12 Osteoarticular Manifestations of Antiphospholipid Syndrome

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Antiphospholipid syndrome (APS) is a multi-system disorder characterized by arterial or venous thrombosis, pregnancy morbidity, and the presence of aPL, namely anticardiolipin antibodies (aCL) and lupus anticoagulant (LA). The syndrome is classified as primary or as secondary when it occurs in the context of other autoimmune disorders, especially systemic lupus erythematosus (SLE). A plethora of clinical manifestations have been associated with APS, some well recognized and others less widely known. Osteoarticular manifestations have not been commonly reported in clinical studies with APS patients, probably because of their uncertain association with the syndrome. Arthralgias represent the most well-defined osteoarticular features of primary and secondary APS, whereas arthritis is mainly described in SLE-related APS. Osteonecrosis has been documented in association with antiphospholipid antibodies (aPL) in SLE patients with or without APS, but usually in the presence of steroid treatment. The existence of osteonecrosis in patients with primary APS (PAPS), in the absence of steroid administration, suggests an association between this disorder and APS.

Osteonecrosis

Osteonecrosis, also known as avascular necrosis or aseptic necrosis, is a disease in which cell death occurs in the components of bone as a result of interruption of the blood supply. It is a multi-factorial disorder associated with various traumatic and non-traumatic conditions and clinical entities (Table 12.1). If the etiology of osteonecrosis can not be identified, the disease is classified as idiopathic. Despite new developments in its diagnosis and treatment, the pathogenetic mechanisms of osteonecrosis remain partially elucidated. The most predominant hypotheses include the presence of mechanical vascular interruption (caused by trauma, fractures), injury to or pressure on a vessel wall (associated with vasculitis, infection, radiation, Gaucher disease), vascular embolism (by fat, nitrogen bubbles, sickle cells), and thrombosis [1].

Osteonecrosis has been associated with autoimmune diseases, including rheumatoid arthritis, systemic sclerosis, systemic vasculitis, and, especially, SLE [2–4]. Small vessel vasculitis or thrombotic microvasculopathy associated with aPL have been suggested as the pathogenetic mechanisms in these disorders.

Table 12.1. Etiologic factors associated with osteonecrosis.

Trauma	Connective tissue diseases
Hematologic disorders	Systemic lupus erythematosus
Sickle cell disease	Antiphospholipid syndrome
Thalassemias	Rheumatoid arthritis
Disseminated intravascular coagulation	Systemic vasculitis
Polycythemia	Systemic sclerosis
Hemophilia	Cytotoxic agents
Clotting disorders	Vincristine
Inherited thrombophilic factors	Vinblastine
Protein C deficiency	Cisplatin
Protein S deficiency	Bleomycine
Antithrombin III deficiency	Methotrexate
Factor V Leiden	Cyclophosphamide
Homocysteinemia	5-fluorouracil
Dysfibrinogenemia	Infections
Tissue plasminogen activator decrease	Human immunodeficiency virus
Plasminogen activator inhibitor increase	Meningococcemia
Acquired thrombophilic factors	Metabolic conditions
APL	Gaucher disease
Nephrotic syndrome	Hyperparathyroidism
Smoking	Hyperlipidemia
Alcohol	Hemodialysis
Pregnancy	Renal transplantation
Estrogens	Diabetes
Obesity	Gout
Diabetes mellitus	Gastrointestinal diseases
Cushing syndrome	Pancreatitis
Corticosteroids	Inflammatory bowel disease
Malignancies	Others
Hepatic failure	Radiation therapy
Hyperlipidemia	Legg-Calve-Perthes disease
	Dysbaric osteonecrosis
	Fabry disease

APL and Osteonecrosis

Ischemia has been postulated as the predominant mechanism resulting in osteonecrosis since the first description of the disease [5]. In 1974, Jones et al suggested that intravascular coagulation with fibrin thrombosis, activated by several factors, is the likely final pathway leading to bone necrosis [6]. The above hypothesis has gained support by numerous studies reporting diverse coagulation abnormalities in the patients with osteonecrosis. Idiopathic osteonecrosis of the femoral head in adults and Legg-Calve-Perthes disease in children has been associated with several thrombophilic factors including protein C, S, or antithrombin III deficiency, activated protein C resistance, factor V Leiden, homocysteinemia, and aPL, as well as with abnormal fibrinolysis [7–11].

aPL are associated with vessel thromboses of all sizes and at multiple organ sites [12–14]. Thus, these antibodies may play an important role in osteonecrosis development, promoting thrombotic vasculopathy in the intraosseous microcirculation. In some patients with non-traumatic osteonecrosis, histopathologic examinations have revealed thrombosis of terminal arteries in the subchondral areas [15].