Antibodies (aCL), although rare, was described in SSc, detected as lupus anticoagulant (LAC) and/or anticardiolipin with SSc. However, the association of thrombosis and aPL, phospholipid antibodies (aPL), and did not focus on patients association of thrombosis and pregnancy loss with anti- the definition of antiphospholipid syndrome (APS) as the et al Uehara.

Precursors. 

in the lumbar spine, suggesting that the addition of MTX to prednisone may cause more bone loss than would be expected from corticosteroid treatment alone. Recently, Uehara et al have shown in vitro that MTX impairs bone formation by inhibiting the differentiation of osteoblast precursors.

In patients with inflammatory arthritis receiving corticosteroids, MTX treatment should be considered as an additional risk factor for stress fractures. As far as we know this is the first reported case of MTX osteopathy in a patient with JIA. Rheumatologists should be aware of this complication as it may be easily confused with synovitis. Involvement of the leg articular or periarticular area should raise diagnostic clinical awareness. A bone scan is particularly useful for the diagnosis. 

Figure 1 Technetium-99m bone scan (anterior and posterior views, late images) showing multiple zones of enhanced uptake in the superior and inferior right pubic ramus, pubic symphysys, left hip, bilateral femoral condyles, and right calcaneum.

More on anticardiolipin and anti-β₂ glycoprotein I in systemic sclerosis

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Patients with systemic sclerosis (SSc) may have arterial and venous thrombosis and, according to the limited and controversial data available, may have an increased incidence of pregnancy losses. These observations preceded the definition of antiphospholipid syndrome (APS) as the association of thrombosis and pregnancy loss with anti-phospholipid antibodies (aPL), and did not focus on patients with SSc. However, the association of thrombosis and aPL, detected as lupus anticoagulant (LAC) and/or anticardiolipin antibodies (aCL), although rare, was described in SSc, supporting the possible existence of a “secondary” APS in SSc. 

In view of the fact that most aCL are directed to β₂ glycoprotein I (aβ₂GPI), the possibility that patients with APS may be negative for aCL, but positive for aβ₂GPI, and considering the scarcity of data examining this issue in SSc, we read with great interest the recent study by Schoenroth et al, who examined the frequency of aβ₂GPI in SSc. The authors found IgM aβ₂GPI in 2/26 (8%) patients and IgG in none. This finding did not seem to be related to any clinical or laboratory features. In another report, 80 patients with SSc were studied using an enzyme linked immunosorbent assay (ELISA) detecting the complex cardiolipin/β GPI. A similar prevalence of aCL/β GPI (10% IgG and 6% IgM), was found and a significant correlation between the presence of aCL/β GPI IgG and isolated pulmonary hypertension. 

Looking retrospectively at our cohort of 115 patients with SSc fulfilling the American College of Rheumatology criteria,
we found that, where clinically indicated, both aCL and aβ2GPI+ had been routinely evaluated in 60 patients (four male, 56 female; mean age 57 years; mean disease duration 13 years, range 1–42). These patients were classified, according to Le Roy (1988), as having limited (ISSc; n=48) or diffuse SSc (dSSc; n=12). Twenty seven patients were anticentromere positive and 16 anti-Scl-70+. Anticardiolipin antibodies were measured by a routine standardised method, and aβ2GPI as described by Balestrieri et al; values higher than the 99th centile of 100 healthy blood donors were regarded as positive.

Positive tests for aCL were found in 8/60 (13%) patients and for aβ2GPI+ in 14/60 (23%) (table 1). The prevalence of aβ2GPI+ was higher than in previous studies, probably because we performed the test only where clinically indicated; therefore, the prevalence in patients with SSc overall may differ.

Among 60 patients, eight had a history of documented venous (four) or arterial (four) thromboses: two were aCL+ aβ2GPI+, two aCL+ aβ2GPI+, one aCL+ aβ2GPI+; and three aCL− aβ2GPI+. aCL and anamnestic thrombosis were significantly related (p<0.01; χ2 with Yates’s correction). Two patients had “primary” (that is, not secondary to lung fibrosis) pulmonary hypertension. One patient was aCL+ aβ2GPI+, whereas the other one was aCL+ and LAC−, but aβ2GPI+; aCL and pulmonary hypertension were significantly related (p=0.02). According to the Sapporo criteria31 three patients had a significant history of pregnancy loss without thromboses: one was aCL− aβ2GPI+; but two were aCL− aβ2GPI+.

In our experience, the presence of aCL in patients with SSc was significantly associated with a history of thrombosis and with pulmonary hypertension. Anti-β2GPI seemed to be less specific, but allowed the identification of a woman with deep vein thrombosis, two miscarriages, and livedo reticularis. Although these events can be related to other thrombophilic conditions, none of these conditions was found in this patient. The association with aβ2GPI+ suggests that she might be defined as having “aCL−, aβ2GPI+ + APS” or “equivocal APS”.32

In conclusion, in patients with SSc and APS related symptoms, the evaluation of aβ2GPI+ can help to define the clinical picture and the specific treatment required.

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Accepted 22 November 2002

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