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CASE REPORT

Primary Adrenal Tuberculosis Causing Adrenal Insufficiency

VV Maller, MO Afzal, S Shankar

Department of Radiology, University of Tennessee Health Science Center, Memphis, Tennessee 38163, USA

ABSTRACT

Addison's disease with bilateral adrenal enlargement can be due to infectious or non-infectious causes. The imaging characteristics of adrenal tuberculosis vary with the duration of Addison's disease and should be differentiated from other causes of bilateral adrenal enlargement. Imaging in tuberculous Addison's disease usually demonstrates bilateral enlarged adrenal glands with calcifications and peripheral enlargement although in later stages the adrenal gland becomes atrophic and calcified. We present a case report of a middle-aged male with histopathologically proven tuberculosis with Addison's disease.

Key Words: *Addison disease; Granuloma; Tuberculosis*

中文摘要

原發性腎上腺結核引致腎上腺功能不全

VV Maller, MO Afzal, S Shankar

阿狄森氏病（Addison's disease）併發雙側腎上腺增大可能是由於感染性或非感染性的病因。腎上腺結核的成像特性隨阿狄森氏病的持續時間而改變，並且應該從雙側腎上腺腫大的其他原因分辨出來。阿狄森氏病結核病的成像一般顯示兩側增大腎上腺鈣化和外圍增大，後期腎上腺變得萎縮並鈣化。本文報告一名患有阿狄森氏病的中年男性患者，病理證實為結核。

CASE REPORT

A 43-year-old male presented with a history of fatigue and left-sided weakness in September 2014. Blood tests revealed low cortisol, elevated adrenocorticotropic hormone and hypokalemia suggestive of primary adrenal insufficiency. The Quanti FERON (Quest Diagnostics, Madison [NJ], USA) gold test for tuberculosis (TB) was positive. Subsequently computed tomography (CT) of chest, abdomen, and pelvis was performed. Contrast-enhanced chest CT did not reveal any signs of active TB. There were a few calcified mediastinal and hilar lymph nodes presumed to be from prior granulomatous disease. Contrast-enhanced CT of the abdomen and pelvis revealed bilateral enlarged adrenal glands with calcifications and heterogeneous enhancement (Figure 1).

Correspondence: *Dr Vijetha Vinod Maller, Department of Radiology, University of Tennessee Health Science Center, 865 Jefferson Avenue, F150, Memphis, Tennessee 38163, USA.*
Email: vijethamaller@gmail.com

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Magnetic resonance imaging (MRI) of the abdomen subsequently revealed bilateral enlarged adrenal glands. The enlarged adrenal glands were isointense on T1-weighted images, and heterogeneously hypointense on T2-weighted images. No loss of signal was seen on out-of-phase imaging. On post-contrast images the enlarged adrenal glands showed peripheral enhancement. The imaging findings favoured adrenal TB (Figure 2).

Adrenal biopsy was performed with the patient in a prone position and from a posterior approach under CT guidance. The biopsy revealed caseating granulomas confirming the diagnosis of adrenal TB.

DISCUSSION

Thomas Addison first described adrenal insufficiency, also known as Addison's disease, in 1855 in patients with adrenal TB.[1] Although adrenal TB is rare, it is the most commonly affected endocrine gland. Patients can present with insidious onset of symptoms or may present with adrenal crisis. Clinical manifestations of tuberculous Addison's disease are seen when 90% of the adrenal gland are destroyed.[2] The most common clinical manifestations are weakness, anorexia, nausea, vomiting, and are often non-specific resulting in delayed diagnosis.[2-4]

Although autoimmune adrenalitis is the most common cause of Addison's disease, accounting for 80% of cases, in which the adrenal glands appear small,[5,6] TB accounts for 10% to 15% of Addison's disease.[7] Bilateral adrenal gland enlargement with Addison's disease strongly suggests infective aetiology as other causes such as primary adrenal tumours, metastatic carcinoma, or haemorrhage are rare.[4,7,8] TB is the most common cause of bilateral adrenal gland enlargement in Addison's disease in developing countries.[9] In developed countries such as the United States, adrenal TB is relatively rare. Histoplasmosis should also be considered a strong differential for bilateral enlarged adrenal glands with calcifications as the disease is endemic in south and central parts of North America.[10,11] Rarer causes of Addison's disease with infectious adrenal enlargement include blastomycosis and various human immunodeficiency–related infections.[8,12]

Adrenal TB usually causes bilateral involvement due to the haematogenous route of spread.[2,7] A study by Wang et al[13] showed that all patients with tuberculous Addison's disease had bilateral adrenal involvement. Guo et al[7] indicated that 91% of patients with tuberculous Addison's disease had bilateral adrenal gland involvement.

A study by Nomura et al[14] revealed that 93% of the patients with adrenal TB had previous extra-adrenal TB and the mean period from previous non-adrenal TB to adrenal TB was 31.9 years. Alevritis et al[15] observed that most cases of adrenal TB were found 10 to 15 years after the initial infection. In the present case, contrast-

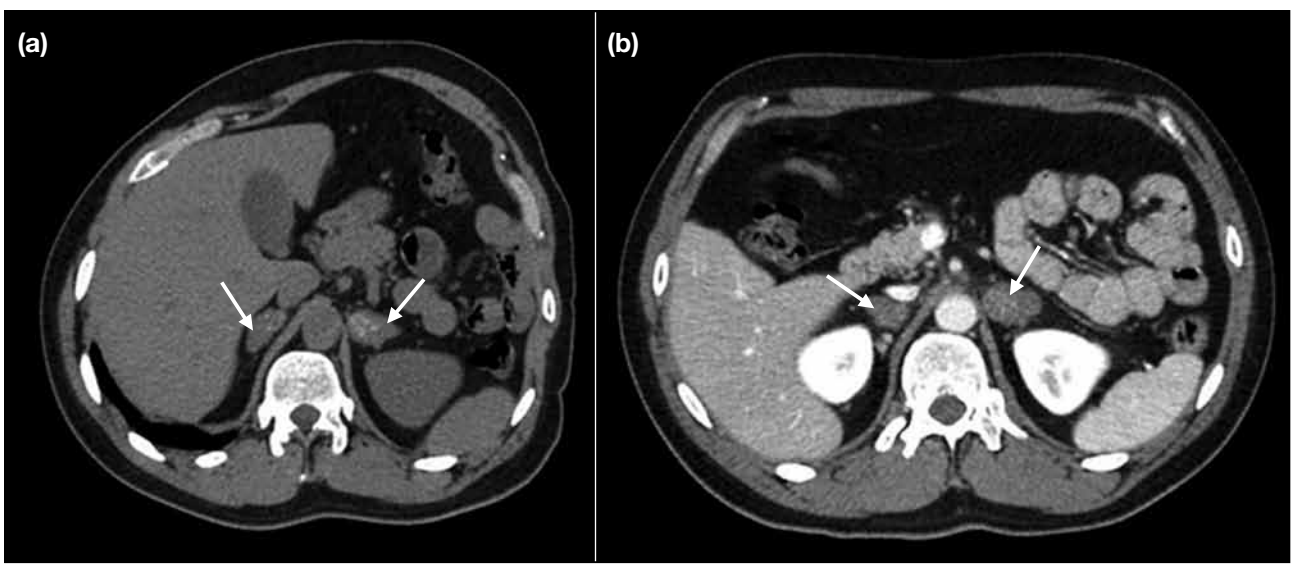

Figure 1. (a) Axial non-contrast computed tomography (CT) shows bilateral enlarged adrenal glands with calcifications (arrows). (b) Axial contrast-enhanced CT shows bilateral enlarged adrenal glands with subtle peripheral enhancement (arrows).

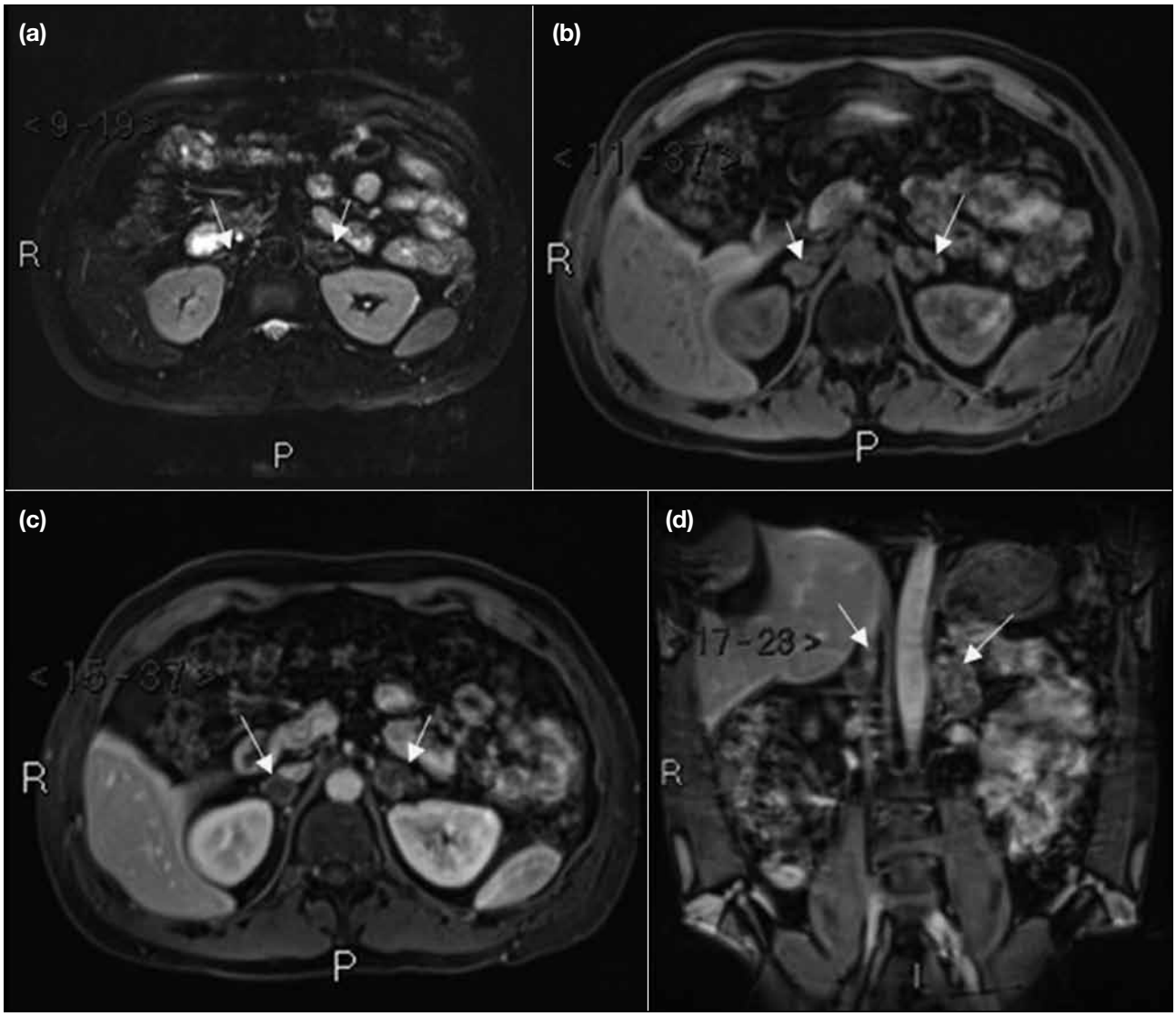

Figure 2. (a) Axial T2-weighted fat-suppressed image shows bilateral enlarged adrenal glands which appears heterogeneously hypointense (arrows). (b) Axial T1-weighted fat-suppressed non-contrast image shows isointense bilateral enlarged adrenal glands (arrows). (c) Axial contrast-enhanced T1-weighted fat-suppressed image and (d) coronal contrast-enhanced T1-weighted fat-suppressed image demonstrate peripheral enhancement of the bilateral enlarged adrenal glands (arrows).

enhanced chest CT revealed some calcified mediastinal and hilar lymph nodes raising the possibility of prior pulmonary TB.

The typical imaging features of adrenal TB on CT are enlarged adrenal glands, calcifications with central low attenuation, and peripheral enhancement.[7,16-18] The imaging appearance in tuberculous Addison's disease varies with the duration of the disease. In the early stages, within 1 year of manifestation of Addison's disease, histopathology usually reveals granuloma with caseous necrosis due to the destruction of the adrenal cortex with CT revealing mass-like enlargement of the adrenals. When the duration of Addison's disease is more than 1 year, there is regression of the mass-like enlargement with return of the contour towards normal.[7,18] Ultimately, the adrenal glands become atrophic and calcified. In a study conducted by Guo et al[7] of 42 patients, 75% of the patients with Addison's disease of less than 1-year duration had mass-like enlargement of the adrenals and 73% of those with duration of Addison's disease of more than 1 year had enlarged adrenals with preserved contour. It is important to differentiate adrenal TB from primary

adrenal tumours. A study conducted by Yang et al[17] of 34 patients with adrenal TB and 74 patients with primary adrenal tumours revealed that 91% of cases of adrenal TB had bilateral adrenal involvement while only 9% of the primary adrenal tumours had bilateral adrenal involvement. They also found that calcifications, low-attenuation centre, and peripheral enhancement were more commonly found in TB with 91% specificity for contour preservation in adrenal TB.[17] In the present study, although the enlargement of the adrenal glands was mass-like, there were calcifications and peripheral enhancement that were helpful to differentiate from the primary adrenal tumours.

The MRI appearance varies with the pathological changes of adrenal TB. Adrenal granuloma without caseation will appear hyperintense on T2-weighted images. Caseating granulomas without necrosis will appear hypointense and as central necrosis occurs within the caseation, the centre appears hyperintense. On T1-weighted images, the enlarged adrenal glands appear hypointense. Peripheral enhancement is seen when there is central necrosis, otherwise heterogeneous enhancement occurs on post-contrast study. In the end stage, as the gland atrophies and calcifies, the adrenal glands will appear as areas of low signal intensity on T1- and T2-weighted images.[3]

Biopsy of the adrenal glands will result in a definitive diagnosis. Histopathological examination shows granulomatous inflammation with Langhans giant cells with or without caseous necrosis.[7,16,19]

CONCLUSION

In patients who present with primary adrenal insufficiency and imaging that shows bilateral enlarged adrenal glands with calcifications and peripheral enlargement, the possibility of adrenal TB is most likely. Knowledge of radiological manifestations of adrenal TB will help the radiologist make a prompt diagnosis in patients where there is a high index of clinical suspicion and enable early treatment and recovery of adrenal function. The standard blood tests for TB and ultimately histopathological confirmation will help in reaching a definitive diagnosis. Treatment with appropriate steroid therapy should be initiated. Anti-TB therapy should be started in patients with adrenal TB and enlarged adrenal size.

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