

Chalky adrenals: a sequelae of antiphospholipid syndrome

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DESCRIPTION

A woman in her 20s presented to us with repeated episodes of giddiness and hypotension requiring multiple hospitalisations in the preceding year. She had an episode of severe abdominal pain followed by a history of easy fatigability, anorexia and progressive hyperpigmentation associated with a weight loss of 5 kg over the past 1 year. On clinical examination, there was diffuse hyperpigmentation and her blood pressure was 90/50 mm Hg with a significant postural drop. The rest of the systemic examination was normal. Blood investigations revealed low sodium (125 mmol/L), hyperkalaemia (5.5 mmol/L), hypocortisolemia (8:00 am cortisol of 2 µg/dL) and an elevated plasma adrenocorticotrophic hormone (ACTH) of >1250 pg/mL. The presence of low serum cortisol in the presence of elevated ACTH was suggestive of a primary adrenal insufficiency. Subsequently a CT scan of the abdomen was done to visualise the adrenal glands, and this showed bilateral chunky calcifications involving the adrenal glands on both sides suggesting the occurrence of a prior adrenal haemorrhage (figures 1 and 2). Furthermore, an aetiological workup was done, which showed a normal prothrombin time and a prolongation in the duration of the activated thromboplastin time (59 s), which did not correct with the addition of normal plasma. She was diagnosed to have an antiphospholipid (aPL) syndrome based on the presence of lupus anticoagulant and anticardiolipin antibodies and antibodies to beta 2 glycoprotein 1. Other blood tests done included a complete haemogram, which showed the haemoglobin to be 10 g/dL (N: 13–15 g/dL), total leucocyte count of 7100/mm³ (N: 4000–11000/mm³, mean corpuscular haemoglobin was 25.2 pg, reticulocyte count of 3.09%, differential count showed 77% neutrophils, 1% eosinophils, 13% lymphocytes and monocytes of 9%. Platelet count was 1.52 lakh/mm³. D-dimer was 233 ng/mL. Fibrinogen and platelet aggregation test were not available in this patient. She was started on hydrocortisone and fludrocortisone. For APS, she was initiated on enoxaparin and then overlapped with warfarin.

Primary adrenal insufficiency is the most common endocrine manifestation of primary aPL syndrome, although its prevalence remains low. On the other hand, APS is diagnosed in less than 0.5% of all patients with Addison's disease. The exact pathogenic mechanism underlying the occurrence of bilateral adrenal haemorrhage in APS is largely unknown. It is postulated that the unique nature of the vasculature of the adrenal glands with a rich arterial supply and restricted

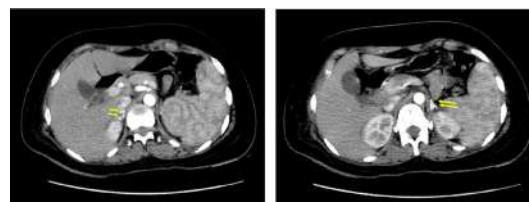


Figure 1 Cross-sectional CT imaging showing calcification of both adrenals.

venous drainage by a single vein may predispose to thrombosis.¹ Apart from APS, the other causes of primary adrenal insufficiency include inflammatory and granulomatous disorders such as tuberculosis, histoplasmosis, autoimmune adrenalitis, Allgrove's syndrome, adrenal haemorrhage secondary to sepsis, genetic causes such as mutations that involve the ACTH receptor.

The anatomical disposition of the adrenal glands is such that the fascicular zone makes up to three-fourth of the adrenal cortex, its cells have high cholesterol content. The endosomal and lysosomal membranes of cells that demonstrate high rates of lipid-trafficking are enriched with lysobisphosphatidic acid (LBPA), which is a potential target for the aPL antibodies. Antibodies directed against LBPA result in cellular accumulation of cholesterol and secretion of lysosomal proteinases, which activates endothelial cells, thereby inducing a procoagulant state. A second possibility is that aPL antibodies increase intracellular cholesterol deposition, resulting in cell death. aPL antibodies could, thus, aggregate locally and alter haemostasis through



Figure 2 Coronal section showing both adrenals calcification.



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the abovementioned pathways, resulting in microthrombosis and postinfarction haemorrhage. Further mechanisms include increased expression of vascular cell adhesion molecule-1 or E-selectin and Annexin V, resulting in thrombosis.² In the setting of APS with adrenal insufficiency, besides anticoagulation, management includes lifelong replacement with adrenal steroids and ensuring periodic follow-up and monitoring of the patient.³

Learning points

- ▶ Adrenal insufficiency remains the most common endocrine manifestation of primary antiphospholipid syndrome.
- ▶ Presence of prolonged activated thromboplastin time, which does not correct with addition of normal plasma along with positive anticardiolipin antibody and lupus anticoagulant in the setting of adrenal insufficiency and chunky adrenal calcification would clinch the aetiology of primary antiphospholipid syndrome.
- ▶ Long-term follow-up and monitoring is warranted in all patients.

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Case reports provide a valuable learning resource for the scientific community and can indicate areas of interest for future research. They should not be used in isolation to guide treatment choices or public health policy.

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