Antiphospholipid Syndrome with Antiβ2glicoprotein-1 Antibodies as the Cause of Recurrent Tibial Vein Thrombosis in SAPHO syndrome

The antiphospholipid antibody syndrome is defined by the presence of antiphospholipid antibodies in patients with recurrent venous or arterial thromboembolism (1). SAPHO syndrome is a rare disease, characterized by specific clinical manifestations of synovitis, acne pustulosis, hyperostosis, and osteitis. It is a disease that manifests with a combination of osseous and articular manifestations associated with skin lesions (2). Venous thrombosis complicating SAPHO syndrome seems to be uncommon with an unclear pathogenesis (3-9). Coexistence of antiphospholipid syndrome and SAPHO syndrome was not previously mentioned in literature.

A 33-year-old white woman was diagnosed with SAPHO syndrome at the age of 31. The patient was previously diagnosed with polycystic ovary syndrome and depressive syndrome. She was treated with sulfasalazin (2 g daily) and methotrexate (20 mg weekly). Seven months before admission to our department she experienced an episode of deep vein thrombosis of the left leg, successfully treated with subcutaneous enoxaparin sodium (40 mg daily) that was continued for the following 6 months as secondary prophylaxis.

Pustular skin changes on palmar surface of the hands and plantar surface of the feet (characteristic for palmo-plantar pustulosis), tenderness of sternoclavicular joints, swelling and restricted motion of both wrists, and pain on motion in both elbows, shoulders, knees, and ankles were found on physical examination. There was also a moderate amount of effusion in her left knee. There was a 3-centimeter difference between the circumferences of the shins. The level of C reactive protein was increased (6.21 mg/L).

The patient was positive for antiβ2glicoprotein-1 (anti-β2G-1) antibodies. Tests for anticardiolipin antibodies (aCL), antiannexin V antibodies, antiphosphatidylserine antibodies (aPS), and antiprothrombin antibodies (aPT) were negative. Prothrombin time, activated partial thromboplastin time, and D-dimer level were normal, and lupus anticoagulant was not present. Serum concentrations of protein C, protein S, factor V Leiden, and antiprothrombin III levels were normal. Tests for antinuclear antibodies, rheumatoid factor, and HLA-27 antigen were negative. Serum vascular endothelial growth factor (VEGF) level was 360 pg/mL, serum epidermal growth factor (EGF) level was 566 pg/mL. Bacteria culture of discharge from pustules was negative.

Doppler ultrasound examination of the left leg confirmed thrombosis of one the posterior tibial veins at its lower third. Subcutaneous enoxaparin sodium was started and later replaced with acenocumarol. The dose of sulfasalazin was increased to 3.0 g daily, and azithromycin 1.0 g daily once a week (for 8 weeks) was added. After 3 months, the patient reported reduction of joint pain. The follow-up Doppler ultrasound examination of the left leg revealed resolution of thrombosis. Three months later, the antiβ2G-1 antibodies were positive, so the patient met the criteria of antiphospholipid syndrome (1). The treatment with acenocumarol was continued and hydroxychlorochine was started.

Venous thrombosis complicating SAPHO syndrome seems to be uncommon with an unclear pathogenesis. There were reports of thrombosis of the following veins: subclavian, mediastinan, iliac, and the superior vena cava (3-8).

We have diagnosed recurrent tibial vein thrombosis in a patient with SAPHO syndrome in the course of antiphospholipid syndrome.

There were suggestions that the reason for some cases of vein thrombosis in SAPHO syndrome is a pressure of the hyperostotic skeleton or inflamed soft tissue on the vein walls (3,4,6,10), which was not the case in our patient. Legoupil *et al*. (6) suggested that the reason for iliac vein thrombosis in SAPHO syndrome was an impressive extension of the inflammatory process to the soft tissues within the lumbar spine. That patient was negative for aCL antibodies (6). Kawabata *et al*. (7) suspected that aCL antibodies could be the reason for thrombosis in this syndrome,

but the patient with multiple venous thrombosis presented in his case report was negative for aCL antibodies; however, he was not tested for anti-β2G-1 antibodies.

There was a paper demonstrating increased level of aCL antibodies in 5 of 12 patients with SAPHO syndrome (11). In our observations of 17 patients with SAPHO syndrome, only 1 had increased level of aCL antibodies without symptoms of thrombosis (12). That patient was negative for aCL antibodies, aPT antibodies, aPS antibodies, and antiphosphatidylserine antibodies, but she was positive twice for anti-β2G-1 antibodies. The presence of anti-β2G-1antibodies may be caused by an infectious agent, but in our case bacteria culture of the discharge from pustules was negative. One year after the first episode of deep vein thrombosis, our patient met the criteria of antiphospholipid syndrome.

We conclude that antiphospholipid syndrome, especially the presence of anti-β2G-1 antibodies, could be the cause of increased risk of vein thrombosis in SAPHO syndrome.

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