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PRIMARY ANTIPHOSPHOLIPID ANTIBODY SYNDROME CAUSING ACUTE PRIMARY ADRENAL INSUFFICIENCY SECONDARY TO BILATERAL ADRENAL HEMORRHAGE: A CASE REPORT AND REVIEW OF LITERATURE

Dr. Samia A Bokhari*, Dr. Nada Nasser, Dr. Patan Murthuza Khan, Dr. Muneera Shareef, Dr. Lamees Ismaeel Felimban and Dr. Maram Mohammed Jehani

Department of Endocrinology, King Fahd Armed Forces Hospital, Jeddah, Saudi Arabia.

***Corresponding Author: Dr. Samia A Bokhari**

Department of Endocrinology, King Fahd Armed Forces Hospital, Jeddah, Saudi Arabia.

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ABSTRACT

Adrenal hemorrhage (AH) is a rare cause of adrenal insufficiency (AI) and considered a fatal event with mortality rate reaching up to 15%.[1] Adrenal hemorrhage can be unilateral or bilateral, and patients may present with mild vague abdominal pain and vomiting or may present with hemodynamically instability and cardiovascular collapse, due to adrenal crisis. Venous thrombosis and/or hemorrhage are leading cause of Primary antiphospholipid syndrome, causing bilateral adrenal hemorrhage is rare cause of acute adrenal insufficiency. We report a case with acute adrenal insufficiency secondary to bilateral adrenal hemorrhage due primary antiphospholipid antibody syndrome.

KEYWORDS: Primary Antiphospholipid antibody syndrome; Adrenal hemorrhage; Primary Adrenal insufficiency.

INTRODUCTION

Primary adrenal insufficiency affects both mineralocorticoid and glucocorticoid production in the adrenal cortex.[2] Acute adrenal insufficiency is a rare complication of antiphospholipid antibody syndrome (APS). Antiphospholipid antibody syndrome manifest with thrombosis, abortion and rarely cause adrenal insufficiency. We are presenting a rare case of primary antiphospholipid syndrome, presented with acute adrenal insufficiency due to bilateral acute adrenal hemorrhage.

CASE REPORT

A 35-year-old male patient, with no known medical illnesses presented to Emergency Department with history of pain and swelling of left lower limb of 3 days duration. No history of trauma, undercurrent infection, prolonged immobilization. Pt is a chronic smoker with a history of three packs a day for 15 years. Physical examination was unremarkable except evidence of swelling and tenderness of left calf muscles and Homan's sign was positive on left leg. The Doppler US performed in ER revealed Deep vein thrombosis in left femoral vein. Patient started on heparin followed by warfarin. Patient was reluctant to stay for further work up and discharged against medical advice. He discontinued warfarin one week of discharge and did not come for scheduled follow up in clinic.

After 2 months from his discharge, the patient presented with fever, cough, pleuritic chest pain and shortness of breath. He was complaining of nausea and dizziness and abdominal pain.. On examination: patient was conscious not distressed. BP: 100/70 mm/hg with postural drop, HR: 95 bpm, SPO: 95% on ambient air, temperature: 37.9^0 C .Systemic examination was unremarkable except respiratory system examination revealing dullness on percussion and absent breath sounds over the left lower zone.

CT Angiography performed and Pulmonary Embolism diagnosed. Patient investigated for hypercoagulable states because of unprovoked DVT and Pulmonary embolism. And for adrenal insufficiency was suspected due to relevant signs and symptoms of adrenal insufficiency. The preliminary investigations (Table: 1, 2) were normal except prolonged aPTT. Case was referred to rheumatologist and full work was performed to detect the cause of hypercoagulable state (Table no: 3) Thrombocytopenia, positive anti cardiolipin antibodies and anti-β2 glycoprotein I antibodies in the absence of evidence of SLE or any other connective tissue disease consistent with API. He was advised lifelong anticoagulation with warfarin, Basal cortisol level was very low and the short synacten test confirmed the diagnosis of adrenal insufficiency (Table: 4). A CT abdomen performed looking for cause of his adrenal insufficiency revealed bilateral adrenal hemorrhages. (Fig No 1.2,).

A final diagnosis of primary APA leading to acute adrenal insufficiency due to bilateral adrenal hemorrhage confirmed. Patient started on therapeutic doses of warfarin and hydrocortisone. Advised to regular follow-ups in outpatient clinic.

Investigations (Table 1):

Chemistry	Patient's value	Normal Range
Urea	4 mmol/L	1.7 – 8.3
Creatinine	75 umol/L	62 – 106
Sodium	123 mmol/L	135 – 147
Potassium	4.2 mmol/L	3.5 – 5.1
ALT	16 U/L	5 – 50
GGT	34 U/L	11 – 49
ALP	100 U/L	90 - 220

Table 2:

Complete Blood Count	Patient's value	Normal Range
WBC	9.9	3.3 – 10.8
HB	9.8 g/L	13.5 – 17
MCV	65 FL	80 – 100
MHC	20.8 PG	23.7 – 32
PLATELET	128 10^9/L	150 – 500
Partial thromboplastin time (aPTT)	72.6 sec	25 – 38
INR	1.4	0.9 – 1.15

Chest x-ray showed: left side pleural effusion

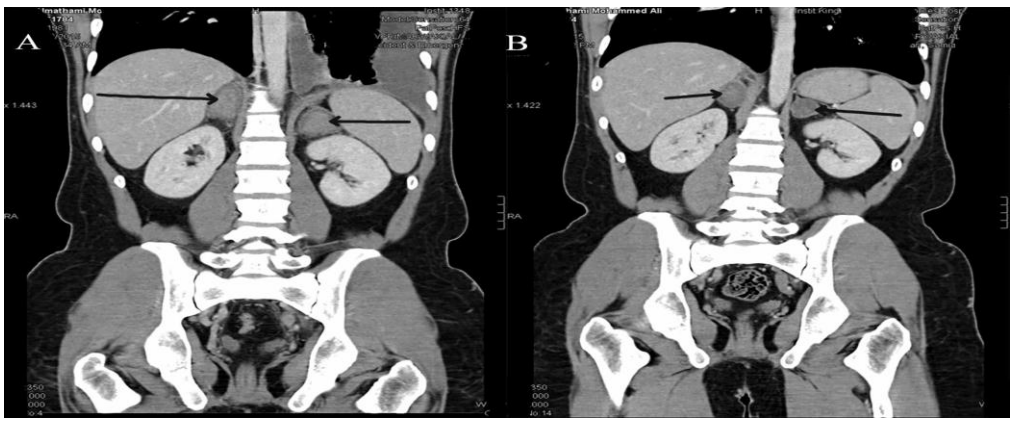
Laboratory investigations done to detect hypercoagulable state (Table 3)

Test	Patient's value	Normal Range
Anti-Beta 2glycoprotient IgG	2429.9 U/ml	<20
Anti-Beta 2glycoprotient IgM	3.2 U/ml	<20
Anti-cardiolipin IgG	reactive	< 15
Anti-cardiolipin IgM	Non-reactive	< 15
ANA	1:60	1:40 – 1:60
Ds-DNA	3.7 IU/ml	< 10
Anti-Smith Ab	0.4 U/ml	< 10

Table 4:

Test	Patient's value	Normal Range
Short synacten test (250 mcg Synacten)		
Basal Cortisol	5.44 nmol/L	171-536 nmol/L
Cortisol 30 minutes	7.83 nmol/L	More than 540 nmol /l
Cortisol 60 minutes	7.89 nmol/L	More than 540 nmpl/l

Figure 1 CT Abdomen with contrast, coronal reformatted images (A) shows bilateral adrenal hemorrhage, (B) Follow up shows decrease in size of the hemorrhage



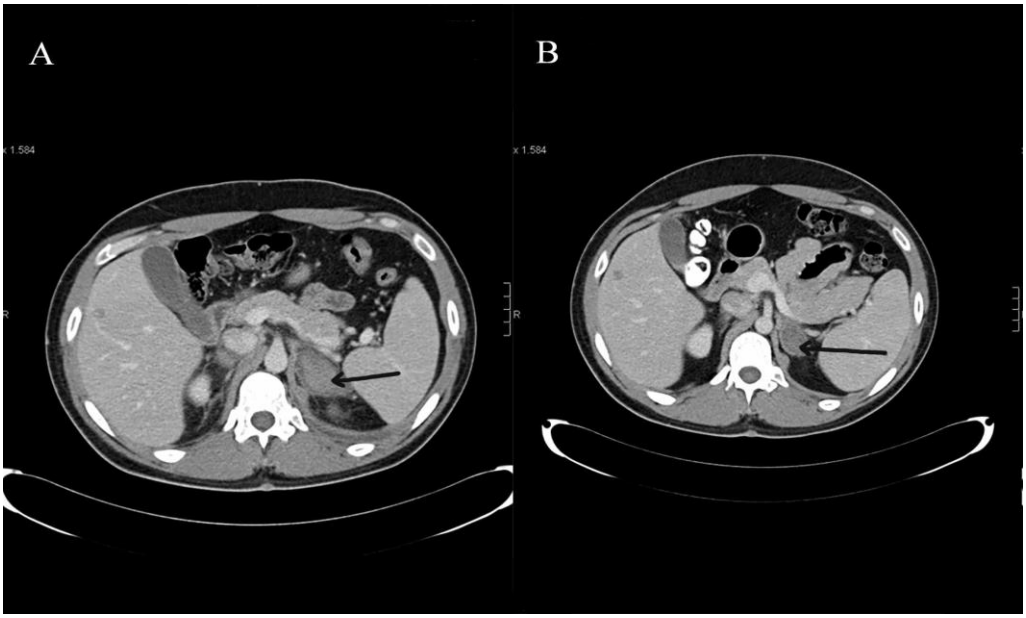


Fig. 2: CT Abdomen with contrast, axial images (A) shows bilateral adrenal hemorrhage, (B) Follow up shows decrease in size of the hemorrhage, Arrow towards the left adrenal gland

DISCUSSION

Antiphospholipid antibody syndrome(APS)is defines by the presence of antiphospholipid antibodies in patients with thrombotic /obstetrical events.[3] API is characterized by the presence of recurrent Thrombotic events.[4] APS may be related to other connective tissue diseases like SLE (secondary APS) or not related any underlying disease(primary APS)APS can cause rarely endocrine complications. Adrenal insufficiency (AI) probably most common complication of API although hypopituitarism and isolated ACTH deficiency were also reported,[5.6] The exact prevalence of AI in API is unknown.[7] In a study by Cervera et al 4 out of 1000 patients with API developed AI.[8] The adrenal glands have extraordinary anatomy, in terms of multiple arterial supplies, but have single venous outflow. This unique vascular supply may result in limited drainage of adrenal glands and predispose patient to thrombosis and hemorrhage.[9] Adrenal glands have a high cholesterol content and rich in lysophosphotitides which are targeted by antiphospholipid antibodies leading to cellular death.[10] Even though prevalence of API is 82% the adrenal involvement is higher in males(55%) consistent our male patient.[3] The incidence of spontaneous AH 0.14%-1.1%, data collected from autopsy reports. Bilateral Adrenal hemorrhage is rare and it is life threatening and carries high mortality up to 15%.Spontaneous bilateral adrenal hemorrhage usually occur in association with severe stress such as meningococcemia, surgery, burns or hypotension.[11] It may also complicate hemorrhagic diathesis, especially from anticoagulant therapy or acquired coagulation disorders such as antiphospholipid syndrome as in our case. The exact pathogenesis of adrenal vein thrombosis is not known in APS. It has been speculated that hypercoagulable state leads to adrenal vein thrombosis which results in in hemorrhagic infarction of adrenal gland. The adrenal gland comprises a rich arterial supply with single vein limiting blood drainage, which when thrombosed leads progressive increase in arterial blood pressure.[12] Bilateral adrenal hemorrhages can cause spontaneous or catastrophic adrenal insufficiency. Our patient had acute adrenal insufficiency precipitated with pneumonia. The main clinical manifestation of primary ADI includes weakness, fatigability, anorexia, dizziness and abdominal pain. Addisonial crisis due to severe adrenal insufficiency can be catastrophic with persistent hypotension and vascular collapse and fatal outcome. Imaging modality like CT scan can detect acute hemorrhage. Acute hemorrhage appear as a hyper dense mass on CT scan (fig: 3).Our patient was started on anticoagulation to avoid further complications of APS. He was also started on prednisolone for adrenal insufficiency. He HAD significant improvement in his clinical condition and discharged to be closely followed in our outpatient clinics.

CONCLUSION

Bilateral adrenal hemorrhage is rare complication of primary anti phospholipid antibody syndrome. High degree of suspicion is needed to diagnose adrenal insufficiency in patients having adrenal insufficiency signs and symptoms. Prompt diagnosis and appropriate management can avoid fatal complications.

REFERENCES

1. Fatima Z, Tariq U, Khan A, Sohail MS, Sheikh AB, Bhatti SI, Munawar K. A Rare Case of Bilateral Adrenal Hemorrhage. Cureus, 2018 Jun 18; 10(6): e2830. doi: 10.7759/cureus.2830. PMID: 30131923; PMCID: PMC6101466.
2. Murat Sahin, Ayten Oguz, Dilek Tuzun, Serife Nur Boysan, Bülent Mese, Hatice Sahin, Kamil Gul,

"Primary Adrenal Failure due to Antiphospholipid Syndrome", Case Reports in Endocrinology, 2015. Article ID 161497, 3 pages, 2015. https://doi.org/10.1155/2015/161497.

3. Mikalis S, Lockshin MD,AtsumiT et.al:International consensus statementon the update of the classification criteria for definite antiphospholid antibody syndrome, JThromb Hemost, 2006; 4: 295-306.
4. Levine JS, Branch DW, Rauch j, The antiphospholipid syndrome, New England Journal of Medicine, 2002; 346: 752-763.
5. Pandolfi C, Gianini a,Fregoni v,et,al: Hypopituitarism and antiphospholipid syndrome. Minerva Endocrinol, 1997; 22: 103-105.
6. Andre M,Aumaitre o, Piette JC, et al:Hypopituitarism and antiphospholipid syndrome AM Rheum,Dis., 1998; 57: 257-258
7. Mehdi AA, Salti I, Uthma I:Antiphosphilipid syndrome and endocrinological manifestations and organ involvement: Semin Throm Hemost, 2011; 37: 49-57.
8. Cervera R, Piette IC, Font J et al;Antiphospholipid syndrome clinical and immunological manifestations and patterns of disease disease expression in cohert of 1000 patients,Arthritis Rheum, 2002; 46; 1019-1027.
9. Espinosa G Cervera R, Font J et al; Adrenal involvement in antiphospholipid syndrome,Lupus, 2003; 12; 569-572.
10. Ashesrson RA.Cervera R,Piette JC et al ;catastrophic antiphospholipid syndrome clues to pathogenesis from a series of 80 patients; Medicine (Baltomore), 2001; 80: 355-377.
11. Xarli VP,Steele AA, Davies PJ,et al; Adrenal hemorrhage in an adult.Medicine, 1978; 57; 211-221.
12. Anastasia M, Canacci, Gregory T,Mac Linnan.Adrenal hemorrhage.J Urol, 2007; 128: 284.