https://doi.org/10.4038/jmj.v35i1.184

Case Report

Primary antiphospholipid syndrome with adrenal insufficiency

S Seyon1, T Peranantharajah1, Nalayini J1, S Rushanthini1, R Pirannavan1

[1]*Teaching Hospital, Jaffna*

Summary

Antiphospholipid syndrome (APS) is a thrombophilic condition leading to multiple complications. Primary APS rarely causes primary adrenal insufficiency, but it can be life-threatening. In the present report, a patient presents with symptoms and signs of adrenal insufficiency and subsequent hormone level tests and radiological findings led to a diagnosis of primary APS with adrenal insufficiency.

Key words

Antiphospholipid syndrome (APS), Adrenal insufficiency, Hyponatraemia

Introduction

Antiphospholipid syndrome (APS) can be defined as a disease characterized by hypercoagulability and pregnancy complications, and linked with a group of antibodies called 'antiphospholipid antibodies that are associated with it.(1)anticardiolipin antibody, anti-beta-2 glycoprotein-I antibody APS can be primary or linked with other autoimmune disorders like systemic lupus erythematosus (SLE).

It can manifest as thromboembolic phenomenon of any vascular segment. Endocrine manifestations of APS are very unusual. When present, primary adrenal insufficiency (Addison's disease) is the commonly reported endocrinological complication. Even though rare, it is life threatening and hence it should be emphasized that APS should be considered in patients with Addison's disease, and vice versa.

Case presentation

A previously well, young female presented with inflammatory type back pain for three weeks duration associated with on and off fever episodes. There were no symptoms suggestive of an infective focus, neither a history of chronic cough, night sweats or contact history of tuberculosis. There was a history of on and off giddiness. The past medical history and surgical history were unremarkable.

On physical examination, there was a significant postural drop in blood pressure. Cardiovascular, respiratory and abdominal examinations were normal. Straight leg raising test was negative bilaterally.

The investigations given below:

FBC	WBC-8, Neu-3.21, Hb-10.1, Plt-328
CRP	32
ESR	110
RFT	S.cre-82, Na-128, K-5.1, B.urea-2.8
LFT	ALT- 59, AST-31, ALP-81, T.Bil-10.6, T. pro-76, S.Albumin-33, S.Glo-43
Blood picture	Marked Roulex formation with thrombocytopenia.
VDRL and TPPA	Negative
HIV 1 and 2	Negative
Blood and urine culture	No growth
Serum 9am Cortisol	<4nmol/l
USS (on 10th feb 2021)	Features were suggestive of mesenteric adenitis.
X ray Lumbo Sacral spine	No abnormality detected
CECT CAP	There was a contrast enhanced lesion in right lower lobe with tiny, smaller lesion seen in left base of the lung. both adrenal glands are enlarged without haemorrhage or calcifications. No focal lesion in the liver
Brochoscopy and BAL	Normal brochial tree BAL for TB PCR, AFB, Culture - negative
CT guided lung biopsy	No evidence of malignancy or TB. Normal lung tissue
Repeat USS abdormen during the ward stay(25/3/2021)	IVC thrombus seen in suprarenal compartment which is extends into the intrahepatic part of the IVC.No DVT seen in elsewhere.
Histology of Adrenalectomy Specimen	Adrenal tissue shows mostly necrosis and a few remaining viable tissue.there is no demonstratable granuloma.

Corresponding Author: S Seyon, Email: 91seyon@gmail.com https://orcid.org/0009-0007-2256-2265 Submitted June 2022, Accepted November 2022

ANA	Negative
Anti phospholipid Antibodies	Both Anti beta 2 glycoprotein IgG and IgM positive and Anti cardiolipin antibody IgG also moderatly positive. Anti Cardiolipin Ab (IgG)- 34.7GPL/ml Anti Cardiolipin Ab (IgM)- 12.9 MPL/ml Anti Beta 2 glycoprotein IgM- 13.5U/ml Anti Beta 2 glycoprotein IgG- 24.6U/ml

With the above investigations, the patient was started empirically on anti-tuberculosis medications and steroids. The patient improved clinically even though the Mantoux test came negative.

But, during the hospital stay she developed abdominal pain and bilateral ankle oedema. A repeat ultrasound scan abdomen and lower extremities was done. It revealed residual thrombus in suprarenal compartment of inferior vena cava extending into the intrahepatic part also. But there was no deep vein thrombosis seen in bilateral legs. Suspecting malignancy, laparoscopic right adrenalectomy was performed.

Since there was venous thrombosis, a suspicion of APS was made and lupus anticoagulant, anticardiolipin antibodies and anti-beta-2 glycoprotein 1 antibodies, were positive.

Twelve weeks apart, again Anti phopholipid antibody was positive. ANA was negative.

A diagnosis of primary APS was made. The patient was started on enoxaparin and registered in the haematology clinic for routine follow up. The patient and relatives were educated about the injection of enoxaparin. Routine follow up with platelet monitoring was arranged.

Endocrine manifestations of APS are rare and can involve adrenals, thyroid, pituitary, pancreatic islet cells, parathyroid, ovaries and testes. Adrenal insufficiency is reported to be the commonest endocrinological manifestation in APS.(3) In undiagnosed APS patients, adrenal insufficiency could be a presenting feature.(3) When considering the occurrence of Adison's disease in patients with APS, it amounts to only 0.4%.(4)acute adrenal insufficiency may ensue from bilateral adrenal haemorrhage in patients with known antiphospholipid syndrome (APS

In order to diagnose APS, patients have to meet at least one clinical sign (vascular thrombosis or pregnancy complications) and one laboratory criterion (anticardiolipin IgG or IgM antibodies, lupus anticoagulant of IgG or IgM classes detected on two or more occasions at least six weeks a part). Lupus anticoagulant antibodies are generally more specific for the APS, whereas anticardiolipin antibodies are more sensitive.(5)

It is reported that only in 5% of the cases have this uncommon disorder of APS leading to primary adrenal insufficiency.(1)anticardiolipin antibody, anti-beta-2 glycoprotein-I antibody

The pathophysiology of adrenal insufficiency in primary APS is still not very clear.(6) A commonly accepted hypothesis is that the adrenal haemorrhagic infarction may be possibly due to the adrenal vein thrombosis, which could occur in the hypercoagulable state of primary APS.(6)

A combination of clinical findings, hormone level assessment and radiological analysis assist in the diagnosis of primary adrenal insufficiency. A low serum cortisol, with elevated ACTH levels and a blunted response to short synacthen test confirm primary adrenal insufficiency. Abdominal CT scan remains the preferred modality to visualize the adrenal glands and can help in diagnosis at earlier stages demonstrating bilateral adrenal haemorrhage.(1) CT scan may not reveal any abnormalities, if done at the beginning of the disease. But it should be repeated if there are persistent symptoms as the morphologic changes may then become prominent in the CT scan.(1)

As for treatment, stress doses of intravenous hydrocortisone are started and carried on for a period of 24-hour, later to be changed to adequate oral dose as for replacement therapy. If there is confirmed aldosterone deficiency, then fludrocortisone can also be commenced in order to replace the mineralocorticoid deficit.(1) Together with that, unfractionated heparin is also started to prevent coagulation. When treating with heparin, platelets and clotting factors are monitored meticulously in order to avoid bleeding manifestations.

The established treatment of choice is oral anticoagulation with warfarin for a long term while maintaining the INR between 2 and 3.

It is estimated that around 3.81% of patients succumb to adrenal insufficiency due to APS.(7) But, when considering the overall outcome, if the patients survive the acute phase then their prognosis is better.(7)

Conclusion

When patients present with adrenal insufficiency and no obvious cause is found, primary APS should be suspected, and screening should be done accordingly. Recognizing the fatal acute phase early, and promptly treating it will help reducing the high mortality of the condition, given that the overall outcome is favourable.

References

1. Bansal R, Nath P V., Hoang TD, Shakir MKM. Adrenal Insufficiency Secondary to Bilateral Adrenal Hemorrhage Associated with Antiphospholipid Syndrome. AACE Clin Case Reports. 2020;6(2):e65–9.
2. Aldaajani H, Albahrani S, Saleh K, Alghanim K. Bilateral adrenal hemorrhage in antiphospholipid syndrome: Anticoagulation for the treatment of hemorrhage. Saudi Med J. 2018;39(8):829–33.
3. Uthman IW, Salti I, Khamashta M. Endocrinologic manifestations of the antiphospholipid syndrome. Lupus. 2006;15(8):485–9.
4. Presotto F, Fornasini F, Betterle C, Federspil G, Rossato M. Acute adrenal failure as the heralding symptom of primary antiphospholipid syndrome: Report of a case and review of the literature. Eur J Endocrinol. 2005;153(4):507–14.
5. Levine JS, Branch DW, Rauch J. The antiphospholipid syndrome. N Engl J Med. 2002 Mar;346(10):752–63.
6. Improda N, Alessio M, Capalbo D, Russo G, Dacunzo I, Palamaro L, et al. Acute adrenal failure as the presenting feature of primary antiphospholipid syndrome in a child. Ital J Pediatr. 2012;38(1):2–5.
7. Mlekuš Kozamernik K, Jensterle M, Ambrožič A, Pfeifer M. Adrenal failure and antiphospholipid syndrome. J Int Med Res. 2020;48(7).