

Case Report

Rare Association of Takayasu Arteritis and Antiphospholipid Syndrome with Severe Thrombocytopenia

A Datta¹, P Sharma², S Ahmed³, S A Haq⁴

Abstract:

The association of Takayasu arteritis (TA) with antiphospholipid syndrome (APS) has rarely been described in the literature. This paper reports the first documented case of TA and APS in a 24-year-old woman in Bangladesh. This patient had claudication pain in upper and lower limbs for four years and Raynaud's phenomenon in right hand for eight months. During the course of her illness, she suddenly developed deep vein thrombosis in left superficial femoral, popliteal and posterior tibial veins. Conventional angiography revealed total occlusion of right subclavian artery and 60-70% stenosis of right common iliac artery. CT angiography of right upper limb also supported these findings along with increased wall thickening in the 2nd part of right subclavian artery and moderate narrowing of the 1st part of right axillary artery. She had persistently positive anticardiolipin antibodies in high titers, positive lupus anticoagulant (LA), prolonged activated partial thromboplastin time (APTT) and severe thrombocytopenia. We started high dose prednisolone (1mg/kg daily). Her platelet count increased rapidly. Based on review of 10 case reports, we considered the rare association of TA and APS. Both conditions should be determined promptly for the sake of early institution of the appropriate therapy.

Key words: Takayasu arteritis, Antiphospholipid syndrome, Deep vein thrombosis, Claudication, Thrombocytopenia.

Introduction:

Takayasu arteritis is an uncommon large-vessel vasculitis of unknown cause that chiefly affects aorta and its major branches. Women are affected eight times more frequently than men. The median age at onset of

TA is 25 years. It occurs most commonly in Japan, China, India, and Southeast Asia with an incidence of nearly 150 per million per year in Japan¹. APS is characterized by two main clinical features -thrombosis in blood vessels and, in women, recurrent miscarriages. In the blood, the defining test is the presence of antiphospholipid antibodies². An association between TA and APS has rarely been described³⁻¹². We report a 24-year-old woman with TA and APS with severe thrombocytopenia.

Case Summary:

A 24-year-old woman presented with exertional pain in upper and lower limbs for 4 years and changes in the color of fingers of right hand on exposure to cold for 8 months. The pain rapidly subsided with taking rest. On exposure to cold, her fingers of right hand initially became pale, followed by bluish discoloration and reddish on rewarming. She also experienced tingling and numbness in affected fingers during changes in color. Her past family, personal, socioeconomic and psychiatric histories were insignificant. She had no history of chest pain, cough, shortness of breath, oral ulcer, photosensitivity, joint pain, pregnancy loss, skin tightening, headache, dryness of eyes and mouth and weakness of limbs. Thereafter, she developed sudden swelling of left lower limb up to knee. Duplex studies

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confirmed the presence of thrombi in superficial femoral, popliteal and posterior tibial veins. Antiphospholipid antibody was positive in high titers (172.4 U/mL). She was treated with intravenous heparin followed by rivaroxaban 20 mg daily. Her limb swelling subsided. Three months later, she developed generalized multiple, non-palpable, non-pruritic purpuric rashes.

On examination, she had mild anemia. Right brachial pulse was absent and blood pressure could not be recorded on that arm. All other pulses were normal and there was no subclavian, carotid, renal and femoral bruits. There was carotidynia and mild tenderness in the epigastric region. Other systemic findings were within normal limits.

Investigations revealed haemoglobin - 9 gm/dL, PCV/HCT - 0.27 l/l, MCV - 67 fl, MCH - 22 pg, MCHC - 32 gm/dL, RDW - 16%, WBC - 5800/mm³, and platelet - 6,000/mm³, ESR - 35 mm in 1st hour and c-reactive protein- not elevated. Investigation for autoantibodies revealed positive ANA, but anti-dsDNA and anti-Smith antibodies were negative. She had a positive direct Coombs test without features of hemolysis and normal serum lactate dehydrogenase. Anti-cardiolipin antibodies (both IgM and IgG) were positive in high titers (IgM- 17.5U/mL, IgG-22.5U/mL). Lupus anticoagulant was also positive and APTT was significantly prolonged (>60 seconds). Peripheral angiography revealed total occlusion of right subclavian artery and 60-70% stenosis of right common iliac artery. CT angiography of right upper limb showed wall thickening resulting complete occlusion of 2nd part of right subclavian artery and moderate narrowing of the 1st part of right axillary artery with evidence of insufficient collateralization from scapula anastomosis. She had normal Doppler echocardiography and other investigation findings.



Figure 1: Purpuric rash.

She fulfilled both the revised Sapporo classification criteria for APS and American College of Rheumatology classification criteria for Takayasu arteritis. She had Indian Takayasu Arteritis Score (ITAS) of 4 and ITAS-A of 5, which indicated active disease.

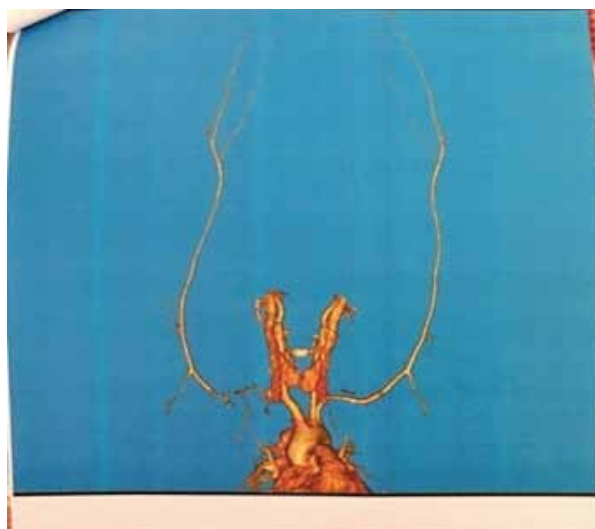


Figure 2: Peripheral angiography showing total occlusion of right subclavian artery.

Discussion:

Our patient had claudication in all four limbs for four years and Raynaud's phenomenon in right hand for eight months. Brachial, radial and ulnar pulsation were absent in the right side. Blood pressure could not be recorded in right arm. Blood pressure in left arm was recorded as 120/70 mmHg. She had noaudible bruits over the subclavian arteries, carotids, abdominal aorta, and femoral arteries. Right subclavian artery was found totally occluded and right common iliac artery was 60-70% stenosed on angiography. CT angiography of right upper limb also showed wall thickening and complete occlusion of 2nd part of right subclavian artery and moderate narrowing of the 1st part of right axillary artery with evidence of insufficient collateralization from scapula anastomosis. She was said to have TA according to American college of Rheumatology criteria for TA as five of six criteria were present¹³.

APS is a systemic autoimmune disorder characterized by arterial and venous thrombosis and/or pregnancy morbidity, associated with the presence of antiphospholipid antibodies (aPL)¹⁴. Our patient had confirmed deep vein thrombosis in left lower limb and after treatment with heparin and rivaroxaban she improved significantly. She had persistently elevated

high titers of anticardiolipin antibodies and in one occasion, she had significantly prolonged APTT and positive lupus anticoagulant. Although she had no history of pregnancy morbidity, she can be considered to have definite APS according to the revised Sapporo classification criteria for APS^{14,15}.

The patient had arthralgia and thrombocytopenia. ANA, aPL, and Coombs test were positive. She was considered to have large vessel vasculitis secondary to SLE as a differential diagnosis of TA. Vasculitis as a manifestation of SLE is not rare (incidence-3.6/million and prevalence- between 11% and 56%)¹⁶. In SLE, cutaneous vasculitis involving small arteries and venules of the skin is most common, accounting for more than 60% of cases. Medium-vessel involvement is less frequent, accounting for less than 10% of cases. Lupus-associated large-vessel vasculitis is rare with a few reported cases of lower extremity large-artery vasculitis and coronary vasculitis. Patients with lupus-associated vasculitis were more commonly male, had onset of disease at early age, and had a longer duration of disease¹⁷. In a large Spanish cohort of SLE subjects, patients with vasculitis had a significantly higher prevalence of high disease activity compared to those without vasculitis¹⁸. Due to lack of common pathological and serological features between SLE vasculitis and TA, it has been suggested that these overlap cases represent random occurrences of two different autoimmune diseases in one individual¹⁹.

Thrombocytopenia is a well-recognized feature of APS and is found in about 29.6% of patients in a large European study (Euro-Lupus Project). It is generally mild, although severe cases have been described. Our patient had severe thrombocytopenia with thrombocytopenic purpuric rashes. Thrombocytopenia is more common in secondary APS (e.g. with SLE) than with primary APS¹⁶⁻¹⁸. The first-line therapy usually includes glucocorticoids (prednisolone, dexamethasone, methylprednisolone), and intravenous immunoglobulin and anti-D¹⁹⁻²². Options of the second-line therapy in failure of the first-line therapy are rituximab, thrombopoiesis-stimulating agents, and splenectomy²³⁻²⁵. As our patient had thrombocytopenic purpura and platelet count of 6,000/mm³, she was urgently transfused platelet concentrates, followed by prednisolone 1 mg/kg daily. With glucocorticoid therapy, her platelet count was increased rapidly to 1,00,000/mm³ after six days and 2,00,000 / mm³ after ten days.

The patient was initially treated with rivaroxaban 20 mg daily for DVT. Thrombocytopenia of <100,000/mm³ or

<50% of baseline occurs in about 3% of patients treated with rivaroxaban. Severe acute thrombocytopenia has also been described in case reports²⁶. Although our patient did not develop thrombocytopenia immediately after rivaroxaban therapy, we stopped rivaroxaban in the setting of severe thrombocytopenia. We also started warfarin after platelet count had increased.

We have reported a rare association of TA and APS complicated with severe thrombocytopenia. High index of suspicion is essential to determine the both conditions to institute appropriate therapy within shortest possible time.

Consent:

Written informed consent was obtained from the patient for the publication of this case report. A copy of the written consent is available for review by editor of the journal.

Conflicts of interest:

There are no conflicts of interest of the authors for the publication of the case report.

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