Episcleritis Associated with Familial Mediterranean Fever

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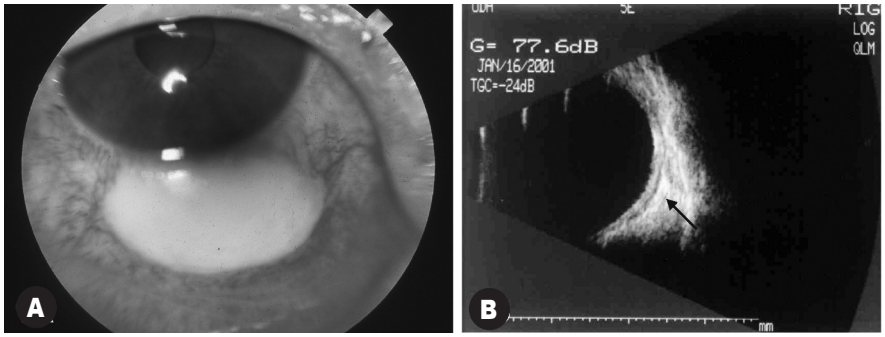
Familial Mediterranean fever is an autosomal recessive disease found predominantly in individuals of Jewish Sephardic*, Armenian, Turkish and Arabic ancestry. It is characterized by recurrent episodes of fever, peritonitis and/or pleuritis. Arthritis, skin lesions and amyloidosis are seen in some patients, the latter leading to nephrotic syndrome and uremia. Attacks of FMF resolve spontaneously, but treatment with colchicine is required to prevent the development of amyloidosis. Reports of ophthalmological manifestations in FMF are few and include retinal colloid-like bodies, panuveitis, anterior uveitis, scleritis, episcleritis and papillitis. We describe a patient with FMF who presented with nodular episcleritis that was successfully treated with local steroids and oral colchicine. The English-language medical literature on episcleritis in FMF is reviewed.

Patient Description

A 40 year old Arab woman with FMF presented with redness and irritation of the left eye of 6 days duration. She was being treated with prophylactic colchicine (tablets 0.5 mg x 3 per day) since age 12. She had no abdominal symptomatology related to inflammatory gastrointestinal disease. Examinations by physicians from the departments of pulmonary diseases and cardiology were also unremarkable. The remainder of her physical examination was unremarkable. Laboratory studies showed that erythrocyte sedimentation rate was 70 mm/hour and C-reactive protein 0.6 mg/dl (normal 0.0–0.5). She had normochromic and normocytic anemia with hemoglobin of 11.0 g/dl. Assays for antinuclear antibody, anti-dsDNA, rheumatoid factor, human immunodeficiency virus and hepatitis antigen were negative. Routine serum chemistry tests and urinalysis were normal. Serum protein electrophoreses was normal. The fibrinogen level at that time was 321 mg/dl (200–400 mg/dl). Tissue typing of the patient for human leukocyte antigen-B27 was negative. We did not perform molecular analysis of her DNA for possible mutations in the MEFV gene. Radiographs of the hands and elbows were normal. Her pelvis X-ray showed no sign of sacroiliitis. Best corrected visual acuity was 6/6 in both eyes and intraocular pressure was normal. Slit-lamp examination revealed no abnormalities in the anterior or posterior segments of the right eye. The left eye showed necrotizing blepharitis combined with nodular episcleritis [Figure A]. Tissue biopsy of the episcleral lesion revealed a non-specific inflammation with moderate dysplasia. No amyloidosis was observed. On B-scan echo of the left eye, thickening of the localized episcleral tissue was noted without scleral involvement [Figure B].



[A] Nodular episcleritis. **[B]** B-scan echo of the left eye.

Treatment consisted of topical and systemic corticosteroids and oral nonsteroidal anti-inflammatory drugs for one month. The oral colchicine dose was increased to 2 mg daily. At follow-up, symblepharon and pseudopterygium at the 6 o'clock position were detected. Injection of 0.1 ml of 0.15 mg/ml mitomycin C into the symblepharon tissue failed to induce any improvement. Therefore, 6 months later, the pseudopterygium and cicatricle tissue of the symblepharon were widely excised, and amniotic membrane was transplanted over the bar sclera. At the 4 months postoperative follow-up, there was no recurrence of the pseudopterygium, and deep lower fornix was formed.

Comment

FMF is very often associated with other autoimmune diseases such as ankylosing spondylitis, rheumatoid arthritis and others, which are chronic progressive diseases of unknown etiology [1]. FMF may manifest as arthritis, pleuritis, pericardits, orchitis or peritonitis. The association of familial Mediterranean fever with juvenile idiopathic arthritis or ankylosing spondylitis, most commonly with negative HLA-B27 antigen, has been described in several previous reports. There is no

* Originating in the Middle East or North Africa

FMF = familial Mediterranean fever

specific biological marker of familial Mediterranean fever that is clinically available. Affected patients lack a specific protease, normally present in serosal fluids, that can inactivate both interleukin-8 and the chemotactic complement factor 5a inhibitor, but the test for this protease is used only in research settings.

Non-specific findings include increases in inflammatory mediators, such as serum amyloid A, fibrinogen and C-reactive protein, during febrile attacks. Michaelson and team in 1959 were the first to report eye manifestations in FMF, consisting of colloid-like bodes, in 56% of their Jewish patients (compared to 11% of the non-Jewish ones). Subsequent studies from the same center of a larger group of patients yielded a lower prevalence (20%), and a later review of 50 Armenian and Arab patients with FMF revealed colloid-like bodies in only 4. Consequently, ophthalmic manifestations were dropped from the clinical criteria of FMF, even as a finding to rule out this diagnosis.

In 1982, Yazici and Pazarli [2] reported a case of anterior uveitis in a woman with FMF who later developed episcleritis. Several years later four additional cases were described, making a total of five reports of seven cases of uveitis and episcleritis in FMF patients. Overall, four cases of episcleritis [2-4], two cases of panuveitis and two cases of anterior uveitis have been reported in the English-language medical literature to date. Both cases of panuveitis were characterized by rhegmatogenous retinal detachment. Topical steroids and mydriatics were used in most of the patients. One case of nodular episcleritis was treated with subconjuctival tiamcenolone [3] and one case of panuveitis was treated with weekly periocular steroid injections [4]. One case of flare-up of panuveitis was completely resolved following an increase in colchicine therapy. The present patient showed a good response to topical and systemic corticosteroids. These findings suggest that episcleritis and uveitis may be associated with FMF. The report of two siblings [4] with FMF and eye symptoms, combined with low prevalence of eye symptoms in large groups of patients may point to a genetic mutation specific to the eye disease.

The patient we have described developed symblepharon and pseudopterygium at 6 o'clock, despite intensive anti-inflammatory treatment (local and systemic). This complication was challenging. Anti-fibrotic (mitomycin C) treatment for symblepharon has been suggested. Our patient had no benefit of such treatment. There are many reports in the ophthalmic literature that present the occurrence of episcleritis and scleritis and the relation of their presence with autoimmune disease [5]. This explains the fact that uveitis, scelritis and panuveitis were reported in FMF cases.

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