Letters to the Editor

Osteonecrosis of the knees in a variable common immunodeficiency

Sirs,

We report a case of osteonecrosis of the knees in a 37-year-old woman suffering from a common variable immunodeficiency since the age of 17. She presented at the age of 17 with spontaneous cutaneous ecchymosis revealing an autoimmune thrombopenic purpura treated by steroids during one year. At the same time a severe hypogammaglobulinemia of 3.5 g/l was discovered. Immunoglobulin G was assessed at 2.95 g/l (normal range: 6.39 - 13.5), IgA at 0.06 g/l (normal range:0.7 - 3.12) with normal IgM. By that time she was receiving polyvalent human intravenous immunoglobulins (IVIg) regularly every 3 weeks. During this period she presented repeated infections of the respiratory upper tract and sinuses.

In 1992 a moderate splenomegaly was discovered and in 1996 an autoimmune haemolytic anaemia responded to steroids in a few weeks. ln February 2000,she presented severe knee pain of sudden onset, increasing with cough. Her clinical examination was normal. The erythrocyte sedimentation rate (ESR) was 4 mm at one hour with normal fibrinogen and moderately increased C reactive protein at 18 mg/l. A full blood count found moderate pancytopenia related to hypersplenism. Antinuclear, anti-double-stranded DNA antibodies and antiphospholipids were normal. Knees radiographs were normal,as was a bone technetium scintigraphy. Because of the persistence of mechanical knee pain, however, a second bone scintigraphy was done and revealed abnormal uptake at the tibial plateaus. Magnetic resonance imaging of the femoral condyles showed metaphysis and diaphysis lesions of the femurs and tibias with a central high signal on T1-weighted images, a polycyclic surround of low signal on T1-weighted images, and a double halo on T2-weighted images. These MRI aspects were consistent with multiple osteonecrosis of the knees.

Common variable immunodeficiency (CVI) is a primary immunodeficiency disease characterized by hypogammaglobulinemia and reccurent bacterial infections (1). The clinical spectrum of CV1 and immunological features are heterogenous. Sometimes CVI is associated for unknown reasons with autoimmune [such as systemic lupus erythematosus (SLE)] or granulomatous diseases (1). Moreover, patients with CVI present an increased risk of neoplasms, particularly lymphoma (1).

Osteonecrosis of the knee is relatively frequent,with two distinct forms:the idiopathic form in which no factors for osteonecrosis can be found, and a secondary form in which predisposing factors can be recognised (2). Aetiological factors in secondary knee osteonecrosis are alcoholism, SLE, administration of systemic steroids, Gaucher's disease, drepanocytosis and thalassemia. Secondary osteonecrosis, such as our case, is more frequent in younger patients, with larger lesions than idiopathic osteonecrosis,affecting both knees in 30-80% of cases but usually with a gradual onset (2). We report here the first case of osteonecrosis described in a patient with a common variable immunodeficiency. ln our case, the possibility of a steroid-induced osteonecrosis could also be considered because the patient frequently received systemic steroids during repeated respiratory upper tract infections and for autoimmune thrombopenia and haemolytic anaemia. Although no cases of osteonecrosis after IVIg have been described, a possible role of hyperviscosity can also be hypothesised as one of the factors contributing to bone medullary ischemia (3). Indeed, retinal vein occlusions following IVIg have been reported (4). Osteonecrosis has also been described in human immunodeficiency viral infection; the mechanism is unknown, but could merely involve an increased frequency of risk factors (5-7). This could support the hypothesis of a relationship between common variable immunodeficiency and osteonecrosis in our case, notwithstanding the fact that a fortuitous association cannot be excluded.

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Detection of anticardiolipin antibodies

Sirs,

The editorial by Drs. Tincani and Meroni gives a rather misleading interpretation of an article that we published in the same issue (1,2). We demonstrated in our study that, whereas using a virtually identical approach other colleagues in our laboratory had been able to detect anti-DNA antibodies in patients with lupus, we had been unable in spite of a dozen different variations in the basic cell culture and antibody visualisation techniques to detect anticardiolipin antibodies in culture supernatants of peripheral blood mononuclear cells from patients with the antiphopsholipid antibody syndrome.

We concluded that other methods of measuring anticardiolipin antibodies produced in culture will need to be explored but not (as Tincani and Meroni implied) that there were no antibodies produced to be measured. We had certainly speculated that this problem might arise through antibody-producing cells being absent from the peripheral blood but concluded that this hypothesis was unlikely. We further concluded that there may have been a methodological problem inherent in our techniques which we had been unable to overcome within the time available and suggested that there was little to be gained from further perseverance. We believe, in fact, it is more likely that the phospholipids present in the culture supernatants, as a result of cell death, are neutralising any antiphospholipid antibodies produced, and thus rendering them undetectable. We would anticipate that similar problems might arise when looking for anti-beta 2GP1 antibodies. Ours was, therefore, intended to be a friendly note of caution to those interested in the field that potentially significant problems exist in trying to identify anticardiolipin antibodies in the supernatant of PBMC compared to the detection of DNA antibodies. We naturally wish any other group who attempt to go