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Sir,

Regression of aneurysmal dilatations in a case of idiopathic retinal vasculitis, aneurysms and neuroretinitis (IRVAN) associated with allergic fungal sinusitis

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Idiopathic retinal vasculitis, aneurysms, and neuroretinitis (IRVAN) is a rare clinical entity characterized by bilateral retinal arteritis, numerous aneurysmal dilatations of the retinal and optic nerve head arterioles, neuroretinitis, and uveitis.[1,2] To the best of our knowledge, only 17 patients have been reported in the literature.[1–4] This syndrome typically affects young healthy individuals, it has a female predominance, and is not associated with any systemic abnormalities.[1–4] Visual loss is caused by exudative maculopathy and neovascular sequelae of retinal ischaemia.[2]

This report describes a patient who presented with features typical of IRVAN in whom medical evaluation disclosed allergic fungal sinusitis. Resolution of arterial sheathing, regression of several of the aneurysmal dilatations, and decrease in lipid exudate deposition were noted over a 3-year period follow-up.

Case report

A 16-year-old boy presented with a 12-month history of decreased vision in both eyes. The patient's medical history was significant for asthma, however, not on regular treatment. He had progressive nasal obstruction associated with headache, sneezing, and itching. Review of systems revealed no history of fever, weight loss, skin lesions, arthritis, or genital ulcers. On examination, visual acuity was 20/60 in the right eye, and 20/100 in the left. Intraocular pressure by applanation was 14 mmHg, bilaterally, and pupillary reactions were normal. External examination and slit-lamp biomicroscopy were normal with clear anterior chambers. There were trace vitreous cells present in both eyes. Fundus examination disclosed bilateral extensive peripapillary and macular lipid exudate deposition. Marked and extensive sheathing of retinal arterioles was present associated with periarteriolar intraretinal haemorrhages. Numerous aneurysmal dilatations were present on the optic nerve head and along the first- and second-order retinal arterioles. The optic discs showed swelling and hyperaemia. Fluorescein angiography accentuated the numerous aneurysmal dilatations on the retinal arterioles, and showed extensive leakage from aneurysmal dilatations on the optic nerve head and on the retinal arterioles, and late staining of the aneurysmal dilatations. Both optic nerve heads demonstrated leakage and stained in the later stages (Figures 1 and 2). Extensive areas of peripheral capillary nonperfusion and adjacent anomalous arteriovenous anastomosis were present in both eyes (Figure 3). The following laboratory investigations were requested: chest X-ray, complete blood count, erythrocyte sedimentation rate, routine blood chemistry, haemoglobin electrophoresis, serum protein electrophoresis, urinalysis, Venereal Disease Research Laboratory test (VDRL), fluorescent treponemal antibody absorption test, Mantoux test, antinuclear antibody, anti-double-stranded DNA antibody, antiphospholipid antibodies including anticardiolipin and lupus anticoagulant antibodies, anti-neutrophil cytoplasmic antibodies, and computed tomographic scan of the brain. A peripheral eosinophilia was present. There were no other laboratory abnormalities. Neurologic and cardiovascular examinations were normal. ENT examination revealed multiple left-sided nasal polyps. Computed tomographic scan of the

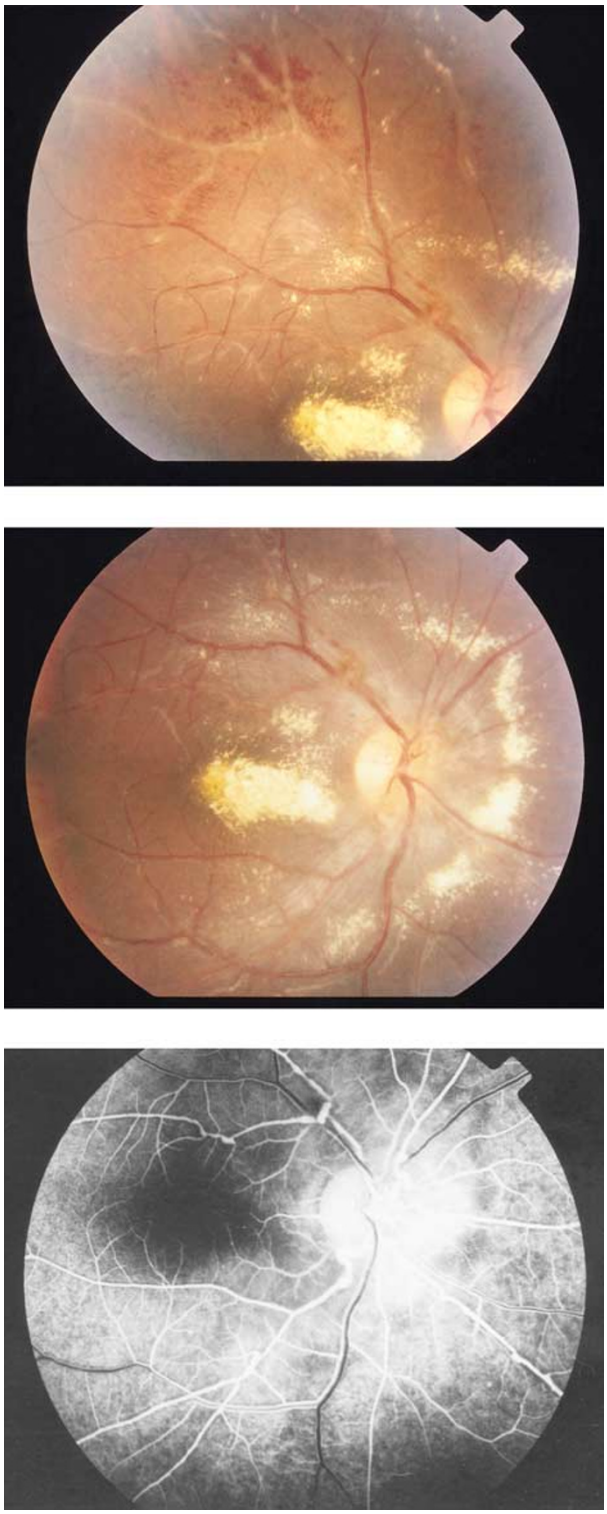

Figure 1 Initial examination (top). Fundus photographs demonstrate extensive peripapillary and macular lipid exudates deposition, aneurysmal dilatations along the retinal arterioles (middle), and perivascular sheathing affecting the retinal arterioles (top). Early-phase fluorescein angiogram showing the aneurysmal changes along the retinal arterioles (bottom).

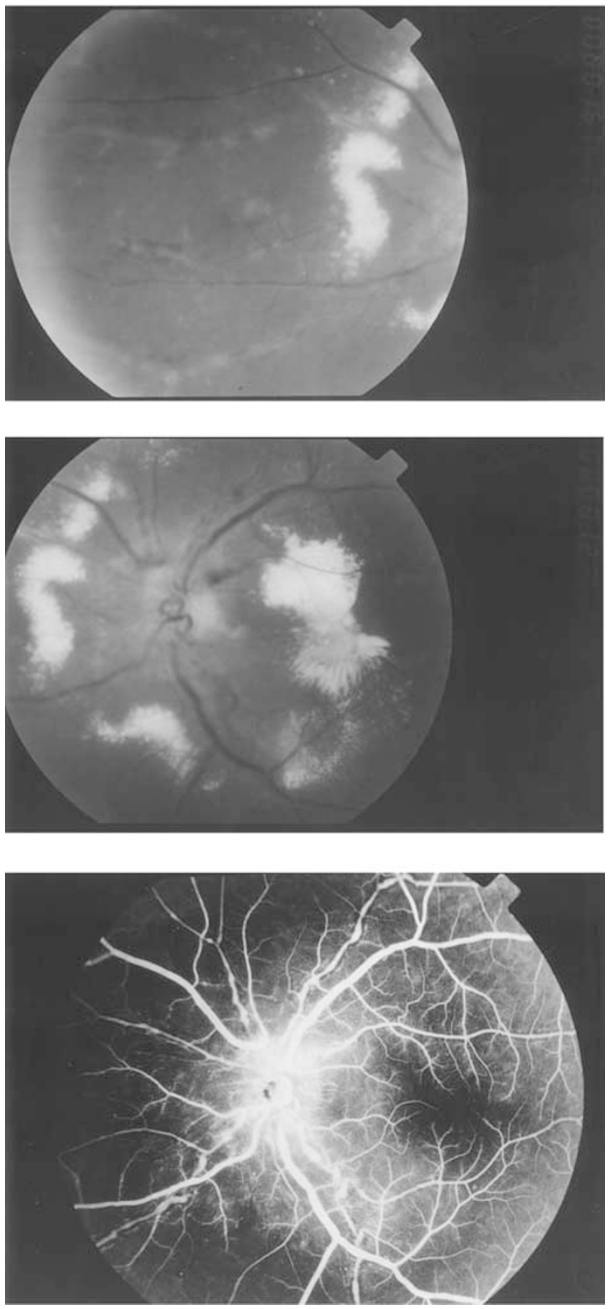

Figure 2 Initial examination (top). Fundus photographs demonstrate extensive peripapillary and macular lipid exudates deposition, aneurysmal dilatations along the retinal arterioles (middle), and perivascular sheathing affecting the retinal arterioles (top). Arteriovenous phase fluorescein angiogram showing leakage from the aneurysmal dilatations and leakage from the optic nerve head (bottom).

paranasal sinuses showed extensive soft-tissue opacity filling and expanding the sphenoid, left ethmoid, and left maxillary sinuses (Figure 4). The involved sinuses showed rarefaction of their bony margins, which was more pronounced in the roof of the sphenoid sinus and

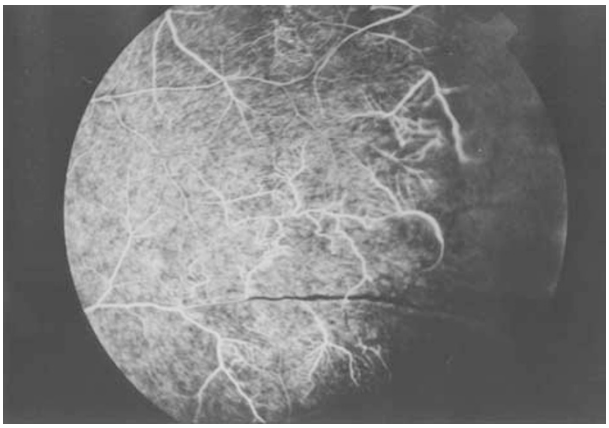

Figure 3 Initial examination. Fluorescein angiography illustrating the large areas of peripheral capillary nonperfusion.

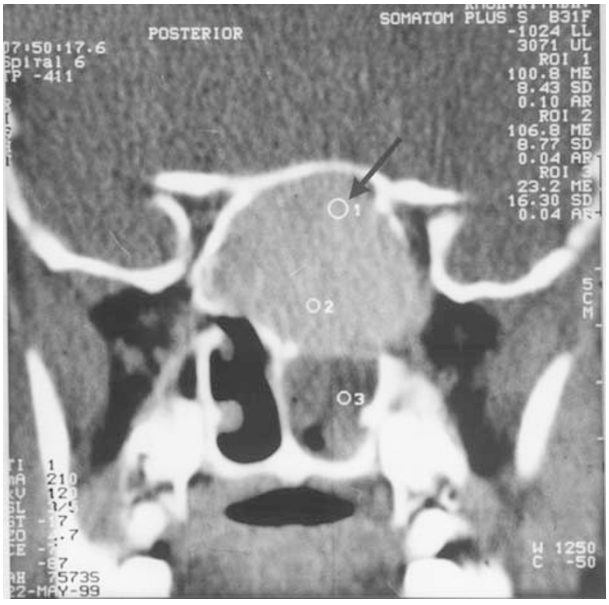

Figure 4 Computed tomographic scan showing soft-tissue opacity filling the sphenoid sinuses (arrow).

the cribriform plate, with the possibility of bony dehiscence and intracranial extension. The patient underwent endoscopic surgical debridement of the diseased sinuses, which revealed typical allergic fungal mucin filling the sinuses. Histopathological examination results showed eosinophilic–lymphocytic mucosal inflammation, and inspissated allergic mucin-containing septate fungal hyphae consistent with allergic fungal sinusitis. *Aspergillus niger* was grown from the sinus contents. After surgical removal of the fungal masses, therapy with oral prednisone 1 mg/kg/day was initiated that was tapered and discontinued 1 year after start of treatment. In an attempt to prevent retinal neovascularization and vitreous haemorrhage, a scattered laser photocoagulation was carried out on the peripheral avascular retina apart from the aneurysmal dilatations. At 3 years after the initial visit, he reached a final visual acuity of 20/20 in the right eye and 20/40 in the left eye. There was a gradual decrease in the size and number of aneurysmal dilatations. This was associated with resolution of arteriolar sheathing and marked decrease in lipid exudate deposition (Figure 5).

Discussion

Allergic fungal sinusitis (AFS) is a noninvasive form of fungal sinusitis that has recently been delineated as a distinct clinicopathologic entity. It is increasingly recognized as a cause of chronic sinusitis, with the primary causative agents being members of the Dematiaceae fungus (dark-pigmented) family. The eosinophil is a prominent inflammatory cell on histologic examination. Retrospective pathologic studies suggest that AFS accounts for approximately 7% of patients with sinus disease requiring surgery.[5] Affected patients typically are immunocompetent, and have a history of asthma, atopic disease, nasal polyposis, and chronic refractory allergic rhinosinusitis unresponsive to medical management. Treatment requires surgery, and postoperative medical management including allergy medications, allergen immunotherapy, and in many cases the addition of oral corticosteroids.[6] The exact pathogenesis of AFS is unknown. It is postulated that these ubiquitous fungi become deposited in a sinus and proliferate under anaerobic conditions. These patients develop an allergic reaction to the fungal elements similar to allergic bronchopulmonary aspergillosis. A type 1 IgE-mediated hypersensitivity and a type 3 immune complex (antibody–antigen)-mediated immune reaction to fungal antigens appear to play a role in AFS.[7]

The exact pathogenesis of IRVAN in the present case is unknown. Given the rarity of both AFS and IRVAN, it is unlikely that this association is a coincidence. One may speculate that an immunologically mediated hypersensitivity reaction to the fungal elements triggered the retinal vasculitis and contributed to the development of IRVAN in a patient already predisposed to the disease. Several studies demonstrated that *Aspergillus fumigatus* antigens mediate both humoral and cell-mediated immune responses in patients with allergic bronchopulmonary aspergillosis[8] supporting this hypothesis. Moreover, *in vitro* and *in vivo* humoral and cell-mediated autoimmune reactions were demonstrated to human acidic ribosomal

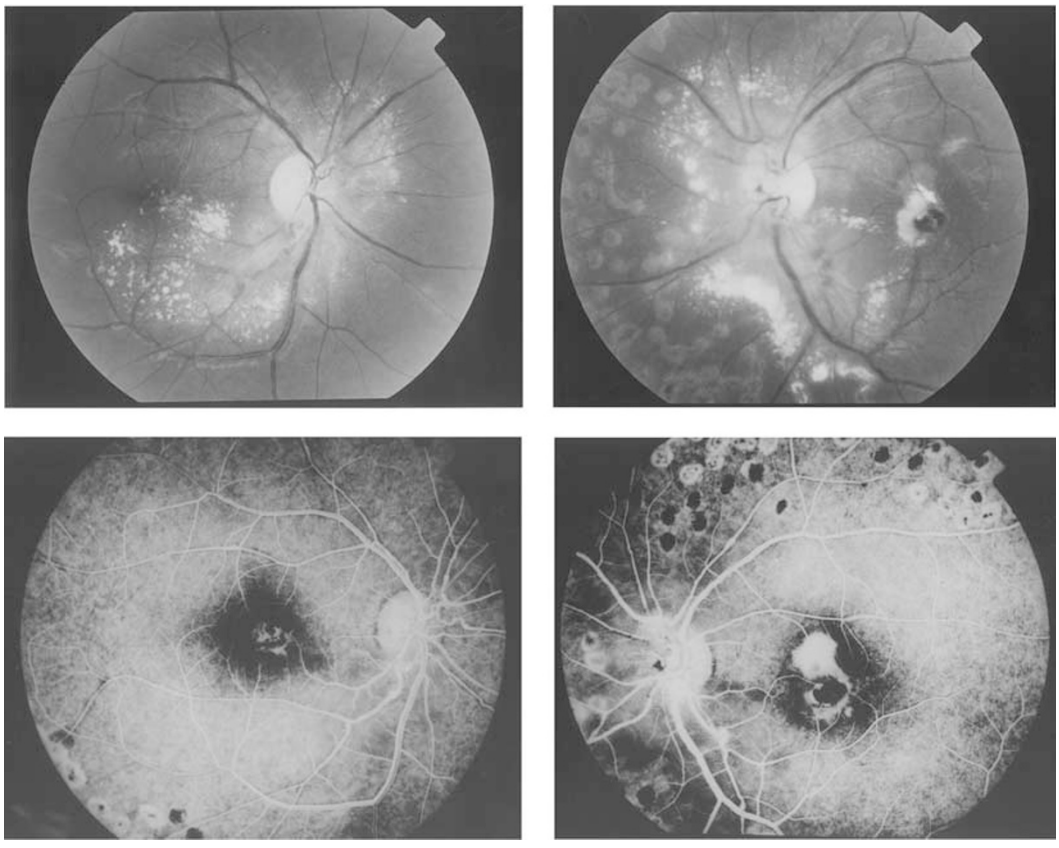

Figure 5 After 3 years. Fundus photographs of the right eye (top left), and left eye (top right) showing resolution of arteriolar sheathing, decrease in the size and number of aneurysmal dilatations, and marked decrease in lipid exudate deposition. Fundus fluorescein angiography of the right eye (bottom left) and left eye (bottom right) showing regression of several aneurysmal dilatations.

phosphoprotein type 2 (P_2 protein) and manganese superoxide dismutase (MnSOD) enzyme in patients suffering from chronic *Aspergillus fumigatus* allergy. Both the human acidic ribosomal P_2 protein and MnSOD enzyme share a high degree of sequence homology to the corresponding *Aspergillus fumigatus* protein and enzyme.[9,10] It is interesting that Stephens *et al*[11] reported a case of allergic bronchopulmonary aspergillosis that after a long latent period developed the classical features of allergic granulomatosis and systemic necrotizing vasculitis (Churg–Strauss syndrome) with continued evidence of aspergillus hypersensitivity. The demonstration of aspergillus hypersensitivity raises the possibility that this fungus contributed to the development of the Churg–Strauss syndrome in this patient.

The resolution of aneurysmal dilatations of the retinal arterioles have been reported in two patients with IRVAN. Owens and Gregor[12] reported resolution of aneurysmal dilatations in a patient treated with systemic steroids, laser photocoagulation, and vitreoretinal surgery. Similarly, Sashihara *et al*[3] reported regression of aneurysmal dilatations in a patient treated with systemic steroids, and peripheral retinal photocoagulation. The resolution of arteriolar sheathing associated with regression of the aneurysmal dilatations, and decrease in lipid exudates deposition in the present case raises the question what influence treatment of AFS had on the regression of the disease. It is possible that debridement of fungal debris and postoperative treatment with oral corticosteroids resulted in suppression of the hypersensitivity inflammatory response to the fungal elements. In addition, retinal photocoagulation of the ischaemic retina may have had a beneficial effect by inducing regression of the posterior retinal vascular lesions.

Acknowledgements

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Sir,

Pseudoxanthoma elasticum and nonarteritic anterior ischaemic optic neuropathy

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Patients with pseudoxanthoma elasticum can have extensive arteriosclerotic changes at an early age. This vascular pathology can result in premature coronary artery disease and cerebrovascular disease.[1–3] We present a young patient with pseudoxanthoma elasticum, who we believe developed nonarteritic anterior ischaemic optic neuropathy secondary to arteriosclerotic changes in the optic disc vasculature.

Case report

A 36-year-old gentleman presented with blurred vision in his left eye. His best visual acuities were 6/9 OD and 6/18 OS. There was a generalized pallor of the optic disc in the right eye with the cup disc ratio being 0.6 in the right eye and 0.3 in the left eye (Figure 1). There was no relative afferent pupillary defect. In the left eye, a superior temporal branch retinal vein occlusion at an arteriovenous crossing was noted along with macular oedema. Angioid streaks were noted in both the fundi. The intraocular pressures were unremarkable at 16 mmHg OD and 18 mmHg OS. Visual field examination revealed superior and inferior arcuate field defects in the right eye and a paracentral scotoma in the left eye. He was also found to have yellow papules arranged in a linear pattern on his neck. A diagnosis of pseudoxanthoma elasticum (PXE) was made. MRI revealed the presence of high signal lesions, suggestive of ischaemic areas, in the left high parietal lobe and adjacent to the anterior horn of the right and left lateral ventricle (Figure 2). There was no evidence of any compressive

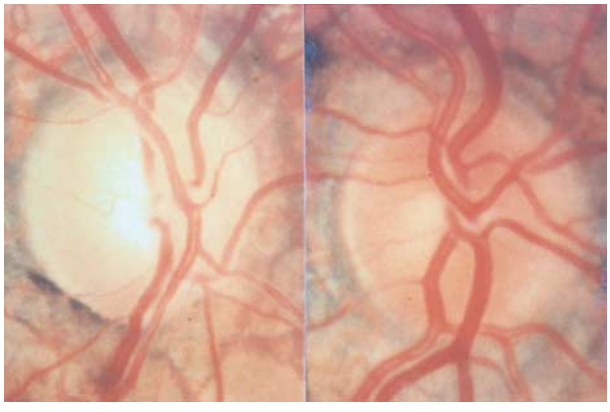

Figure 1 Optic disc photographs showing the pale, cupped disc in the right eye (right) and the normal optic disc in the left eye (left).