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Inflammation and infection

Primary bilateral adrenal tuberculosis with Addison's disease: A case report

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A B S T R A C T

Primary adrenal tuberculosis is an extremely rare benign lesion that typically presents with no clinical symptoms in its early stages, making it prone to clinical misdiagnosis. We report a case of a middle-aged man initially thought to have adrenal nodules, which further examination revealed to be adrenal tuberculosis accompanied by Addison's disease. This report discusses the diagnostic approach, progressive features, and treatment options for this rare disease.

1. Introduction

Adrenal tuberculosis is a rare clinical condition. Extra-adrenal tuberculosis is present in 94.7 % of patients diagnosed with adrenal tuberculosis, while only 5.3 % of patients have primary adrenal tuberculosis, which lacks extra-adrenal lesions.[1] In its early stages, adrenal tuberculosis typically presents with no clear symptoms and is often detected incidentally during routine physical examinations or the diagnosis of other conditions, leading to frequent clinical misdiagnosis. Notably, adrenal tuberculosis is the second cause of primary adrenocortical insufficiency, also known as Addison's disease (AD).[2] However, due to its extremely low incidence, no consistent clinical treatment standards have been established.

2. Case presentation

In September 2023, a 45-year-old male patient presented to our hospital with a 5-month history of bilateral adrenal masses. In April 2023, the patient visited another hospital due to experiencing left lumbar and back pain. During a CT scan, bilateral adrenal masses were detected. However, further treatment was not pursued for reasons related to the patient. Five months later, the patient sought medical attention in our department with a desire to address this situation. The patient did not report any abdominal pain, bloating, poor appetite, nausea, or vomiting upon admission. He had no history of tuberculosis symptoms and denied any history of tuberculosis or contact with individuals affected by it. Physical examination revealed sparse body hair, pigmentation of the skin, lips, and mucous membranes, but no notable findings in the abdomen. His vital signs were as follows: temperature 36.4 °C, pulse 76 beats per minute, blood pressure 111/82 mmHg, and respiration 19 breaths per minute. Upon admission, the patient's adrenocorticotropic hormone (ACTH) level was significantly elevated at 2035.69pg/ml (Normal range: 7.2–63.4pg/ml), while the cortisol hormone level was notably reduced to 1.84 μg/dl (8:00 *a.m.*). The interleukin-6 (IL-6) was mildly elevated at 8.26pg/ml. The tuberculosis infection T cell spot test (T-SPOT) returned positive. The erythrocyte sedimentation rate increased to 20 mm/h. Multiple sputum smear acid-fast staining and sputum cultures were negative. Aldosterone, renin, angiotensin II, blood cell analysis, urine routine, metabolic panel, and tumor markers showed no remarkable findings. Further examination revealed no obvious abnormalities in the lungs on chest CT. However, abdominal unenhanced and contrast-enhanced CT indicated that both adrenal glands were enlarged and thickened, with disorganized structures and areas of cystic necrosis (Fig. 1A and B). The CT value of the right adrenal mass was 27HU and that of the left adrenal mass was 36HU on the CT scan. Contrast-enhanced CT imaging showed slow washout (right absolute percentage washout is 11 %, left side is 22 %, right relative percentage washout is 6.4 %, left side is 8.6 %). CT images can not determine whether adrenal tumor or adrenal tuberculosis. Subsequently, an adrenal magnetic resonance imaging (MRI) scan was performed, which showed that both adrenal glands were enlarged and thickened with mixed signals. There were multiple soft tissue masses with restricted diffusion and uneven enhancement. Within the lesions, there were multiple areas of cystic necrosis without enhancement (Fig. 1C and D). The imaging diagnosis was considered to be adrenal tuberculosis. Additionally, electrocardiograms and 24-h ambulatory

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blood pressure monitoring were within normal limits, revealing no significant abnormalities.

Based on the patient's medical history, physical examination, and auxiliary examinations, primary bilateral adrenal tuberculosis with AD was considered. Considering the patient's condition, an anti-tuberculosis treatment regimen comprising isoniazid, rifampicin, pyrazinamide, and ethambutol was initiated. Isoniazid 0.3g/day + rifampicin 0.5g/day + pyrazinamide 1.5g/day for two months in the strengthening stage, isoniazid 0.3g/day + rifampicin 0.45g/day for six months in the consolidation stage. Due to the fact that rifampicin accelerates the metabolism of steroid hormones leading to insufficient steroid hormone blood levels, the dosage of hydrocortisone tablets was increased to 50mg per day, administered in two divided oral doses in the morning and evening. No adrenal crisis occurred during treatment. After two months of treatment, the patient's symptoms were alleviated, and all indicators approached normality: ACTH of 667.75pg/ml, the cortisol hormone of 3.85 μg/dl, IL-6 of 7.16pg/ml, T-SPOT showed a weak positive result, the erythrocyte sedimentation rate of 16 mm/h, and liver and kidney functions were essentially normal. After six months of consolidation treatment, the patient's body hair was denser than before, and the pigmentation of the skin, lips, and oral mucosa had subsided. All indicators were normal: ACTH of 75.67pg/ml, the cortisol hormone of 14.56 μg/dl, IL-6 of 4.05pg/ml, T-SPOT was negative, the erythrocyte sedimentation rate of 10mm/h. Abdominal CT revealed that the bilateral adrenal glands were slightly thickened, the relevant lesions had been absorbed, the soft tissue shadow was significantly smaller than previously, and no obvious calcification spots were detectable (Fig. 1E and F). No hormone replacement therapy is currently being administered and the patient is being followed up.

3. Discussion

Tuberculosis of the adrenal glands was first discovered in 1855 by Thomas Addison through an autopsy.[3] Patients with unilateral adrenal tuberculosis often have no obvious symptoms and occasionally present with low back pain on the affected side. In bilateral adrenal tuberculosis, the adrenal structures are typically destroyed, leading to insufficient secretion of adrenal cortical hormones and resulting in AD. When more than 90 % of the adrenal glands are severely compromised, the patient may exhibit signs and symptoms of AD.[1] Typical clinical symptoms of AD include fatigue, loss of body mass, loss of appetite, a high-sodium diet, nausea, vomiting, diarrhea, or recurrent abdominal pain, and most patients have hypotension and postural vertigo. In addition, almost all AD patients will have skin and/or mucosal pigmentation, but the degree of pigmentation varies. Primary adrenal tuberculosis complicating AD in cases such as this one is relatively rare.

Laboratory tests for adrenal tuberculosis include adrenal function and indicators of tuberculosis. Adrenal function parameters include ACTH, plasma renin, aldosterone (standing and lying down), plasma cortisol, electrolytes, and catecholamine levels. Indicators related to tuberculosis include tuberculin test, blood sedimentation and TSPOT.[4] For imaging, CT is superior to color ultrasound, and adrenal tuberculosis is more clearly visualized on CT, especially with regard to the identification of calcified spots.[5] A CT-guided aspiration biopsy of the adrenal gland can be performed to confirm the diagnosis.[6] At present, there is no uniform diagnostic standard for adrenal gland tuberculosis, and it is usually analyzed according to the patient's medical history, clinical manifestations, relevant laboratory tests and imaging changes for reference, and the misdiagnosis rate is high. If adrenal tuberculosis is highly suspected, anti-tuberculosis and hormone therapy can be given for 6–18 months with regular observation. The adrenal glands have a strong regenerative capacity and generally offer a good prognosis. However, if adrenal cortical function does not improve, it may be due to irreversible damage caused by tuberculosis.[7] Surgery may be recommended to clarify the diagnosis in patients with adrenal nodules >2 cm in diameter that do not heal easily if they cannot be differentiated from tumors.[1]

The main methods of treatment for adrenal tuberculosis are pharmacologic therapy and surgical intervention. Pharmacologic therapy mainly includes early, regular, full, moderate, combined antituberculosis and long-term hormone replacement therapy.[8] In patients undergoing surgery, perioperative hormone replacement therapy can prevent

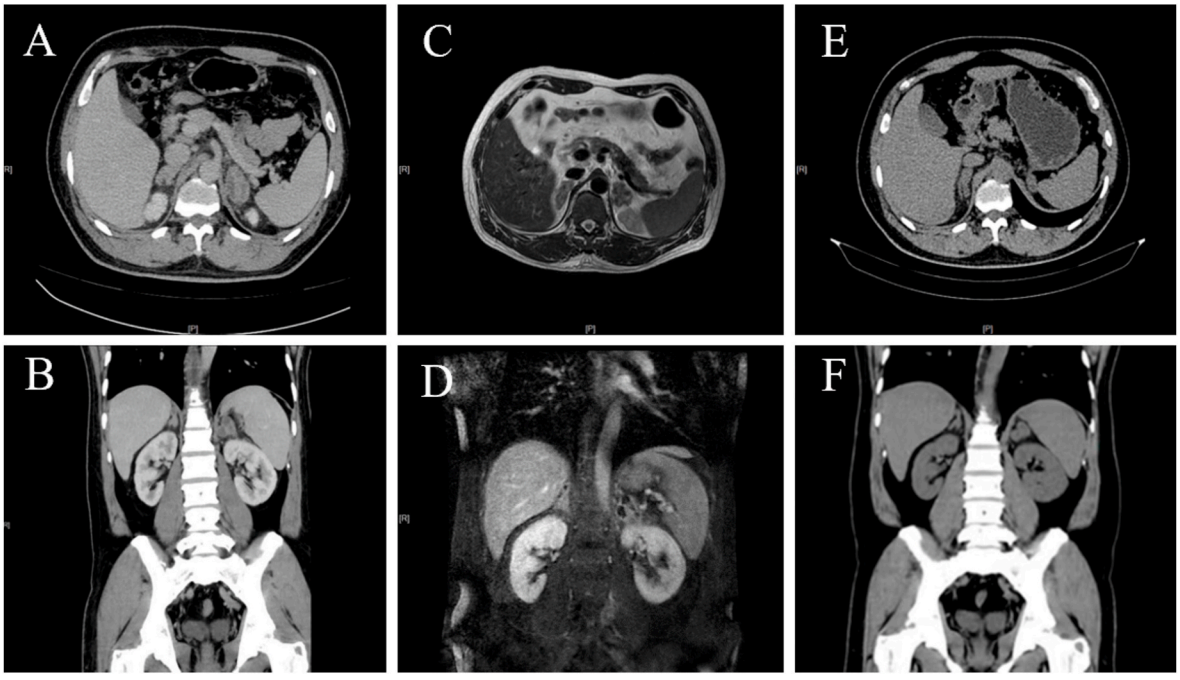

Fig. 1. Imaging findings of primary adrenal tuberculosis with Addison's disease before and after treatment. A-B) CT indicated that the adrenal glands on both sides were enlarged and thickened, with disorganized structure and cystic necrosis in part of the tissue. C-D) MRI revealed bilateral adrenal gland enlargement and thickening, with multiple soft tissue masses and areas of cystic necrosis. E-F) CT revealed that the bilateral adrenal glands were slightly thickened, the relevant lesions had been absorbed, the soft tissue shadow was significantly smaller than previously.

adrenal crisis, and then the dosage should be reduced and gradually changed to oral administration. Although adrenal tuberculosis is a benign lesion, it should be closely monitored and treated with regular anti-tuberculosis therapy after surgery. Follow-up of patients with adrenal tuberculosis includes enhanced CT of the chest and whole abdomen, and close monitoring of blood pressure, heart rate, ACTH, plasma renin, aldosterone (standing and lying down), plasma cortisol, blood sedimentation, electrolytes, and catecholamine levels. For the patient, after 2 months of treatment, the patient's skin symptoms improved, and follow-up tests showed near normal results.

4. Conclusion

Diagnosing primary adrenal tuberculosis is challenging because of its rarity and overlapping symptoms with adrenal tumors. It should be done to combine the patient's medical history and auxiliary examination and other relevant indicators to make a comprehensive judgment, especially through imaging to identify, if necessary, puncture biopsy to clarify the diagnosis, to avoid misdiagnosis and reduce the burden on patients. During treatment, vigilance for adrenal crisis and early steroid hormone replacement therapy are required.

Conflicts of interest

The authors declare no conflict of interest.

CRediT authorship contribution statement

Yu Huang: Writing – original draft. **Yawei Zhang:** Writing – original draft. **Haifeng Wang:** Writing – review & editing. **Nan Zhang:** Writing – review & editing.

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