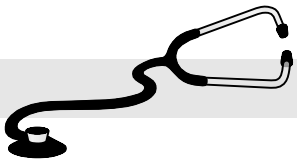

Orbital Myositis in a Patient with Primary Biliary Cirrhosis: Successful Treatment with Methotrexate and Corticosteroids

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Key words: primary biliary cirrhosis, orbital myositis, methotrexate, corticosteroids

IMAJ 2003;5:825–826

Primary biliary cirrhosis is a progressive autoimmune disease of unknown etiology. It often coexists with other autoimmune diseases and several cases of polymyositis have been reported in association with PBC. We present the first case of orbital myositis developing in a patient with long-standing PBC. Treatment with pulsed intravenous methylprednisolone and methotrexate led to resolution of the myositis and improvement in liver enzyme levels.

Patient Description

A 67 year old woman was admitted to the neurology department because of a persistent headache unresponsive to non-steroidal anti-inflammatory drugs. Pain developed initially around the left orbital region and was followed by shaded vision and general malaise. She had a 10 year history of PBC confirmed by liver biopsy, which was consistent for stage II-III PBC according to accepted criteria [1]. Her major complaints at the time of referral were fatigue, generalized pruritus and steatorrhea. Itching was worse at night, under constricting coarse garments, and was associated with dry skin. She denied alcohol consumption and had no history of recent foreign travel. At that time there was no serologic evidence of viral hepatitis. Biochemical tests of liver function revealed a typical cholestatic pattern: alkaline phosphatase and gamma-glutamyltranferase levels were disproportionately higher than the amino-transferase levels. Antimitochondrial antibody tests were positive. She had been treated initially with colchicine withdrawal for bowel symptoms, which was substituted with ursodeoxycholic acid .

On admission her temperature was 37.5°C; she denied recent infections, there was no serologic evidence of viral hepatitis (A, B and C) or trauma, and she was not taking any medications. Physical examination disclosed diplopia on downward gaze. Saccadic velocity and other ocular motions appeared normal Cranial nerves V and VII were intact.

Among the laboratory investigations, liver function tests were abnormal: ALP 710 UI/L (normal <275), γ-GGT 235 UI/L (normal 8–35), aspartate aminotransferase 72 UI/L (normal 0–35) and alanine aminotransferase 45 UI/L (normal 0–35). Immunoglobulin G was 1,850 mg/dl (normal 700–1,350) and IgM 426 mg/dl (normal 56–352), a polyclonal hypergammaglobulinemia was present (3.28 g/L) and erythrocyte sedimentation rate was 98 mm in the first hour. Antinuclear antibodies, anti-DNA antibodies, antismooth muscle antibodies and antiparietal cell antibodies were negative, but antimitocondrial antibodies were positive (titer 1:80) as were anticardiolipin antibodies (64 M phospholipid units, normal <10).

A brain magnetic resonance imaging scan showed soft tissue infiltration in the sphenoidal and maxillary sinuses. An ultrasound of the orbital region revealed enlargement of the left superior rectum muscle (5.7 mm) with enhanced reflectivity of the sheath of the left lateral rectum muscle which looked fibrotic [Figure]. On the basis of the clinical presentation, laboratory abnormalities and ultrasound of the orbital region, a diagnosis of orbital myositis was made.

She was given weekly pulsed intravenous methylprednisolone (125 mg) and methotrexate (15 mg) associated with oral daily fluocortolone (20 mg). After 2 weeks the liver function tests were already decreased: AST 55 UI/L (normal 0–35), ALT 35 UI/L (normal 0–35) and γ-GGT 193 UI/L (normal 8–35). After 1 month, the clinical picture had completely resolved; liver enzymes had reverted to normal (AST 25 and ALT 19 UI/L), except for ALP and γ-GT that had only moderately decreased (ALP 312 and γ-GGT 154 UI/L). Pulsed methylprednisolone and methotrexate were continued and after 3 months both ALP and γ-GGT decreased further (ALP 165 and γ-GGT 64 UI/L). The polyclonal hypergammaglobulinemia had reverted to normal (1.25 g/L). The therapy remained unchanged for another 3 months after which the parenteral drugs were stopped and oral steroids were progressively tapered.

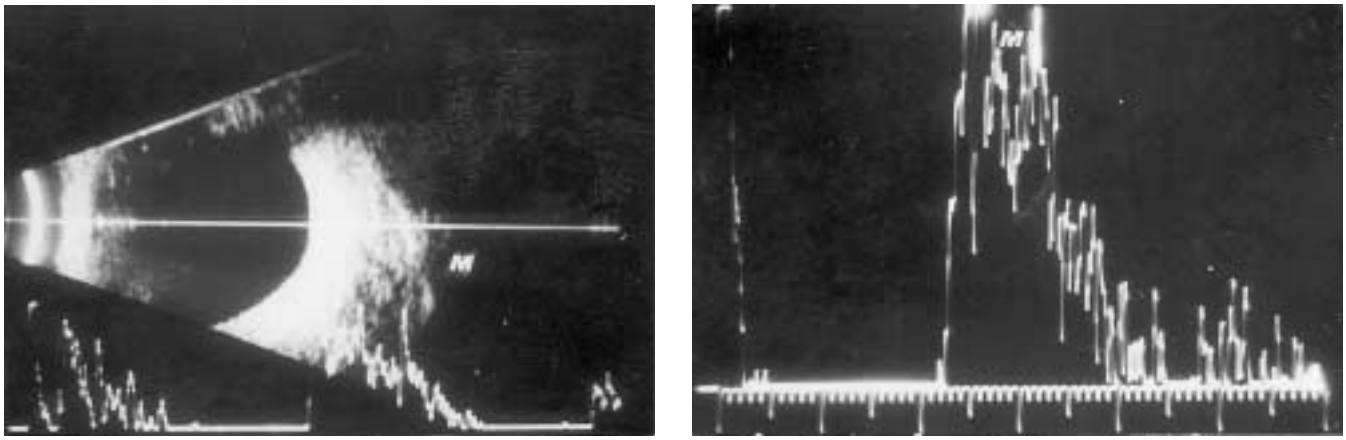
Comment

Idiopathic orbital myositis is a non-specific inflammation affecting primarily one or

PBC = primary biliary cirrhosis

ALP = alkaline phosphatase
γ-GGT = gamma-glutamyltransferase
Ig = immunoglobulin

AST = aspartate aminotransferase
ALT = alanine aminotransferase



Echograms of left superior rectus muscle. Longitudinal B scan (top) shows a large muscle (M) with irregular internal structure. Standardized A scan (bottom) shows high internal reflectivity of enlarged muscle (M). Thickness is 6.0 mm.

more of the extraocular muscles, and is the most common cause of extraocular muscle enlargement secondary to thyroid ophthalmopathy. IOM generally presents with acute orbital pain exacerbated by eye movements. Affected patients have varying degrees of eye movement restriction unrelated to the severity or duration of symptoms. Orbital myositis has been found in association with Crohn's disease, rheumatoid arthritis, systemic lupus erythematosus, vitiligo, autoimmune diabetes mellitus and asthma. The diagnosis is suggested by the clinical presentation and confirmed by MRI or ultrasonographic evidence of enlargement of one or more extraocular muscles, with or without involvement of the tendon sheath [2].

Although spontaneous resolution may be anticipated within 3 to 6 weeks, prompt treatment may expedite symptomatic relief and, most importantly, prevent muscle fibrosis by inhibiting prolonged inflammation. The treatment of myositis relies on systemic corticosteroids. Although the pathogenesis of IOM is still unknown, its prompt response to steroids suggests an immunologic basis [3].

To the best of our knowledge this is the first description of an association between orbital myositis and PBC. In recent years several authors have reported on the association between PBC and polymyositis. In some cases muscle biopsy specimens showed the presence of myopathy with mitocondrial alterations [4]. AMA represents the most specific serologic marker of the PBC. The antigens recognized by AMA are distributed in all tissues, even if the main target organ of the disease is the liver. One could speculate that in some patients with myositis, AMA could be reacting with muscle tissue, initiating a chain of events leading ultimately to muscle damage and inflammation.

Polymyositis associated with primary biliary chirrosis has been successfully treated with methotrexate [5]. Moreover, some cases of subacute and chronic IOM were found to respond to immunosuppressive agents such as cyclosporine and methotrexate [2]. In agreement with these reports and bearing in mind the reported 50% relapse rate, we administered methotrexate and corticosteroids to our patient from the very onset of myositis, hoping for rapid symptomatic relief and a long-lasting clinical remission. After 9 months follow-up our patient is still in remission, liver function tests are persistently normal (AST 28, ALT 30, γ-GGT 31 and ALP 195 UI/L), and although anedoctal, our case illustrates the benefit of a combined and protracted regimen with methotrexate and corticosteroids in the treatment of orbital myositis associated with PBC.

IOM = idiopathic orbital myositis

AMA = antimitochondrial antibodies

Acknowledgments. The authors thank Dr. Paul R.J. Ames for his advice in preparing the manuscript.

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A good writer of history is a guy who is suspicious. Suspicion marks the real difference between the man who wants to write honest history and the one who'd rather write a good story.

Anonymous