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Case Report

Unilateral Non-Haemorrhagic Adrenal Infarction in a Non-Pregnant Female with Antithrombin III Deficiency

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Abstract

A white non-pregnant female in her late 20s presented with a few hour history of new onset left sided abdominal pain, nausea and vomiting to the emergency department. On examination, she was haemodynamically stable and her abdomen was soft, with tenderness and guarding in the epigastrium, left upper quadrant and left flank. Initial investigations revealed an elevated white cell count and lactate, and mildly elevated C-reactive protein. Initial CT imaging revealed adrenal pathology, which was confirmed to be unilateral non-haemorrhagic acute left sided adrenal infarction through further CT and MRI scans. Antithrombin III deficiency was identified to be the precipitating cause, and thus the patient was started on lifelong warfarin. To our knowledge there is no literature describing unilateral non-haemorrhagic adrenal infarction (NHAI) in a non- pregnant female, or NHAI secondary to antithrombin III deficiency was found, making this case unique in its presentation.

Keywords: *Antithrombin III Deficiency; Non-Haemorrhagic Adrenal Infarction (NHAI); Non-Pregnant Female*

Case Presentation

A white non-pregnant female in her late 20s presented with a few hours history of new onset left sided abdominal pain. The pain was initially in the epigastric region which then started to radiate to the left upper quadrant and flank down to the left groin. This was associated with nausea, multiple episodes of vomiting and chills and rigours on the day of presentation. The patient also reported multiple episodes of diarrhoea the day before, and having had an asymptomatic urinary tract infection 3 weeks prior, which was untreated. She denied documented fever, dysuria, urinary frequency, gross haematuria and trauma.

The patient was a known case of hypertension on amlodipine. She had no past surgical history or relevant family history. She denied previous thromboembolic events. The patient was a non- smoker and denied alcohol and illicit drug misuse. She reported weight gain of 10 kg over 1 year.

On physical examination the patient appeared to be in pain and unable to find a comfortable position. Her abdomen was obese, soft, with tenderness and guarding in the epigastrium, left upper quadrant and left flank. The renal punches were negative bilaterally. Her blood pressure was 161/89 mmHg, pulse 81 bpm, respiratory rate 16 breaths/min, oxygen saturation 98% on room air, and temperature of 36.6°C.

Initially the patient was administered analgesia, fluid hydration, anti-emetics and an anti- spasmodic.

Once initial CT imaging investigations revealed left adrenal pathology, with a differential of necrosis, infection or haemorrhage, she was admitted, and treated with co-amoxiclav, analgesia and IV fluids. The patient remained haemodynamically stable.

MR imaging done whilst the patient was in hospital confirmed a diagnosis of unilateral non- haemorrhagic acute left sided adrenal infarction. Further investigations revealed that this was not precipitating an Addisonian crisis and the cause to be antithrombin III deficiency.

The patient was discharged home after 7 days.

Investigations

Initial investigations

Blood investigations

These showed an elevated white cell count of 19.8 x 10^9, platelet count of 454 x 10^9, c-reactive protein of 19.6 mg/L, normal renal profile, APTT Ratio of 1.0, and INR of 1.09. Venous blood gas showed an elevated of Lactate 5.1 and was otherwise normal.

Urinalysis

This revealed a pH of 5, with negative white blood cells, negative nitrites and erythrocytes of 10 uL.

HIT test

This was negative for pregnancy.

Imaging

- CT KUB was the primary imaging done on the day of presentation, which showed no urinary tract calculi and normal bilateral kidneys, however revealed a swollen upper pole of the left kidney, with fat stranding around the upper pole of left kidney, in anterior pararenal space and around the left adrenal gland which were reported as possibly due to infection or a vascular insult.
- CT abdomen and pelvis with contrast (Image 1) was done in view of the CT KUB findings which showed a swollen, enlarged and hypodense left adrenal gland associated with reactive perinephric and Gerota's fascia fat stranding. Acute left adrenal gland necrosis was suspected however infection or haemorrhage was included in the differential diagnosis.
- MR Adrenals (Image 2) was performed two days after presentation. It showed an oedematous left adrenal gland which showed no enhancement, with peripheral reactive changes seen around it with late peri-adrenal enhancement following administration of contrast. The right adrenal gland showed a normal appearance. This was compatible with a unilateral non-haemorrhagic acute left sided adrenal infarction.

Further work up

To identify any adrenal insufficiency

A standard short synacthen test, aldosterone-renin ratio and repeat sodium and potassium levels were taken which were normal, indicating no adrenal insufficiency.

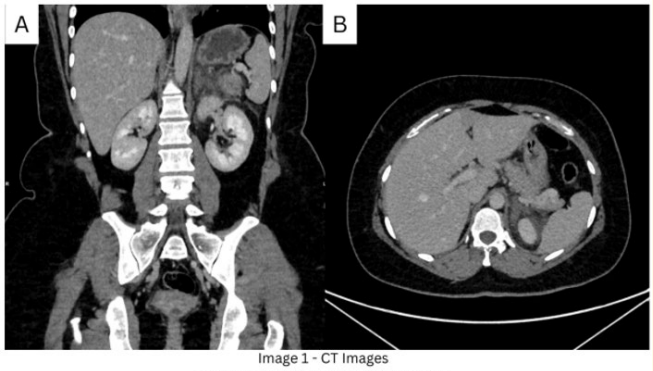

Image 1 - CT Images
A: Coronal Section; B: Sagittal Section

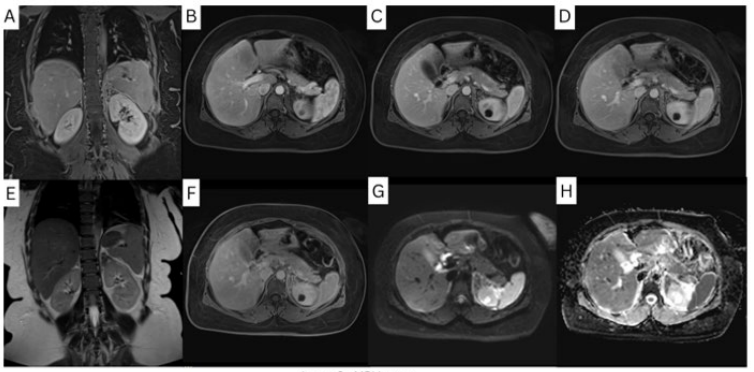

Image 2 - MRI Images
A: T1 Coronal Section ; B: T1 Arterial Phase ; C: T1 Venous Phase; D: T1 Delayed Venous Phase;
E: T2 Coronal Section ; F: T1 Delayed Phase; G: Diffusion Weighted Imaging; H: Apparent Diffusion Coefficiant Map

To identify cause of infarction

The tests described in table 1 were done, identifying the cause to be a severe antithrombin III deficiency.

Test	Result	Range
Thrombophilia Screen		
Prothrombin time	11.00	9.96-11.24 sec
INR	1.04	0.94-1.06 ratio
APTT (sec)	26.0	19.26-25.59 sec
APTT Ratio	1.09	0.86-1.14 ratio
Actin FSL/APTT Ratio	1.09	>1.23 ratio
Lupus Inhibitor Screen	0.93	>1.05 ratio
Antithrombin III Activity	48.0	84.3-138.5%
Protein C Activity	100.1	74.3-137.1%
Protein S Activity	83.2	44.8-105.4%
Protein S Free Antigen	65.9	75.2- 138.8%

Genetic Screen		
JAK -2 V617F	No mutation	
Factor V Leiden Screen	No mutation	
FII gene mutation G20210A	No mutation	
Antibody Screen		
Anti B2 glycoprotein (IgG)	<2.0	0.0-19.9 RU/ml
Anti B2 glycoprotein (IgM)	3.1	0.0-19.9 RU/ml
Anti-cardiolipin (IgG)	2.1	0.0-11.9 U/ml
Anti-cardiolipin (IgM)	2.5	0.0-11.9 U/ml

Table 1

Differential diagnosis

The initial top differential diagnoses were renal colic and pyelonephritis. Other less likely differentials which were considered included pancreatitis, splenic pathology, gastroenteritis, mesenteric ischaemia or infarction and diverticulitis.

In view of the presenting signs and symptoms, patient age and sex, and top differentials a CT KUB was the imaging of choice. The findings indicated a possible infective or vascular cause; therefore, these then became the top differential diagnoses.

The follow up CT abdomen and pelvis with contrast showed adrenal pathology with a differential of adrenal necrosis, infection or haemorrhage. Adrenal infarction was confirmed with MR imaging.

Treatment

Admission and management of symptoms

The patient was initially managed through hospital admission, during which she was administered co-amoxiclav due to the initial differential diagnoses including an infective cause, anti-emetics due to the presence of nausea and vomiting, intravenous fluids to supplement fluid losses, anti-hypertensive medications including doxazocin to manage uncontrolled blood pressure.

Specific treatment for antithrombin III deficiency

Once the cause for adrenal infarction was identified as thrombus formation secondary to antithrombin III deficiency, lifelong anticoagulation was required to prevent future thrombosis. The agent of choice was warfarin which was dosed according to local guidelines to achieve a target INR range of 2-3.

Outcome and follow-up

After discharge, the patient was followed up at Haematology and Endocrinology outpatients with appointments at 3 months, 6 months, and 1.5 years. A repeat CT abdomen and pelvis was done at 6 months which demonstrated no adrenal pathology bilaterally. The patient initially complained of left sided abdominal discomfort which resolved after 6 months. The patient was advised life-long Warfarin treatment.

Discussion

The adrenal glands play a crucial role in producing hormones such as cortisol, aldosterone, and adrenaline, which are essential for regulating various physiological processes, including metabolism, electrolyte balance, and stress response. Adrenal infarction is the

interruption of blood supply to the adrenal gland can disrupt hormone production, leading to adrenal insufficiency or other endocrine abnormalities.

Adrenal infarction can be either unilateral or bilateral and either haemorrhagic or non- haemorrhagic. It is usually a bilateral disorder most often associated with haemorrhage, with the most common risk factors being antiphospholipid syndrome or haemodynamic variation. Non-haemorrhagic adrenal infarction is a rare event. Furthermore, unilateral non-haemorrhagic adrenal infarction is even less common [1].

A literature search for unilateral non-haemorrhagic adrenal infarction (NHAI) was done. Only a few cases have been described and those that have are in pregnant females [1-21]. Only one case describing a unilateral non-haemorrhagic adrenal infarction was found however it was in a male with polycythaemia vera [21]. No literature describing unilateral non-haemorrhagic adrenal infarction (NHAI) in a non-pregnant female or NHAI secondary to antithrombin III deficiency was found, making this case unique in its presentation.

The aetiology of unilateral non haemorrhagic adrenal infarction can vary, but it is often associated with conditions that affect blood flow to the adrenal gland, such as thromboembolism, vasculitis, or arterial thrombosis. Other predisposing factors may include trauma, surgery, coagulation disorders, pregnancy or underlying systemic diseases [22-24]. When unilateral, adrenal infarct more commonly occurs in the right gland, due to a short, direct venous drainage into the inferior vein cava, which favours venous stasis and thrombosis [25]. While less common than bilateral adrenal infarction or adrenal haemorrhage, it is still a significant clinical entity that warrants attention due to its potential impact on adrenal function and overall health [1].

Clinically, patients with unilateral non-haemorrhagic adrenal infarct may present with nonspecific symptoms such as abdominal or flank pain, fatigue, weakness, nausea, or vomiting. These symptoms can mimic other conditions, making diagnosis challenging [3]. Imaging studies, such as computed tomography (CT) or magnetic resonance imaging (MRI), are often used to confirm the diagnosis by revealing characteristic findings, such as focal gland enlargement with decreased enhancement due to ischemia [23].

Management of unilateral non-haemorrhagic adrenal infarct typically involves addressing the underlying cause, if identified, and providing supportive care. In cases of adrenal insufficiency, hormone replacement therapy may be necessary to restore hormonal balance and alleviate symptoms. Close monitoring of adrenal function and regular follow-up are crucial to assess response to treatment and prevent complications [4].

Further research is needed to better understand the pathophysiology, risk factors, and optimal management strategies for unilateral non-haemorrhagic adrenal infarct, particularly in light of its rarity and potential consequences for affected individuals. Collaboration among clinicians, radiologists, and researchers is essential to improve diagnosis, treatment, and outcomes for this condition.

Learning Points/Take Home Messages

- Unilateral non-haemorrhagic adrenal infarction is a rare condition with severe potential consequences on adrenal function and overall health
- Clinical signs are not specific and may mimic other more common conditions and therefore should be included in the differential diagnosis of abdominal pain
- Definite diagnosis can only be made by focused adrenal imagining using CT or MRI
- Unilateral non-haemorrhagic adrenal infarction can occur in both pregnant and non- pregnant individuals.
- Patients identified with unilateral non-haemorrhagic adrenal infarction should be worked up to identify the cause including a thrombophilia screen and consideration of anticoagulation treatment.

Bibliography

1. Jerbaka M., *et al*. "Left Flank Pain During Pregnancy With an Unpredictable Etiology: Think of Nonhemorrhagic Adrenal Infarction". *Future Science OA* 7.8 (2021): FSO718.

2. Junghans E. "Hemorrhagic infarct of the adrenal glands and symmetrical necrosis of the adrenal cortex in pregnancy". *Zeitschrift für Geburtshilfe und Gynäkologie* 151.2 (1958): 200-219.

3. Guruli M and Kantorovich V. "Adrenal Infarct as a Presenting Finding in Polycythemia Vera (PV)". *Journal of the Endocrine Society* 5.1 (2021): A109.

4. Green P-AD., *et al*. "Unilateral adrenal infarction in pregnancy". *BMJ Case Reports* (2013): bcr2013009997.

5. Hynes D., *et al*. "Nonhemorrhagic adrenal infarction in pregnancy: magnetic resonance imaging and computed tomography evaluation". *Journal of Computer Assisted Tomography* 43.6 (2019): 884-886.

6. Ryan MF., *et al*. "MRI diagnosis of bilateral adrenal vein thrombosis". *British Journal of Radiology* 76.908 (2003): 566-569.

7. Agarwal KA and Soe MH. "Cryptogenic adrenal infarction: a rare case of unilateral adrenal infarction in a pregnant woman". *BMJ Case Reports* 12.3 (2019): e228795.

8. Reichman O., *et al*. "Non-hemorrhagic adrenal infarct in pregnancy-a rare clinical condition diagnosed by non-contrast magnetic resonance image". *European Journal of Obstetrics and Gynecology and Reproductive Biology* 198 (2016): 173-174.

9. Lamba A. "And you thought hormones were the problem in pregnancy". *Journal of the Louisiana State Medical Society: Official Organ of the Louisiana State Medical Society* 167.3 (2015): 151.

10. Yuen KCJ., *et al*. "Adrenal insufficiency in pregnancy: challenging issues in diagnosis and management". *Endocrine* 44.2 (2013): 283-292.

11. Molière S., *et al*. "Usefulness of diffusion-weighted imaging for diagnosis of adrenal ischemia during pregnancy: a preliminary report". *Emergency Radiology* 24.6 (2017): 705-708.

12. Aljenaee KY., *et al*. "Unilateral adrenal infarction in pregnancy secondary to elevated factor VIII". *Saudi Medical Journal* 38.6 (2017): 654.

13. Chasseloup F., *et al*. "Unilateral nonhaemorrhagic adrenal infarction as a cause of abdominal pain during pregnancy". *Gynecological Endocrinology* 35.11 (2019): 941-944.

14. Shah N., *et al*. "Unilateral adrenal infarction in pregnancy with associated acute hypoadrenalism and subsequent spontaneous biochemical and radiological resolution". *Clinical Case Reports* 10.2 (2022): e05442.

15. Weyrich P., *et al*. "Acute adrenocortical insufficiency due to heparin-induced thrombocytopenia with subsequent bilateral haemorrhagic infarction of the adrenal glands". *VASA. Zeitschrift für Gefässkrankheiten* 30.4 (2001): 285-288.

16. Riddell AM and Khalili K. "Sequential adrenal infarction without MRI-detectable hemorrhage in primary antiphospholipid-antibody syndrome". *American Journal of Roentgenology* 183.1 (2004): 220-222.

17. Cunningham TK., *et al*. "Adrenal infarction in the immediate postnatal period". *Journal of Obstetrics and Gynaecology* 39.3 (2019): 410-411.

18. Cesmebasi A., *et al*. "A review of the anatomy and clinical significance of adrenal veins". *Clinical Anatomy* 27.8 (2014): 1253-1263.

19. Warda F., *et al*. "Acute Unilateral Nonhemorrhagic Adrenal Infarction in Pregnancy". *AACE Clinical Case Reports* 7.3 (2021): 228-229.

20. Muhammad ZUH., *et al*. "Unilateral nonhemorrhagic adrenal infarction presenting as acute abdomen in a pregnant woman". *Endocrine Abstracts* 94 (2023): P310.

21. Ornaghi S., *et al*. "Acute spontaneous non-hemorrhagic adrenal infarction in pregnancy: case-report and literature review". *Gynecological Endocrinology* 39.1 (2023): 2234492.

22. Sormunen-Harju H., *et al*. "Adrenal infarction in a healthy pregnant woman". *Obstetric Medicine* 9.2 (2016): 90-92.

23. Guenette JP and Tatli S. "Nonhemorrhagic adrenal infarction with magnetic resonance imaging features during pregnancy". *Obstetrics and Gynecology* 126.4 (2015): 775-778.

24. Chagué P., *et al*. "Non-hemorrhagic adrenal infarction during pregnancy: the diagnostic imaging keys". *Tomography* 7.4 (2021): 533-544.

25. Mathew R., *et al*. "Adrenal infarction in pregnancy secondary to elevated plasma factor VIII activity". *Cureus* 13.11 (2021): e19491.

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