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(CASE REPORT)

Acute adrenal insufficiency revealed by pulmonary tuberculosis: A rare association, a case report

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Abstract

Aims: Acute adrenal insufficiency (AAI) is a rare but potentially life-threatening complication of pulmonary tuberculosis (TB). We report a case highlighting the importance of considering this diagnosis in patients with severe TB and unexplained hydro-electrolytic disturbances.

Presentation of Case: A 37-year-old man, chronic smoker (3 pack-years), was admitted for severe deterioration of general condition with recent-onset dyspnea (mMRC stage 3), post-prandial vomiting, major weight loss, anorexia, asthenia, low-grade fever, and night sweats. On examination he was febrile (38 °C), drowsy, tachypneic (26 cycles/min), hypotensive (90/50 mmHg), and hypoxemic (SpO2 70% on room air). Laboratory tests showed hyponatremia (118 mmol/L), hyperkalemia (5.6 mmol/L), and a markedly depressed morning serum cortisol level of 29.5 nmol/L (reference range approximately 138–690 nmol/L), consistent with acute adrenal insufficiency. Chest imaging revealed bilateral macronodular consolidations predominating in the upper and middle lung zones, associated with a "mimosa flower" micronodular pattern and mediastinal lymphadenopathy, together with a positive QuantiFERON-TB test, leading to a clinical diagnosis of pulmonary tuberculosis.

Discussion: AAI complicating TB may result from direct tuberculous destruction of the adrenal cortex or from a functional cortisol response inadequate to the demands of severe infectious stress, further aggravated by rifampicin-induced acceleration of cortisol clearance. Prompt recognition and immediate glucocorticoid replacement are essential to prevent hemodynamic collapse.

Conclusion: Substitutive hydrocortisone therapy combined with standard antituberculous chemotherapy (2RHZE/4RH) led to marked clinical improvement. Clinicians should systematically consider AAI in patients with severe TB presenting with marked general impairment and electrolyte disturbances.

Keywords: Pulmonary tuberculosis; Acute adrenal insufficiency; Addison's disease; Hyponatremia; Hydrocortisone; Case report

1. Introduction

Pulmonary tuberculosis (TB) remains a major public health concern in endemic countries and is responsible for a broad spectrum of respiratory as well as systemic manifestations. Beyond classical pulmonary involvement, tuberculous infection can induce metabolic and endocrine disturbances, particularly in severe or advanced disease. Among these complications, acute adrenal insufficiency (AAI) is rare but potentially fatal. It may result either from tuberculous destruction of the adrenal glands, now an exceptional finding since the introduction of effective antituberculous

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chemotherapy or from a functional impairment of the cortisol response to infectious stress, which is often unmasked by the initiation of rifampicin-containing regimens [1–3]. Because adrenal tuberculosis and TB-related functional AAI are uncommon and their clinical presentation largely overlaps with that of severe sepsis, the diagnosis is frequently delayed, exposing patients to the risk of adrenal crisis and hemodynamic collapse [4,5]. We report a case of AAI revealed concomitantly with pulmonary tuberculosis in a young adult, and discuss the underlying pathophysiological mechanisms and therapeutic implications.

2. Presentation of case

A 37-year-old man, with a smoking history of 3 pack-years and no other relevant medical history, was admitted for major deterioration of his general condition. The clinical picture combined recent-onset dyspnea (mMRC stage 3) with post-prandial vomiting and gastro-esophageal reflux, occurring in a context of major weight loss, anorexia, asthenia, low-grade fever, and night sweats.

On admission, physical examination found a temperature of 38 °C with drowsiness and marked asthenia, tachypnea at 26 cycles/min, arterial hypotension at 90/50 mmHg, and severe hypoxemia with an SpO2 of 70% on room air. The remainder of the physical examination was unremarkable.

Laboratory investigations revealed severe hyponatremia at 118 mmol/L, hyperkalemia at 5.6 mmol/L, and a markedly depressed morning serum cortisol level at 29.5 nmol/L (reference range approximately 138–690 nmol/L), a biochemical pattern consistent with acute adrenal insufficiency. No adrenocorticotropic hormone (ACTH) assay or corticotropin stimulation test was available at the time of the acute presentation, given the need for immediate glucocorticoid replacement in a hemodynamically unstable patient.

Chest computed tomography (Figures 1–3) demonstrated multiple bilateral macronodular consolidations predominating in the upper and middle lung zones, associated with centrilobular and “mimosa flower” micronodules together with a few small, subcentimeter mediastinal lymph nodes (prevascular, paratracheal, and aortopulmonary window regions). This radiological pattern, combined with the clinical presentation and a positive interferon-gamma release assay (QuantiFERON-TB), was highly suggestive of pulmonary tuberculosis, and the diagnosis was established based on the overall clinical and radiological findings.

The patient was managed with substitutive glucocorticoid therapy consisting of an intravenous bolus of hydrocortisone 100 mg followed by 50 mg every 6 hours, together with fluid and electrolyte resuscitation using normal saline, 5% dextrose, and hypertonic (3 g) sodium chloride solutions. Antituberculous chemotherapy was initiated according to the standard regimen (2 months of rifampicin, isoniazid, pyrazinamide, and ethambutol, followed by 4 months of rifampicin and isoniazid; 2RHZE/4RH). This combined management resulted in significant clinical improvement, with hemodynamic and respiratory stabilization and progressive correction of the electrolyte disturbances.

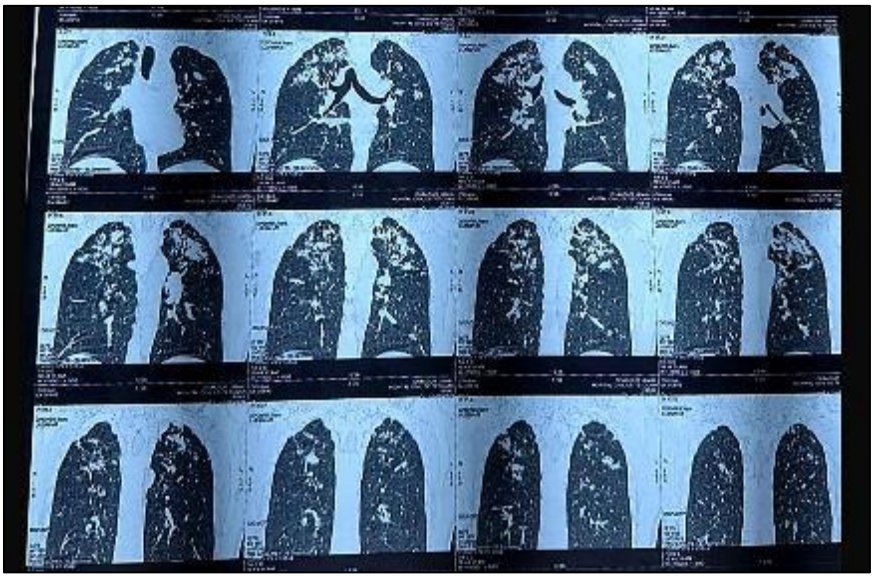

Figure 1 Chest CT scan, multiplanar sagittal reconstruction, showing bilateral macronodular lesions predominating in the upper and middle lung zones.

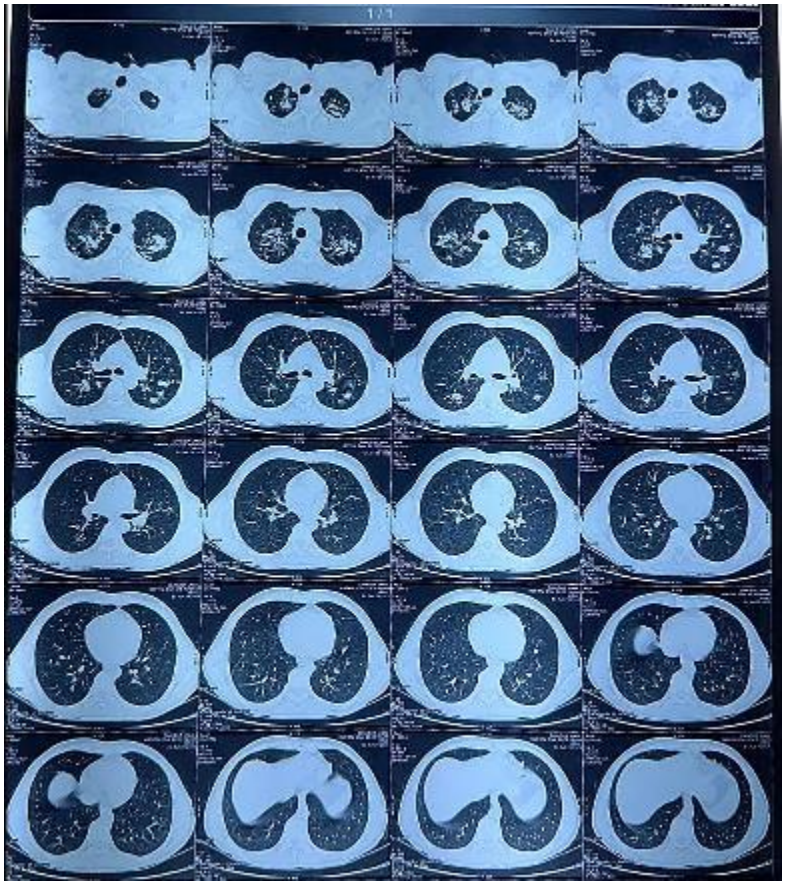

Figure 2 Chest CT scan, axial parenchymal window, showing bilateral macronodular consolidations associated with a "mimosa flower" micronodular pattern.

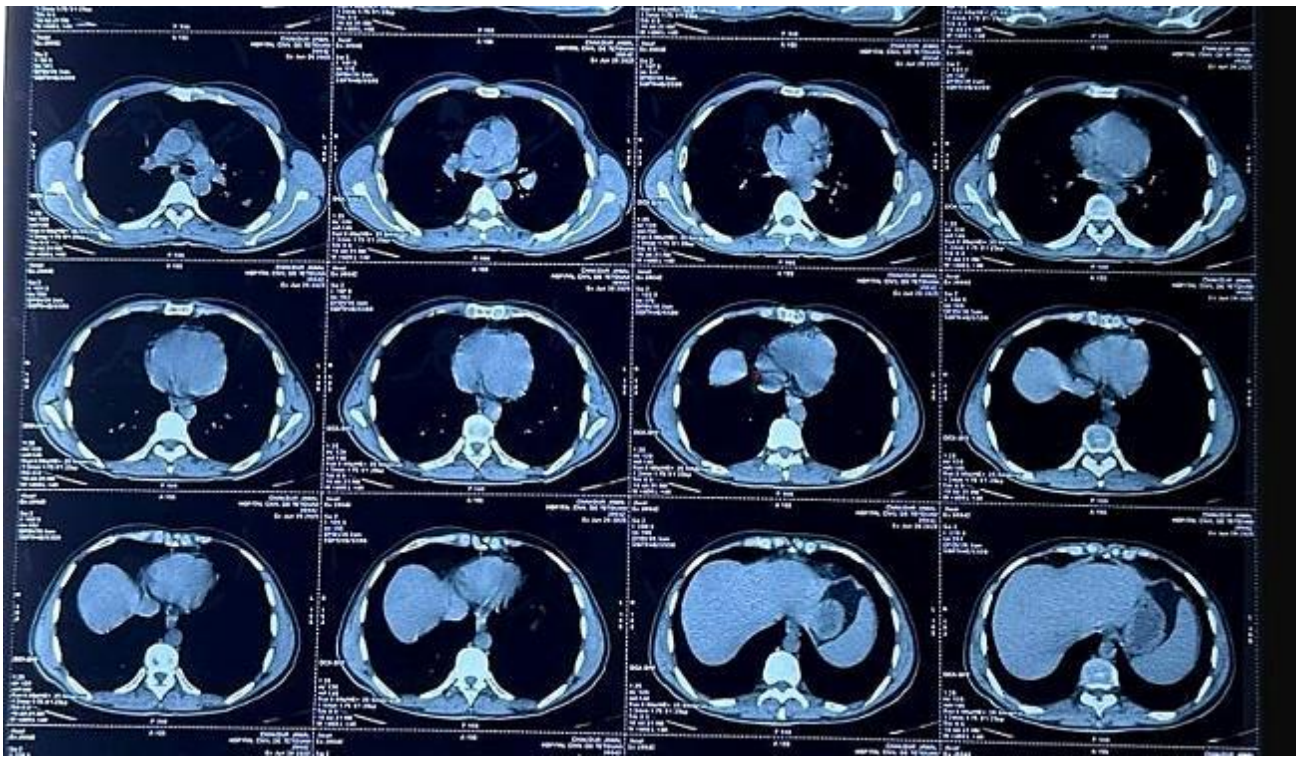

Figure 3 Chest CT scan, axial mediastinal window, at the level of the great vessels and hila, corresponding to the region where a few small (subcentimeter) prevascular, paratracheal, and aortopulmonary window lymph nodes were reported.

3. Discussion

Acute adrenal insufficiency is an uncommon but severe complication of tuberculosis. Historically, tuberculosis was the leading cause of primary adrenal insufficiency: Thomas Addison himself, in his original 1855 description of the disease that now bears his name, identified tuberculous destruction of the adrenal glands in the majority of his patients, and autopsy series from the early twentieth century subsequently found tuberculous adrenalitis in up to 70% of cases of Addison's disease [6,7]. With the advent of effective antituberculous chemotherapy, the relative contribution of tuberculosis to primary adrenal insufficiency in developed countries has declined to approximately 10–15% of cases, autoimmune adrenalitis having become the predominant etiology; tuberculosis nevertheless remains a leading cause of Addison's disease in TB-endemic, resource-limited settings such as Morocco and much of the developing world [1,2,6]. A recent Swedish population-based case-control study confirmed that, even in a modern, low-incidence setting, adrenal involvement in tuberculosis is associated with a substantially increased mortality risk compared with tuberculosis without adrenal involvement, underlining the clinical importance of recognizing this complication irrespective of local TB prevalence [4].

Two distinct, and potentially overlapping, pathophysiological mechanisms may explain the association observed in our patient. The first is direct destruction of the adrenal cortex by caseating granulomatous inflammation secondary to hematogenous dissemination of Mycobacterium tuberculosis, usually a late manifestation occurring years after the initial infection and typically requiring destruction of more than 90% of adrenal tissue before clinical signs of insufficiency become apparent; bilateral adrenal enlargement with peripheral rim enhancement is the characteristic early imaging finding of this form, evolving toward adrenal calcification in the chronic, burnt-out stage [6,7]. Because adrenal tuberculosis is frequently asymptomatic until advanced destruction has occurred, and because our patient's presentation was acute and concomitant with the pulmonary diagnosis rather than a late sequela, dedicated adrenal imaging (abdominal CT or MRI) would be a valuable adjunct in this case to determine whether structural adrenal involvement is present, and should be considered on subsequent follow-up imaging.

The second mechanism, arguably more relevant to the acute, early presentation described here, is a functional inadequacy of the hypothalamic-pituitary-adrenal (HPA) axis relative to the intense stress of severe systemic infection. Contrary to earlier assumptions of adrenal “exhaustion,” physiological studies indicate that the HPA axis is typically activated rather than suppressed in active pulmonary tuberculosis, with elevated baseline cortisol; however, this activation can be functionally insufficient relative to the metabolic demand of severe sepsis-like illness, a state now recognized as critical illness-related corticosteroid insufficiency (CIRCI) [11,12]. This relative insufficiency is compounded, once antituberculous therapy is initiated, by rifampicin-induced acceleration of hepatic cortisol clearance. Rifampicin is a potent inducer of hepatic cytochrome P450 (CYP3A4) and 6β-hydroxylase activity, which markedly increases the conversion of cortisol to inactive 6β-hydroxy cortisol; in patients with limited adrenal reserve, whether from subclinical adrenal tuberculosis or from the functional exhaustion of severe illness, this can precipitate overt adrenal crisis within days of starting treatment, and has been repeatedly documented since the earliest reports of this interaction in the 1980s [8–10]. In our patient, the temporal relationship between disease onset and biochemical presentation suggests that functional insufficiency related to severe infectious stress was the dominant early mechanism, though a component of subclinical adrenal tuberculous involvement cannot be excluded and would need to be reassessed once antituberculous treatment is well underway.

The clinical presentation of AAI is notoriously nonspecific, combining asthenia, anorexia, weight loss, gastrointestinal symptoms, and hypotension, which readily overlap with the constitutional symptoms of tuberculosis itself and may delay recognition until frank cardiovascular collapse occurs [3,6]. This overlap is a major contributor to diagnostic delay: fatigue, weight loss, and low-grade fever are common to both conditions, and hypotension may initially be attributed to volume depletion from vomiting and poor oral intake rather than to glucocorticoid deficiency. The combination of hyponatremia and hyperkalemia, as observed in our patient, is a particularly valuable biochemical clue, as it points toward primary (rather than secondary or tertiary) adrenal insufficiency, reflecting the combined glucocorticoid and mineralocorticoid deficiency characteristic of primary adrenal failure. This distinguishes it from the syndrome of inappropriate antidiuretic hormone secretion (SIADH), which is also common in severe pulmonary and central nervous system tuberculosis and can likewise present with hyponatremia, but which is typically associated with normal or low-normal serum potassium rather than hyperkalemia; this distinction is clinically important, as the two conditions require markedly different fluid and electrolyte management. Urgent cortisol measurement, ideally obtained before glucocorticoid administration, together with paired plasma ACTH when feasible, allows biochemical confirmation and localization (primary versus secondary) of the deficiency; however, in a hemodynamically unstable patient, treatment must never be delayed while awaiting these results [3,6].

Management relies on immediate parenteral hydrocortisone replacement, which simultaneously provides glucocorticoid activity and, at the high doses used in the acute setting, sufficient mineralocorticoid activity via cross-

reactivity at the mineralocorticoid receptor, together with aggressive correction of hypovolemia and electrolyte disturbances using isotonic and, where indicated, hypertonic saline. Antituberculous therapy should be initiated concurrently once the patient is hemodynamically stabilized, with close awareness that rifampicin may increase steroid requirements; some authors have advocated temporary substitution of rifampicin with a non-enzyme-inducing regimen during the acute phase in patients with confirmed adrenal insufficiency, followed by careful reintroduction with an increased hydrocortisone dose once tolerated [8–10]. Careful monitoring of serum sodium is also warranted during the recovery phase, since rapid correction of hyponatremia after starting hydrocortisone, or unmasking of an associated central diabetes insipidus in more complex presentations, has been reported and can itself pose risks if not anticipated.

Long-term follow-up with a formal corticotropin (Synacthen) stimulation test is warranted once the acute infectious and inflammatory stress has resolved and glucocorticoid replacement can be safely and transiently withheld under close supervision, to determine whether the adrenal insufficiency observed at presentation was transient, related to the acute infectious stress and CIRCI, and reversible after treatment completion, or represents established primary adrenal failure of tuberculous or other origin requiring lifelong hormone substitution [6,7,12]. In patients found to have persistent primary adrenal insufficiency, education on sick-day dosing, an emergency hydrocortisone injection kit, and a medical-alert device are essential components of long-term care to prevent future adrenal crises.

This report has the inherent limitations of a single-case observation: adrenal imaging and a formal corticotropin stimulation test were not performed during the acute phase, precluding definitive distinction between direct tuberculous adrenal involvement and a purely functional mechanism, and no long-term follow-up data are yet available to establish whether adrenal function normalized after treatment completion. Nonetheless, the case illustrates a clinically important and likely underrecognized association that merits systematic consideration in similar presentations.

4. Conclusion

Acute adrenal insufficiency is a rare but serious complication of severe pulmonary tuberculosis. This diagnosis should be systematically considered whenever tuberculosis is associated with marked impairment of general condition and unexplained hydro-electrolytic disturbances, particularly the combination of hyponatremia and hyperkalemia. Early measurement of serum cortisol allows rapid confirmation, and prompt initiation of substitutive corticosteroid therapy significantly improves vital prognosis by preventing hemodynamic decompensation.

Compliance with ethical standards

Acknowledgments

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Disclosure of conflict of interest

The authors declare that they have no conflict of interest.

Statement of ethical approval

This case report was conducted in accordance with the ethical standards of the institutional review board of Mohammed VI University Hospital, Tangier, and with the 1964 Declaration of Helsinki and its later amendments.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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