Letters to the Editors

Mikulicz's disease: a long-term follow-up case report

Sirs,

In the last few years a renewed interest has arisen in IgG4-related diseases, a wide variety of disorders characterised by elevated serum IgG4 concentration and tissue infiltration by IgG4 plasma cells (1-3). Mikulicz's disease (MD), a clinical entity of unknown aetiology characterised by lachrymal and salivary glands enlargement, is considered the most representative among IgG4-related diseases (4-6). However, its real incidence, clinical impact and long-term follow-up in European countries is still debated (7, 8).

Herein, we report the case of a 70-year-old Caucasian woman who had been clinically followed up in our institution for 7 years after a diagnosis of MD. The history of the patient had started in 2002 with a persistent monolateral enlargement of her left lachrymal gland. From an ophthalmologist's perspective, Schirmer's test and green Lissamine were negative, whereas an orbital CT revealed a moderate enlargement of the left lachrymal gland associated with an aspecific thickening of periorbital soft tissue. Ocular ultrasound (OUS) and MRI also showed a smaller enlargement of the right gland. In April 2005 the patient was first referred to our Unit in order to exclude that the ocular problem could be related to a systemic disorder. The patient complained of a mild xerophtalmia and xerostomia but she denied constitutional symptoms including arthralgias/arthritis, fever, malaise and asthenia or other symptoms suggestive for a connective tissue disease. Comorbidities were represented by arterial hypertension and hypercholesterolemia. No other relevant diseases were detectable. Clinical examination revealed an asymmetric soft tumour of the left supra-eyelid region more prominent than the controlateral in the absence of any other pathological finding. Routine laboratory tests showed no abnormalities. Neoplastic and hepatitis B and C markers were negative. Thyroid tests were normal. Non-organ specific autoantibodies were negative. A diagnosis of sarcoidosis, malignancies and hereditary angioedema were ruled out. A repeated MRI showed no progression of glandular involvement. To deeply investigate the xerostomia a minor gland biopsy was performed revealing an aspecific chronic inflammatory infiltration with multifocal aggregates of lymphocytes (focus score 1.23). IgG subclasses were assessed and the evidence of a significant increase in IgG4 (173 mg/dl) together with the negativity of the ocular tests and of the autoantibodies profile, were suggestive of a diagnosis of MD (1). In June 2005, the patient started medium-low doses of oral methylprednisolone. After two months, the patient referred a general improvement of the subjective symptoms and presented a significant reduction of the lachrymal gland enlargement.

In January 2006, a new OUS demonstrated a reduction in gland volume (from 8.8 to 5.6 mm, left side; from 6.7 mm to 5.3 mm, right side), with a complete remission of the initial sicca symptoms. Glucocorticoids were tapered and stopped in April. In August a mild worsening of the supra-eyelid tumour was detected but was completely controlled by reintroducing low-dose methylpredisolone. A new flare occurred in January 2008 when xerophtalmia, xerostomia and OUS findings worsened (left lachrymal gland 6.73 mm; right lachrymal gland 7.65 mm). Azathioprine 100 mg/daily was introduced with an initial good response. Because of gastrointestinal adverse events, after eight months, azathioprine was replaced by methotrexate 10 mg/weekly. A complete clinical remission was achieved and glucocorticoids were stopped in May 2010. After two years the patient is still on remission.

In conclusion, despite MD rarity, the research of IgG4 should be included in the differential diagnostic algorithm of patients with exocrine gland enlargement and negative non-organ specific autoantibodies also in European countries (9). Over long-term follow-up the clinical course of MD is generally benign but relapses are common. Glucocorticoids could be ineffective in monotherapy in maintaining a sustained remission over the follow-up period and the addition of DMARDs could be necessary

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