usually deferred for 1–2 weeks, although the timing is a controversial issue.[6] For an anticoagulated patient on warfarin, this allows time for the warfarin to be stopped or the patient to be heparinised prior to surgery.

Our patient had systemic risk factors associated with suprachoroidal haemorrhage, namely advanced age and atherosclerosis. In this case, we hypothesize that the macular disciform lesion bled and the haemorrhage extended extensively due to the increased clotting time induced by the warfarin.

This case illustrates the risk of visual loss due to ocular haemorrhage in patients on anticoagulant therapy. Medical staff should be aware of the potentially devastating visual consequences of anticoagulation above the normal therapeutic range.

References

1 Manuchehri K, Loo A, Ramchandani M, Kirkby GR. Acute suprachoroidal haemorrhage in a patient treated with streptokinase for myocardial infarction. *Eye* 1999; **13**: 685–686.
2 Edwards P. Massive choroidal hemorrhage in age-related macular degeneration: a complication of anticoagulant therapy. *J Am Optom Assoc* 1996; **67**: 223–226.
3 Alexandrakis G, Chaudhry NA, Liggett PE, Weitzman M. Spontaneous suprachoroidal hemorrhage in age-related macular degeneration presenting as angle-closure glaucoma. *Retina* 1998; **18**: 485–486.
4 Khawly JA, Ferrone PJ, Holck DEE. Choroidal hemorrhage associated with systemic tissue plasminogen activator. *Am J Ophthalmol* 1996; **121**: 577–578.
5 Wong JS. Spontaneous suprachoroidal haemorrhage in a patient receiving low-molecular-weight heparin (fraxiparine) therapy. *Aust NZ J Ophthalmol* 1999; **27**: 433–434.
6 Chu TG, Green RL. Suprachoroidal hemorrhage. *Surv Ophthalmol* 1999; **43**: 471–486.

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Sir,

Orbital nodular-granuloma annulare in a juvenile diabetic

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Granuloma annulare is a benign granulomatous process of the dermis that commonly occurs in children and young adults, but may occur in any age group.[1] The common, superficial lesions consist of small, firm, asymptomatic papules grouped in a ring-like or circinate fashion.[1] The less common variants are: a generalised form consisting of hundreds of papules, perforating granuloma annulare, erythematous granuloma annulare, subcutaneous granuloma annulare and a very rare deep destructive granuloma annulare.[1] Granuloma annulare involving the peri-ocular dermis has been well documented.[2–7] However orbital granuloma annulare is very rare.[2,4,8,9] Although an association between dermal granuloma annulare and diabetes has been documented, orbital granuloma annulare in insulin-dependent diabetes had not been reported previously.[10,11] We report a case of orbital, nodular-granuloma annulare occurring in a juvenile diabetic associated with a partial third nerve palsy.

Case report

A 29-year-old female insulin-dependent diabetic presented with a 10-day history of left-sided red eye, double vision, abnormally large left pupil and ptosis. The visual acuity was normal in both eyes. In the left proptotic eye, there was soft tissue mass bulging through the superior and inferior bulbar conjunctiva of the left eye (Figures 1 and 2). The eye was proptotic.

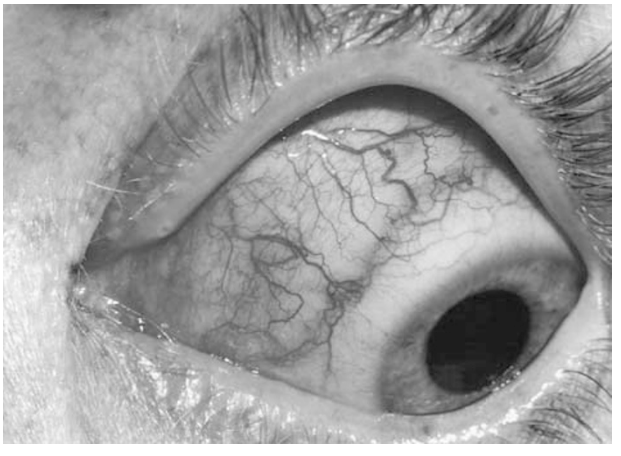

Figure 1 Photograph of the left eye showing the soft tissue mass bulging through the superior bulbar conjunctiva—left down gaze.

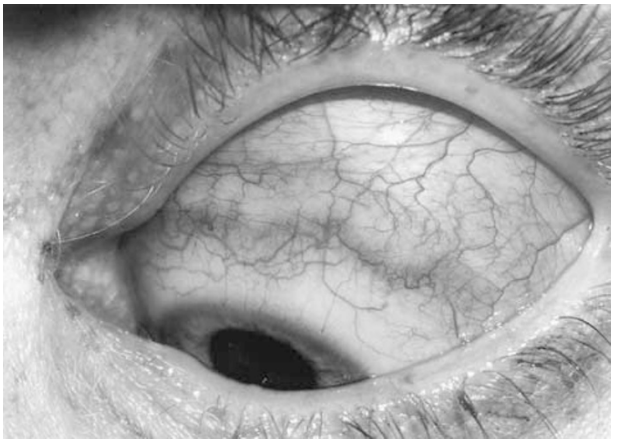

Figure 2 Photograph of the left eye showing the soft tissue mass bulging through the superior bulbar conjunctiva—right down gaze.

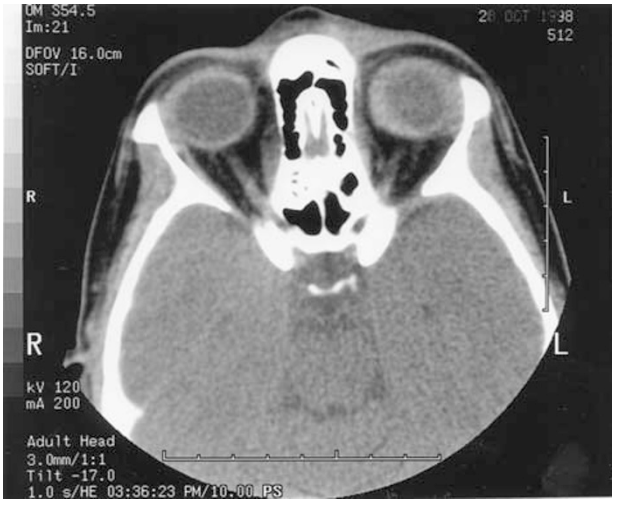

Figure 3 A CT scan of the orbit showing soft tissue thickening circumferential and right around the globe.

In addition, adduction and vertical eye movements were limited in the left eye. The pupil was dilated on the left side with an efferent pupillary defect. A Hess chart recording was in keeping with partial third nerve palsy. Except for background diabetic retinopathy there were no other intra-ocular abnormalities. Also the patient had a papular rash over the legs but there was no systemic evidence of any connective tissue disease or arthritis. The ESR was 9 mm for the first hour and the full blood and differential count was within normal range. Serum rheumatoid factor was negative on two occasions 6 months apart. Liver function tests were normal. A chest x-ray was within normal limits without any evidence of hilar shadowing. The serology for ANF, ANCA, double stranded DNA, anti-treponemal antibodies were negative and angiotensin converting enzyme was within normal range. CT and MRI scans of the orbit showed soft tissue thickening circumferential and right around the left globe (Figures 3 and 4). Scanning of the brain was normal. A biopsy of the lesion was performed through a superior and inferior conjunctiva and fixed in formaldehyde.

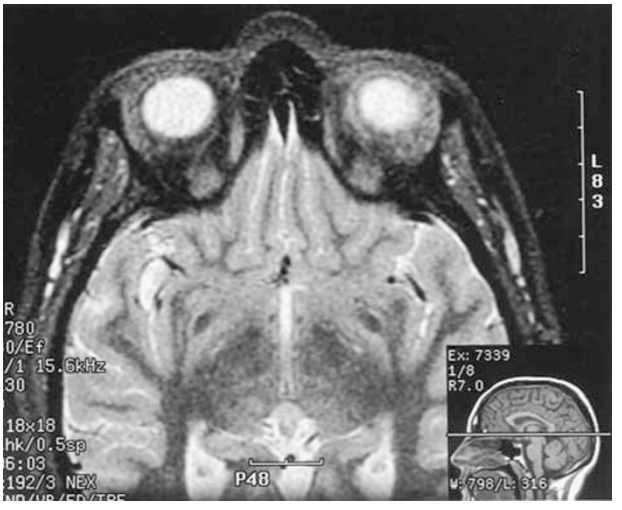

Figure 4 An MRI scan of the orbit showing soft tissue thickening circumferential and right around the globe.

Pathological examination

A biopsy was obtained through an inferior approach. The biopsy consisted of fibrous connective tissue showing focal fibrinoid degeneration of collagen in which occasional karorrhectic nuclear fragments were seen. This was surrounded by a palisade of epithelioid macrophages, forming a granulomatous response (Figure 5). Surrounding lymphocytes were also present but neutrophils were not conspicuous. The necrotic centre of the granuloma showed a positive staining reaction with alcian blue, a stain for mucin. Special stains for organisms including bacteria, mycobacterium, atypical mycobacterium and fungi, were negative. Immunohistochemistry demonstrated expression of the macrophage marker CD68 in many cells. Immunohistochemistry to CD3 demonstrated a moderate number of T cells, but very few B cells (CD 20) were present. The biopsy through the superior conjunctival biopsy also showed similar granuloma.

Postoperatively the eye was treated with topical steroid drops. The orbital lesion and the partial third nerve palsy resolved spontaneously over a period of 6 months. Based on the clinico-pathological evidence a diagnosis of orbital nodular granuloma annulare was made which was thought to cause a partial third nerve palsy.

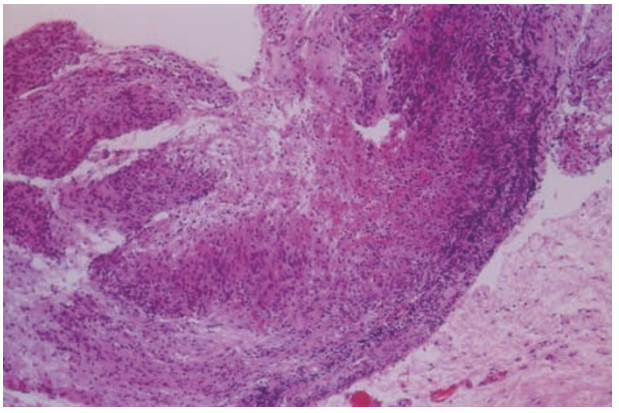

Figure 5 Phtomicrograph showing focus of necrosis with fibrinoid material surrounded by a palisade of epitheliod cells forming a granuloma (H&E × 200).

Comment

Granuloma annulare is a benign necrobiotic granuloma which commonly affects the dermis in a localised or disseminated form.[1] Clinically the presentation may be classified into papular, annular, perforating, erythematous and subcutaneous forms. The deep and disseminated form of granuloma annulare was very uncommon.[1] Histologically, granuloma annulare shows infiltrates of macrophages and epithelioid cells that may vary between a spectrum of an interstitial pattern and a well-developed palisading granuloma. These surround areas of collagen degeneration which show increased amounts of dermal mucin.[1,2,6–8] This feature, a hallmark of granuloma annulare, may be identified by a mucin stain such as alcian blue.[1]

The subcutaneous form of granuloma annulare histologically resembles the nodules of rheumatoid arthritis and rheumatic fever, which is characterised by areas of collagen degeneration in mucinous matrix surrounded by palisading macrophages with epitheliod features.[1,12] The aetiology and pathogenesis of these lesions are not clear. Cell-mediated immune response appears to be involved and is associated with release of lysosomal enzymes from macrophages into the extracellular space.[1] Although vascular deposits of IgM and the third component of complement (C3) have been observed by some investigators, existence of a vasculitic process has not been substantiated.[1]

Mesara *et al* introduced the term pseudorheumatoid nodule to describe subcutaneous nodules in children, indistinguishable from rheumatoid nodules, who had no evidence of rheumatoid arthritis or rheumatic fever.[12] In the ophthalmic literature, clinically and pathologically, identical ocular lesions have been independently reported as pseudorheumatoid nodules[3,7–9,13] and granuloma annulare.[4–6] To describe these identical ocular lesions and to unify general pathological, dermatological and ophthalmic description, Burnstine *et al* proposed the term granuloma annulare-nodular type.[2]

Granuloma annulare may occur as an isolated process, but a clear association has been found between granuloma annulare and insulin-dependent diabetes.[1,11,12]

Less commonly, similar lesions have been associated with a variety of conditions that include insect bites, herpes zoster, sarcoidosis, AIDS, systemic lupus erythematosus, and immunoglobulin mediated vasculitis.[1,10] Histopathologically granuloma annulare may resemble necrobiosis lipodica and both types of granulomas are known to occur in insulin-dependent diabetics.[1,10] Lipid-laden macrophages and fat necrosis are distinguishing features of necrobiosis lipoidica, and the absence of these features eliminates necrobiosis lipoidica in our patient.

The ophthalmic literature contains five cases of orbital granuloma annulare or pseudorheumatoid nodules in otherwise healthy young patients.[4,7–9,13] Although Roa *et al* were probably the first to describe orbital involvement, their report lacked clinical information and the anatomical site was not clearly stated.[7] Floyd reported the first well-defined case of granuloma annulare in a healthy 8-year-old boy with recurrent redness, proptosis and swelling of the right lower lid simulating orbital cellulitis.[9] In this child orbital extension from the lower lid was noted during surgical exploration. Ross *et al* reported a case of granuloma annulare involving the orbit and epi-sclera in a 29-year-old female patient with radiological evidence of retrobulbar extension.[13] Orbital granuloma annulare, occurring as an isolated nodule in the lateral rectus has been recorded in a 13-year-old otherwise healthy boy.[8] The youngest patient with orbital involvement reported was 2 years old presenting with non-tender right superotemporal orbital mass.[4] The orbital involvement is usually non-tender and may be associated with proptosis.[4,8,9,13] Orbital granuloma annulare can be associated with episcleral, peri-ocular and general cutaneous involvement.[4,13] Clinically granuloma annulare may simulate lymphomas, leukaemia, orbital pseudo tumours and metastatic tumours and histological confirmation is essential. In the case we report, the CT and MRI scan of the brain were normal and the partial third nerve palsy was very likely to be due to involvement of the nerve in the orbit. Although orbital inflammatory conditions may involve orbital nerves, similar involvement in orbital granuloma annulare has not been reported previously. Recovery of the nerve palsy occurred spontaneously, without any intervention and coincided

with the resolution of the orbital lesion. The nerve palsy was painless and did not relate to diabetes. The other causes of third nerve palsy were excluded. Based on these observations we believe the nerve palsy could be related to the orbital granuloma. Resolution occurred spontaneously and many authorities have advised simple observation, while others advocate intra-lesional corticosteroids.[2]

In the case we report, no evidence for connective tissue diseases was found and infective causes were eliminated. Although orbital granuloma annulare in diabetes mellitus has not been reported previously, the association between granuloma annulare in several other sites including the lid has been well documented.[1,14,15] In this patient the orbital granuloma annulare may be related to diabetes. While orbital granuloma annulare is rare, it should be considered in the differential diagnosis of granulomas affecting the orbit, especially diabetic patients.

References

1 Shapiro PE. Noninfectious granulomas. In: Elder D (ed). *Lever's Histopathology of the Skin*. 8th edn. Lippincott-Raven: Philadelphia, 1997, pp 317–340.
2 Burnstine MA, Headington JT, Reifler DM, Oestreicher JH, Elner VM. Periocular granuloma annulare, nodular type. Occurrence in late middle age. *Arch Ophthalmol* 1994; **112**: 1590–1593.
3 Ferry AP. Subcutaneous granuloma annulare ('pseudorheumatoid nodule') of the eyebrow. *J Pediatr Ophthalmol* 1977; **14**: 154–157.
4 Lawton AW, Karesh JW. Periocular granuloma annulare. *Surv Ophthalmol* 1987; **31**: 285–290.
5 Mauriello JA Jr, Lambert WC, Mostafavi R. Granuloma annulare of the eyelid. *Ophthal Plast Reconstr Surg* 1996; **12**: 141–145.
6 McFarland JP, Kauh YC, Luscombe HA. Periorbital granuloma annulare. *Arch Dermatol* 1982; **118**: 190–191.
7 Rao NA, Font RL. Pseudorheumatoid nodule of the ocular adnexa. *Am J Ophthalmol* 1975; **79**: 471–478.
8 Choi KH, Wilbur AC, Duvall J, Miale TD, Tan WS. Orbital pseudorheumatoid nodule. *Am J Neuroradiol* 1985; **6**: 828–829.
9 Floyd BB, Brown B, Isaacs H, Minckler DS. Pseudorheumatoid nodule involving the orbit. *Arch Ophthalmol* 1982; **100**: 1478–1480.
10 Magro CM, Crowson AN, Regauer S. Granuloma annulare and necrobiosis lipoidica tissue reactions as a manifestation of systemic disease. *Hum Pathol* 1996; **27**: 50–56.
11 Romaine R, Rudner EJ, Altman J. Papular granuloma annulare and diabetes mellitus. Report of cases. *Arch Dermatol* 1968; **98**: 152–154.
12 Mesara BW, Brody GL, Oberman HA. 'Pseudorheumatoid' subcutaneous nodules. *Am J Clin Pathol* 1966; **45**: 684–691.
13 Ross MJ, Cohen KL, Peiffer RL Jr, Grimson BS. Episcleral and orbital pseudorheumatoid nodules. *Arch Ophthalmol* 1983; **101**: 418–421.
14 Jelinek JE. Cutaneous manifestations of diabetes mellitus. *Int J Dermatol* 1994; **33**: 605–617.
15 Haim S, Friedman-Birnbaum R, Shafrir A. Generalized granuloma annulare: relationship to diabetes mellitus as revealed in 8 cases. *Br J Dermatol* 1970; **83**: 302–305.

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