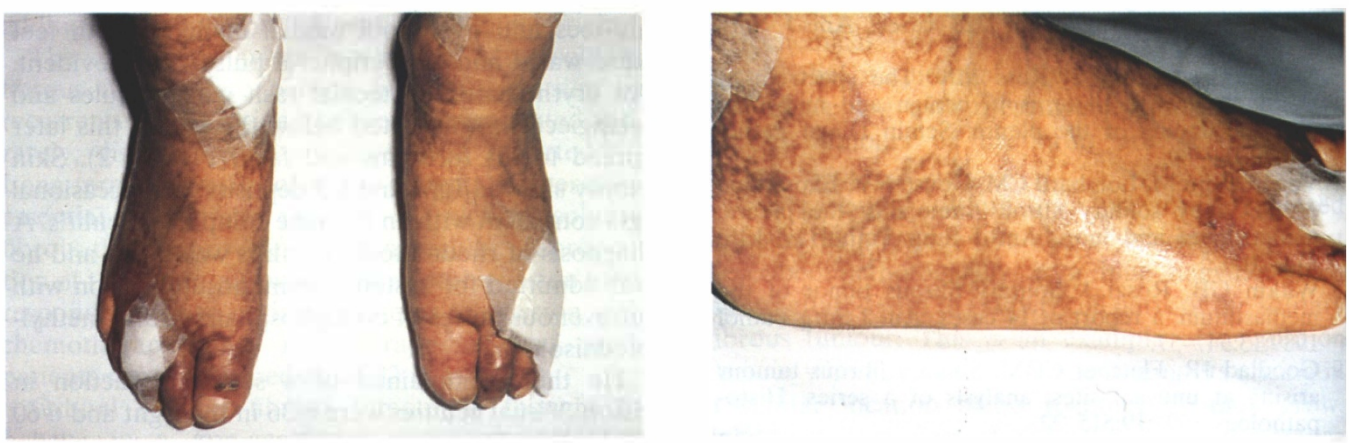
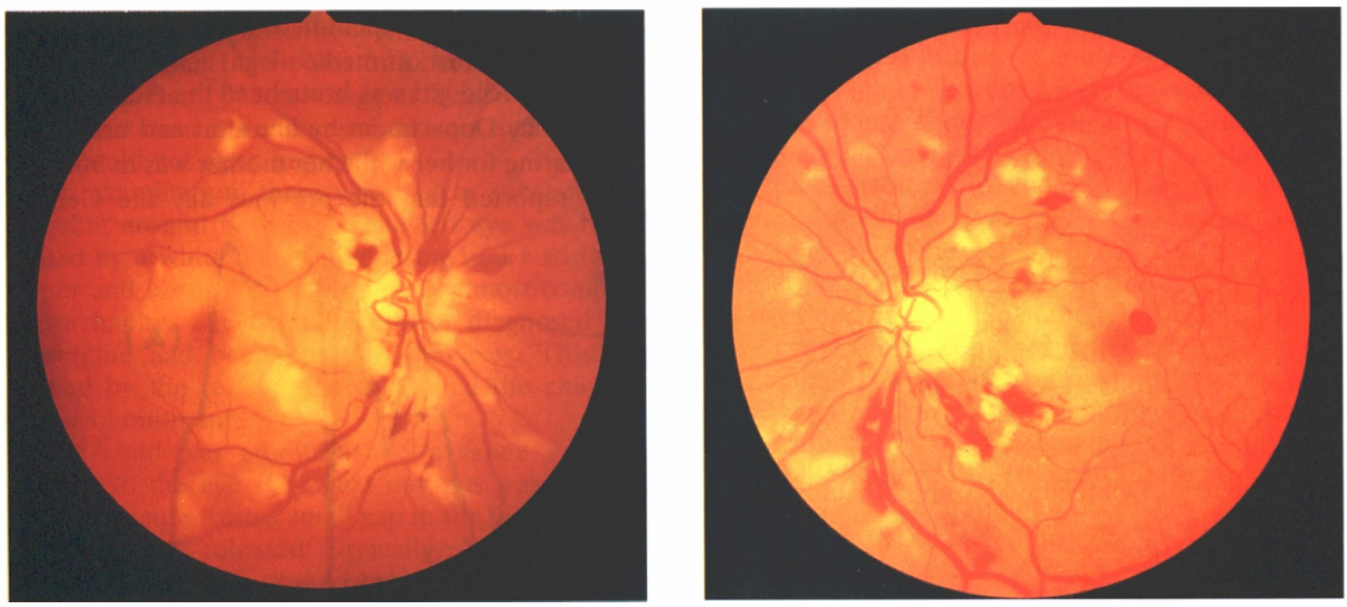


Fig. 2. *Feet showing the vasculitic rash. The dressings hide black necrotic ulcers.*



(a) (b)

Fig. 3. *The right (a) and left (b) fundi showing pale oedematous maculae, retinal haemorrhages and cotton wool spots. Note in particular the peripapillary distribution of the cotton wool spots, suggesting partial central retinal arterial occlusions.*

cleared leaving pale retina, arteriolar narrowing and slight disc pallor.t

Discussion

This patient was suffering from the systemic effects of cryoglobulinaemia as demonstrated clinically and by renal and skin biopsy. We therefore conclude that the retinal appearance was most likely due to cryoglobulinaemia. The differential diagnosis is discussed and a pathological process by which this appearance may have occurred is proposed.

Cryoglobulins are serum immunoglobulins with temperature-dependent solubility. They can occur in association with stem cell abnormalities such as multiple myeloma or Waldenstrom's macroglobulinaemia; with certain infections, such as bacterial endocarditis; and with vasculitic conditions such as systemic lupus erythematosis or polyarteritis nodosa. In some cases they are not associated with an underlying disease.[1] Cryoglobulinaemia was first described in 1933 in a 56-year-old woman with multiple myeloma who presented with Raynaud's phenomenon, purpura, hepatosplenomegaly and a central retinal vein occlusion.[2] Ocular features have rarely been reported since then, but include central retinal artery occlusion[3] and uveitis. Retinal haemorrhages, exudates and cotton wool spots have been reported with cryoglobulinaemia rarely, but in association with markedly dilated and tortuous veins.[4] Such signs have much more commonly been reported in Waldenstrom's macroglobulinaemia and occasionally in multiple myeloma, but usually due to hyperviscosity or anaemia.[5] This patient had only mild hyperviscosity and the retinal vessels were not dilated or tortuous.[6] Hyperviscosity could, however, be a factor in causing the retinal appearance.

A cotton wool spot retinopathy is a recognised feature of some systemic vasculitic conditions, such as systemic lupus erythematosus and polyarteritis nodosa, although the pattern in our case was not typical of that found in such conditions. Such a retinopathy has rarely been reported in rheumatoid arthritis[7] or cryoglobulinaemia.[5] However, cryoglobulinaemia is a form of systemic vasculitis and we would suggest it should be included in the differential diagnosis of systemic vasculitides affecting the eye.

The differential diagnosis of the retinal features would also include atypical presentations of a retinal microvasculopathy, venous occlusions, anaemia and posterior scleritis, but there was no clinical evidence to strongly support any of these diagnoses.

The most striking feature of the retinopathy was the unusual peripapillary distribution of the cotton wool spots. This clinical appearance has been described in association with the syndrome of partial central retinal artery occlusion.[8] This has been reported with temporal arteritis, severe hypertension and with emboli. In the case reported in association with temporal arteritis it was proposed that there was vasculitis affecting the central retinal and posterior ciliary circulations.[9] Our patient had widespread features of an active vasculitis, confirmed on skin and renal biopsy. He therefore may have had a vasculitic process affecting his extraocular central retinal arteries and posterior ciliary arteries. The pathogenesis of the systemic features of cryoglobulinaemia involves immune complex deposition triggering a vasculitis.[1] This has been detected in the

brain,[10] which supports the possibility that cryoglobulins could have caused a central retinal artery or posterior ciliary artery vasculitis.

This case highlights the importance of close collaboration between physicians and ophthalmologists in the management of patients with eye complications as a result of systemic disease.

We would like to acknowledge the help of Prof. A. Bird in preparing this case.

S. J. Talks, MRCP, FRCOphth
P. Shah, FRCOphth
H. E. Willshaw, FRCOphth
R. W. Jubb, FRCP

Departments of Ophthalmology and Rheumatology
Selly Oak Hospital
Birmingham, UK

Correspondence to:
Mr S. J. Talks
The Eye Hospital
Radcliffe Infirmary
Woodstock Road
Oxford OX2 6HE, UK

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Sir,

Superglue Lids: Possibly Non-accidental and a Medico-legal Problem

We report a case of a child who had possible *non-accidental* instillation of Superglue in both eyes. The glue was eventually identified, using infra-red spectroscopy, to ward off medico-legal action.

A 2-year-old girl was brought to the Accident and Emergency Department by her aunt and uncle who were caring for her while her mother was in hospital. They reported that the previous day the General

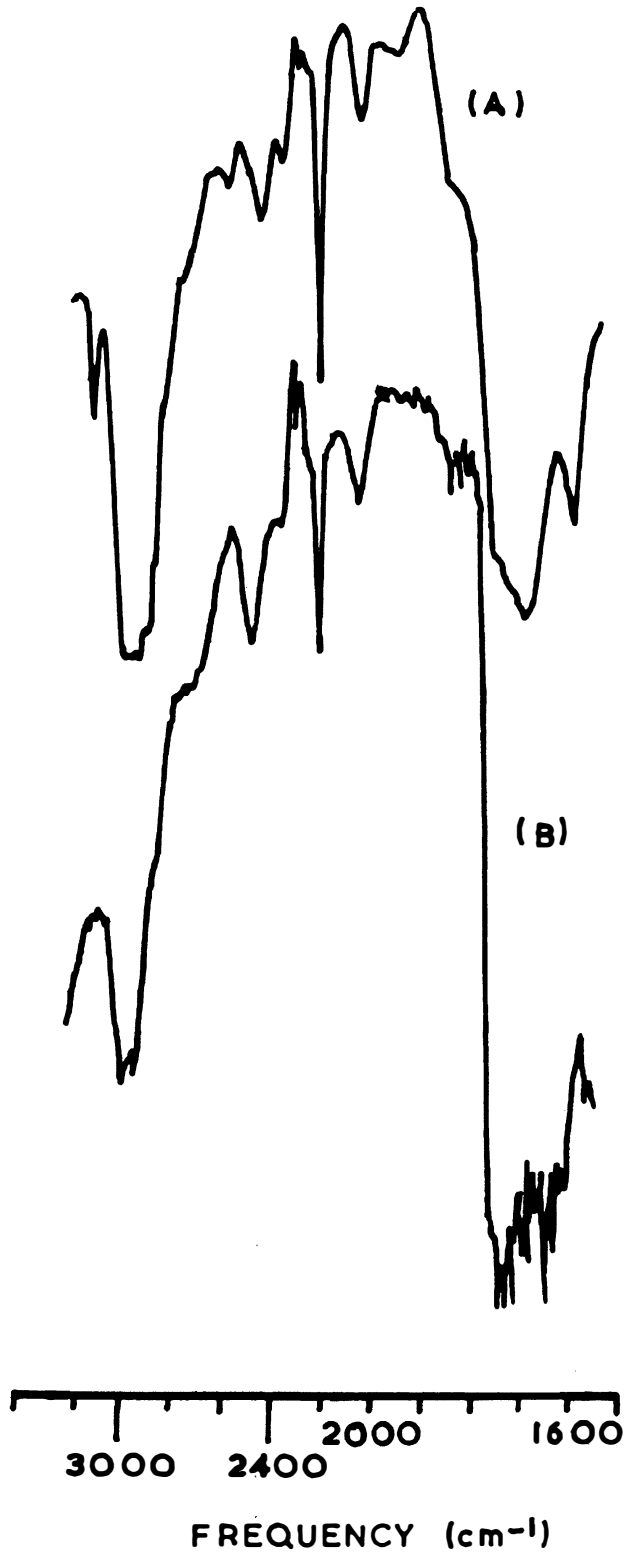

Fig. 1. *Infra-red spectra of a sample from the child (trace A), and of Superglue mixed with skin (trace B).*