The Royal Society of Medicine

Journal of the Royal Society of Medicine Open;
5(12) 1–2
DOI: 10.1177/2054270414562985

Primary anti-phospholipid antibody syndrome causing recurrent venous thrombosis and thrombocytopenia in a patient with Addison's disease

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Lesson

We report a case of Addison's disease presenting with recurrent deep venous thrombosis and thrombocytopenia and proved to have primary anti-phospholipid antibody syndrome. The case report highlights the shared autoimmune nature of both diseases.

Keywords

anti-phospholipid antibody syndrome, Addison's disease, Thrombocytopenia, Venous thrombosis

Case report

A 36-year-old male patient was referred to our internal medicine unit because of severe thrombocytopenia. He is known to have had Addison's disease for 11 y and was kept on oral dexamethasone 0.5 mg daily; as a replacement therapy. Six years before he had right lower limb deep venous thrombosis, for which he was prescribed warfarin for six months. Three years before he had another deep venous thrombosis in the left lower limb and was given warfarin for three months. Three months before presenting to our unit, he had another right lower limb deep venous thrombosis and was kept on warfarin till he was admitted. A few weeks before admission, he started to notice a rash over both forearms, but gave no history of spontaneous bleeding. No similar conditions were reported in his family.

On admission, his blood pressure was 120/75 with no postural drop. His weight was 72 kg and body mass index 25.8 kg/m^2. Purpuric rash was visible over both upper and lower limbs. Initial laboratory investigation showed platelet count 14,000/cmm, prothrombin time 32 s and international normalized ratio 3.4 (on warfarin 5 mg/day). His haemoglobin level, white cell count and blood chemistry and thyroid function test results were all within normal limits. Lupus anticoagulants were positive but antinuclear, anti-ds DNA and anti-cardiolipin antibodies were all negative. Peak cortisol level was 1.9 µg/dL; 60 min after adrenocorticotropic hormone stimulation. Adrenal haemorrhage was ruled out by magnetic resonance imaging, which revealed marked thinning of both suprarenal glands. Duplex ultrasonography showed remnants of old femoral and popliteal thrombi in both lower limbs.

The patient was diagnosed to have primary anti-phospholipid antibody syndrome. Dexamethasone was stopped and oral prednisolone 60 mg/day was started. Warfarin was also stopped, and low-molecular weight heparin was given instead. Significant improvement of the platelet count was noticed within two weeks. When platelet count reached >100,000/cmm, gradual tapering of prednisolone dose was started.

Discussion

Autoimmune adrenalitis is the principle cause of primary adrenal dysfunction, accounting for approximately 80% of cases.[1] Anti-phospholipid antibody syndrome may show adrenal involvement and is considered as one of the rare causes of adrenal failure.[2] Addison's disease is reported in only 0.4% of patients with anti-phospholipid antibody syndrome,[3] while anti-phospholipid antibody syndrome is diagnosed in less than 0.5% of all patients with Addison's disease.[4]

Anti-phospholipid antibody syndrome is characterised by the presence of both venous and arterial recurrent thrombotic events associated with the repeated detection of antibodies directed against phospholipid–protein complexes. To fulfill the diagnosis of anti-phospholipid antibody syndrome, the patient has to meet one clinical sign (vascular thrombosis or pregnancy complication) and one laboratory criterion (anti-cardiolipin immunoglobulin G or immunoglobulin M antibodies, lupus anticoagulant of immunoglobulin G or immunoglobulin M classes detected on two or more occasions at least six weeks apart). Lupus anticoagulant antibodies are more specific for anti-phospholipid antibody syndrome while anti-cardiolipin antibodies are more sensitive.[5]

Adrenal insufficiency is a rare manifestation of anti-phospholipid antibody syndrome, but it could be the heralding one.[4] In their review of literature, Espinosa *et al.*[2] reported that in 31% of cases of primary adrenal insufficiency associated with anti-phospholipid antibody syndrome hypoadrenalism was the first clinical manifestation and that adrenal hemorrhage was the main finding in imaging techniques.

Thrombocytopenia is frequently found in patients with the anti-phospholipid antibody syndrome and is usually mild. In a group of 171 patients with anti-phospholipid antibody syndrome, 23.4% were found to have thrombocytopenia. A causal relationship between anti-phospholipid antibodies and thrombocytopenia was unclear and data on this issue are still controversial.[6] Increased concentrations of anti-phospholipid antibodies were reported in patients with idiopathic thrombocytopenic purpura but no clinical significance or role in the mechanism of thrombocytopenia could be established.[7]

Our patient experienced his first thrombotic event five years after being diagnosed with Addison's disease. His clinical and laboratory findings (recurrent deep vein thrombosis and positive lupus anticoagulants) are consistent with primary anti-phospholipid antibody syndrome with no evidence to suggest secondary causes (anti-nuclear antibody and anti-ds DNA were both negative). Despite being kept on warfarin with prolonged international normalized ratio and low platelet count, he did not report any spontaneous bleeding and magnetic resonance imaging revealed no evidence of adrenal hemorrhage. The good response of platelet count to steroid therapy confirms the autoimmune nature of the thrombocytopenia in the presented case. Despite the fact that a definite causal relationship between anti-phospholipid antibody syndrome and Addison's disease could not be established in our patient, the shared autoimmune nature of both diseases cannot be ignored.

Declarations

Competing interests: None declared

Funding: None declared

Ethical approval: Written informed consent for publication was obtained from the patient.

Guarantor: AS

Contributorship: All authors (IE, EY and AS) were involved in the care of the patient. AS prepared the manuscript and all authors approved the final version.

Provenance: Not commissioned; peer-reviewed by Harit Buch.

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