CASE REPORT

A Rare Case of Antiphospholipid Syndrome (APLS) Presented as Bilateral Adrenal Hemorrhage

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ABSTRACT

A 37-year-old man presented with bilateral adrenal hemorrhage, an uncommon clinical scenario often linked to conditions such as antiphospholipid syndrome (APLS). He reported experiencing lower and bilateral abdominal pain for one week, along with symptoms indicative of an adrenal crisis. Subsequent investigations revealed a significantly low AM cortisol level of 67 nmol/L, and a CT scan of the abdomen confirmed bilateral adrenal hemorrhage. The patient tested positive for anti-cardiolipin, anti-Beta 2 glycoprotein, and lupus anticoagulant, affirming the diagnosis of APLS. Treatment with glucocorticoid and mineralocorticoid replacement led to clinical improvement. This case underscores the importance of maintaining a high index of suspicion for APLS in patients presenting with unexplained abdominal pain, with or without adrenal crisis symptoms, as bilateral adrenal hemorrhage can be a rare but serious manifestation. The CT scan remains a crucial diagnostic tool in detecting such hemorrhages.
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Keywords: Bilateral adrenal hemorrhage, Antiphospholipid Syndrome, APLS, Adrenal crisis, Thrombosis, Abdominal pain

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INTRODUCTION

Antiphospholipid syndrome (APLS) is an autoimmune disorder characterized by antiphospholipid antibodies, increasing the risk of thrombosis and pregnancy complications. It typically presents with deep vein thrombosis, pulmonary embolism, stroke, and miscarriages, but can also have non-thrombotic symptoms1. A rare manifestation of APLS is adrenal hemorrhage, which can be unilateral and asymptomatic, or bilateral and potentially fatal if unnoticed. Bilateral adrenal hemorrhage might be the initial sign of APLS, necessitating careful clinical evaluation and management.

CASE REPORT

A 37-year-old man, presented with lower and bilateral flank abdominal pain for 1 week. The pain was described as dull ache pain, progressively worsening with a pain score of 8/10 and no radiation. It was associated with nausea, vomiting, and lethargy. Otherwise, he had no fever, shortness of breath, chest pain, and altered mental state. He had a history of motor vehicle accident (MVA) 2 weeks before the onset of abdominal pain. His motorbike skidded and he sustained an open fracture of the proximal phalanx of his little finger. Wound debridement and K-Wired were done for his injury. On examination, he was alert but dehydrated. His blood pressure was hypotensive, BP: 90/46, Heart rate (HR): 114, Temperature: 37 degrees Celsius, and Oxygen saturation (spO2): 99% under room air (RA). There was tenderness over the bilateral flank area but no bruises or hematoma. Other systemic examination was unremarkable. CT abdomen was ordered to look for any evidence of traumatic intrabdominal injury. The finding was bilateral adrenal hemorrhage without any other solid organ and bowel injury (Figure 1). The blood investigations revealed thrombocytopenia, isolated prolongation of activated partial thromboplastin time (APTT), and a lack of correction in the mixing test, suggesting a possible autoimmune etiology (Table I). He had no previous history or signs and symptoms of a hematological disorder. Serum cortisol was sent, and the result was low with a level of 67 nmol/L. Intravenous hydrocortisone 100 mg stat and 200 mg infusion over 24 hours was started. His blood pressure was normalized with Intravenous hydrocortisone and hydration. Further workup for etiology of bilateral adrenal hemorrhage

related to hematological disorders i.e. antiphospholipid syndrome (APLS), Idiopathic thrombocytopenia purpura (ITP), and Heparin-induced thrombocytopenia (HIT) were done. Apart from bilateral adrenal hemorrhage, he also developed left-hand gangrene due to digital artery thrombosis (Figure 2). Antibodies for Antiphospholipid Syndrome (APLS), which include anti-cardiolipin, anti-beta 2 glycoprotein, and lupus anticoagulant, are all positive and remain positive after three months. No other thromboembolism events. In conclusion, he had Primary Adrenal Insufficiency secondary to bilateral adrenal hemorrhage secondary to APLS. As for adrenal insufficiency, it was stable with glucocorticoid (T. Hydrocortisone 10 mg OM and 5 mg in afternoon) and mineralocorticoid (T. Fludrocortisone 0.1 mg OD) replacement. Repeated CT adrenal also showed resolving hemorrhage without evidence of the existence of an adrenal tumour. For the left-hand gangrene, it could not be salvaged despite clexane and illosprost administration and he ended up with left-hand amputation.

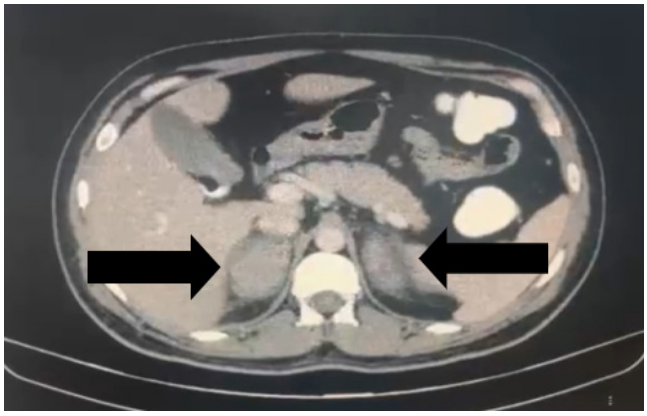

Figure 1: Bilateral heterogeneously enlarged and dense adrenal glands (arrow) with surrounding streakiness suggestive of adrenal hemorrhage.

Figure 2: Left hand gangrene due to digital artery thrombosis

Table I: Summary of laboratory investigations

Laboratory Test	Result	Normal Range
Total White Cell	9.8 x 10^9/L	4 – 10 x 10^9/L
Haemoglobin	14 g/dL	13.0 – 17.0
Platelet	60 x 10^9/L	150 – 410 x 10^9/L
Urea	6.6 mmol/L	3.2-7.4
Serum Sodium	118 mmol/L	136 - 145
Serum Potassium	4.9 mmol/L	3.5 – 5.1
Serum Creatinine	66.4 umol/L	64 - 104
Albumin	33 g/l	35 - 50
Total Protein	65 g/l	64 - 83
Total bilirubin	14.2 umol/L	3.4 – 20.5
Alanine transaminase	45 U/L	0 -55
Alkaline phosphatase	150 U/L	40 - 150
Aspartate transaminase	28 U/L	5 - 34
PT	10.1 seconds	11.6 – 14.9
INR	1.56 ratio	
APTT	107.2 seconds	30.3 – 46.5
Corrected Calcium	2.44 mmol/L	2.2 – 2.60
C3	142 mg/dL	79 - 152
C4	36.1 mg/dL	16 - 38
Lupus anticoagulant	Positive	
Anti-cardiolipin Antibody	Positive	
Anti-B2 glycoprotein Antibody	Positive	
Anti-nuclear Antibody	Positive 1:320, Speckled Pattern	
Anti-Double Stranded DNA Antibody	Negative	
Extractable Nuclear Antibodies (Panel)		
- SSA/Ro52	Negative	
- SSA/Ro60	Negative	
- SSB/La	Negative	
- Cenp-B	Negative	
- Histone	Negative	
- PCNA	Negative	
- AMA M2	Negative	
- PM Scl	Negative	
- U1-snRNP	Negative	
- Nucleosome	Negative	
- Ribosomal P	Negative	
- SmD1	Negative	
- Scl-70	Negative	
- Jo-1	Negative	

DISCUSSION

Bilateral adrenal hemorrhage (BAH) is a rare and life-threatening condition if not treated properly. Diagnosis of adrenal hemorrhage is very challenging because the fact that it is rare, and the presentation can mimic other diseases i.e. sepsis. Hence, a thorough history, clinical examination with appropriate investigation, and a high index of suspicions can help to identify this condition. Adrenal hemorrhage has been associated with various

entities, such as antiphospholipid syndrome (APLS), heparin-induced thrombocytopenia, adrenal tumor, Covid-19 infection and vaccine, trauma, and surgery. In the context of APLS, bilateral adrenal is a rare manifestation observed in 0.4% of APLS patients1. The literature also mentions that bilateral adrenal hemorrhage can be the first presentation of APLS like our patient. The adrenal glands possess a unique vascular anatomy, characterized by a rich arterial supply and a single central vein, rendering them particularly susceptible to congestion and hemorrhage, especially under conditions of high blood flow. In the context of Antiphospholipid Syndrome (APLS), the hypercoagulable state significantly increases the risk of adrenal vein thrombosis, leading to hemorrhagic infarction. This infarction results in tissue death and bleeding, compounded by the adrenal glands' complex blood supply. Moreover, antiphospholipid antibodies may specifically target the zona fasciculata of the adrenal gland, inducing cell death and further promoting coagulation. Consequently, these mechanisms contribute to the increased vulnerability of the adrenal glands to bilateral hemorrhage and subsequent primary adrenal insufficiency. The clinical presentation is usually nonspecific, and most symptoms are due to adrenal insufficiency because of adrenal hemorrhage. This condition can be precipitated by various triggers, such as physical trauma from motor vehicle accidents, as seen in this case, or more common triggers like infection. Based on the systemic review by Lee et al, abdominal pain (39.04%) was the most common clinical presentation, followed by fever of unknown origin (33.33%), vomiting (23.81%), nausea (19.05%), weight loss (13.33%) and general weakness (9.52%)3. Some patients may be presented with acute adrenal crisis with hypotension and altered mental state. Hyponatremia was present in 77.94% of patients, and hyperkalemia was present in 49.15%. Cortisol levels were low (84% of patients) with more than half of patients having levels less than 3 µg/dL. ACTH level also high in most of the patients. Lupus anticoagulant and anticardiolipin were present in 97% and 93% of patients respectively2. Before this, many cases of adrenal hemorrhage were diagnosed post-mortem. But nowadays, CT and MRI contribute significantly to the investigation of adrenal pathology and hemorrhage. In the series of APLS cases with adrenal involvement, adrenal hemorrhage was present on imaging in 57% of cases. The second most common finding is adrenal infarction (14%), usually with a hemorrhagic component. In the CT scan, acute adrenal hemorrhage is characterized by the development of a non-contrast-enhancing high-or mixed-attenuation adrenal lesion within hours to a few days3. In early hemorrhage, the adrenal gland maintains its configuration and preserves its contrast enhancement peripherally but with hemorrhagic central hypodensity (tram-track appearance). Surrounding ill-defined soft tissue stranding and retroperitoneal hematoma can be an important clue to the diagnosis. In the chronic phase, the adrenal glands are typically atrophied and show low attenuation on CT4. This is due to the replacement of the adrenal tissue with fibrous tissue. Whereas for MRI, it's very useful to determine the age of adrenal hemorrhage. For our patient, early detection of bilateral adrenal hemorrhage was by CT scan, and proper treatment was delivered to him. Espinosa et al and Presotto et a reported that in the setting of APLS, more than 40% of adrenal involvement (adrenal hemorrhage or infarction) are precipitated by other factors namely surgical procedures, infections, postpartum, trauma, and biopsies. Like our patient, he was developed adrenal hemorrhage after involved in motor vehicle accident (MVA) and surgical procedure. Patients with adrenal crisis need to be treated with parenteral corticosteroids, such as hydrocortisone. The usual starting dose is 100 mg given as a bolus, followed by 200 mg every 24 hours. This can be given as a continuous infusion or as intravenous or intramuscular injections every 5 hours. In addition, it is important to give intravenous fluids early, such as 1000 mL of crystalloid fluids within the first hour. If the patient's blood sugar is below 70 mg/dL, then 5% dextrose should also be given intravenously. Once the adrenal crisis has resolved, the hydrocortisone dose should be gradually reduced to the usual maintenance dose over 3 days before changing to oral hydrocortisone therapy. In addition, it is also recommended to give mineralocorticoid replacement with fludrocortisone at a mean dose of 100 µg/day (typically 50–200 µg/day). As with this patient, who was discharged with oral hydrocortisone and fludrocortisone, repeated CT imaging of the adrenal glands demonstrated resolution of the hemorrhage and no evidence of an adrenal tumor. It is likely that the patient will require long-term oral hormone supplementation until full recovery of adrenal function is achieved. On the other hands, Patients diagnosed with Antiphospholipid Syndrome (APS) and experiencing current thrombosis should be placed on lifelong anticoagulation treatment to prevent further thrombotic events and complications. Moreover, this patient presents with triple positivity for antiphospholipid (aPL) antibodies, which significantly heightens the risk of thrombosis. Warfarin remains the anticoagulant of choice, as there is currently no strong evidence supporting the effectiveness of alternative oral anticoagulants. In cases of APLS involving bilateral adrenal gland haemorrhages like this, which are understood to be caused by thrombosis, the recommended treatment is meticulous anticoagulation therapy using unfractionated heparin and warfarin, with a target INR of 2-3, to avert further thrombosis5. However, the timing of anticoagulant administration remains a topic of clinical debate and should involve a multidisciplinary approach and shared decision-making.

CONCLUSION

Bilateral adrenal hemorrhage is a rare but serious manifestation of antiphospholipid syndrome (APLS). Clinicians should maintain high suspicion for APLS in

patients with unexplained abdominal pain and adrenal crisis. Prompt CT diagnosis and timely treatment are crucial for improved outcomes, emphasizing the need to consider autoimmune disorders in atypical cases.

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REFERENCES

1. Cervera, R., Piette, J.-C., Font, J., Khamashta, M.A., Shoenfeld, Y., Camps, M.T., Jacobsen, S., Lakos, G., Tincani, A., Kontopoulou-Griva, I., Galeazzi, M., Meroni, P.L., Derksen, R.H.W.M., de Groot, P.G., Gromnica-Ihle, E., Baleva, M., Mosca, M., Bombardieri, S., Houssiau, F., Gris, J.-C., Quéré, I., Hachulla, E., Vasconcelos, C., Roch, B., Fernández-Nebro, A., Boffa, M.-C., Hughes, G.R.V. and Ingelmo, M. (2002), Antiphospholipid syndrome: Clinical and immunologic manifestations and patterns of disease expression in a cohort of 1,000 patients. Arthritis & Rheumatism, 46: 1019-1027. doi: 10.1002/art.10187
2. Walz B, Ho Ping Kong H, Silver R. Adrenal failure and the primary antiphospholipid syndrome. The Journal of Rheumatology. 1990 Jun;17(6):836-837. PMID: 2388207.
3. Espinosa G, Santos E, Cervera R, Piette JC, de la Red G, Gil V, Font J, Couch R, Ingelmo M, Asherson RA. Adrenal involvement in the antiphospholipid syndrome: clinical and immunologic characteristics of 86 patients. Medicine. 2003 Mar 1;82(2):106-18. doi: 10.1097/00005792-200303000-00005.
4. Vella A, Nippoldt TB, Morris JC 3rd. Adrenal hemorrhage: a 25-year experience at the Mayo Clinic. Mayo Clin Proc. 2001;76:161-168. doi: 10.4065/76.2.161.
5. Aldaajani, H., Albahrani, S., Saleh, K., & Alghanim, K. (2018). Bilateral adrenal hemorrhage in antiphospholipid syndrome. Anticoagulation for the treatment of hemorrhage. *Saudi medical journal,* 39(8), 829–833. doi: 10.15537/smj.2018.8.22437