CASE REPORT

Synchronous presentation of two rare forms of extrapulmonary tuberculosis

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SUMMARY

Tuberculosis (TB) remains one of the leading infectious causes of death throughout the world. Extrapulmonary forms, namely adenitis and prostatitis, are rare presentations of TB and pose a difficult diagnostic challenge, given their non-specific manifestations. The authors present a case of a 42-year-old man with long-standing symptoms of fatigue, anorexia, weight loss, nightly fever and diaphoresis. He also suffered from sporadic vomiting and episodic hypotension, and had skin hyperpigmentation, as well as frequent urination, perineal discomfort and pain at ejaculation. Laboratory investigation confirmed primary adrenal failure. On CT scan there were two hypodense right adrenal nodules and bilateral lung condensations with a tree-in-bud pattern. Another hypodense nodule was seen in the prostate. TB was diagnosed by isolating *Mycobacterium tuberculosis* following cultures of bronchoalveolar lavage, bronchial secretions, urine and ejaculate. Antibacterial treatment resolved the infectious lesions but the patient remained on corticosteroid replacement therapy for ongoing adrenal failure.

BACKGROUND

Tuberculosis (TB) is one of the leading causes of death by infectious disease in adults, representing a major public health issue, especially in developing countries. Portugal is a country of intermediate incidence. Clinical suspicion remains the crucial diagnostic tool, and uncommon forms of presentation must be kept in mind, even in immunocompetent hosts. We present a case of disseminated TB in a patient diagnosed as having new onset Addison disease with pulmonary, prostate and adrenal involvement. The typical pulmonary infection was a minor clinical feature with the main symptoms being from the extrapulmonary sites of disease.

There is a necessity to raise awareness of one of the oldest diseases known to mankind, as it remains a health and economic burden in modern times; outcome without treatment being fatal in 50–65% of cases.

CASE PRESENTATION

A 42-year-old man presented with a 3-month history of non-selective anorexia, weight loss (13.5% of total body weight), low grade fever and night sweats. He had one episode of near syncope with moderate effort.

As the disease progressed, postprandial fullness and persistent vomiting were noticed, as well as non-specific urogenital symptoms with frequent

urination, perineal pain and discomfort during ejaculation.

Additionally, he had a productive cough with sputum production similar to his regular pattern.

He had a history of previous hepatitis B and C infections (with spontaneous clearance) and rheumatic fever during childhood. There was also a history of intravenous drug use with sustained abstinence for more than 20 years, and a smoking habit of 30 pack-years. Serology for HIV infection was negative.

The patient was admitted several times in the emergency department and ultimately diagnosed with urinary tract infection (leukocyturia and elevated C reactive protein). Amoxicillin/clavulanate was prescribed and he completed standard duration antibiotic therapy.

The symptoms persisted and he was admitted to an Internal Medicine ward.

On physical examination, blood pressure was 101/73 mm Hg, heart rate 80 bpm and oxygen saturation 98%. The patient was severely dehydrated, appeared unwell and had cutaneous hyperpigmentation. Cardiopulmonary examination was normal. The abdomen was diffusely tender without any palpable masses. A digital rectal examination detected a nodule in an otherwise normal prostate gland.

INVESTIGATIONS AND DIFFERENTIAL DIAGNOSIS

Blood tests were normal apart from an acute kidney injury (creatinine 1.74 mg/dL (normal 0.66–1.25 mg/dL), urea 75 mg/dL (normal 19–43 mg/dL)), euvolaemic hypo-osmolar hyponatraemia (serum sodium 128 mmol/L, serum osmolality 269 mmol/L (normal 280–300 mmol/L), urinary sodium 136 mmol/L and urinary osmolality 595 mmol/L (normal 300–900 mmol/L)), mild hyperkalaemia (potassium 5.8 mmol/L) and an elevation of inflammation markers (C reactive protein 10.2 mg/dL (normal <0.5 mg/dL), erythrocyte sedimentation rate 92 mm/1st hour).

Morning serum cortisol was 5.34 µg/dL (normal 5–25 µg/dL). Standard dose cosyntropin test showed no rise in cortisol following injection of an adrenocorticotrophic hormone (ACTH) analogue (250 µg intravenous): 0, 30 and 60 min serum cortisol 4.71, 4.47 and 4.35 µg/dL, respectively; confirming adrenal insufficiency. ACTH of 1393 pg/mL (normal <46 pg/mL) and aldosterone <1.1 ng/dL (normal 1–16 ng/dL) established the adrenal failure as primary. Gonadotrophic hormones, prolactin

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Figure 1 CT imaging showing nodular lung opacities in tree-in-bud pattern.

and thyroid function tests were within the normal range. Serology for HIV 1 and 2 was negative.

Urinalysis: pH 5.5, leukocyturia and negative urinary nitrite. The urine cultural examination was negative. Prostate-specific antigen 3.69 µg/mL (normal <4 µg/mL).

The tuberculin skin test was positive (15 mm induration in a non-vaccinated patient). Chest radiography was normal.

Full body CT revealed multiple peribronchial nodules in the lung (in a tree-in-bud pattern), with two nodules in the right adrenal gland and a nodule in the prostate gland (figures 1–3).

Finally, *Mycobacterium tuberculosis* complex (MTB) was identified in mycobacterial culture of material from a bronchoalveolar lavage, bronchial secretions (obtained by fiberoptic bronchoscopy), urine and ejaculate.

TREATMENT, OUTCOME AND FOLLOW-UP

The patient was started on adrenal hormonal replacement with hydrocortisone. He was discharged after a good clinical recovery with normalisation of the hyponatremia and hyperkalemia.

Antituberculous therapy consisted of a standard quadruple regimen (isoniazid, rifampicin, pyrazinamide and ethambutol) for 2 months, followed by extended treatment with isoniazid and rifampicin for 10 additional months.

During follow-up, the patient still reported of periods of weakness and hypotension; following this, he was started on flu-drocortisone. An ACTH value nearly 1 year after diagnosis was lower but still elevated at 365 pg/mL (normal <46 pg/mL), with no symptoms of TB. Control CT at this point showed no lung nodules (only residual fibrotic changes), the right adrenal gland had only one nodule, which had significantly reduced in size, and there were no visible nodules in the prostate gland.

DISCUSSION

TB, first described by Robert Koch in 1882, is caused by bacteria of the MTB.¹ The disease usually affects lungs, although extrapulmonary forms (EPTB) occur in up to 30% of cases, with adrenal and prostate glands being rare sites of symptomatic disease, especially in immunocompetent patients.²

Adrenal glands are the fifth most commonly involved organ in EPTB. Adrenal failure (Addison's disease) is mainly autoimmune in aetiology in the Western world, but in up to 20% of cases it can be caused by MTB infection.³ The rich vascularisation allows haematogenous spread and high local concentration of corticosteroids inhibits cell-mediated immunity, making these glands an easy target.⁴ Although the glands are frequently involved in TB, adrenal insufficiency is rarely seen.^{3 5–7}

Clinical features are multiple and non-specific, as a result of loss of glucocorticoid and mineralocorticoid secretion. These effects become evident when up to 90% of the gland is destroyed.⁵ Cutaneous hyperpigmentation is frequent as a result of overproduction of ACTH leading to pro-opiomelanocortin stimulation and melanin secretion.

Hyponatraemia is seen in 80% of cases (lack of cortisol-induced inhibition of vasopressin secretion) and hyperkalaemia in 40% (absent secretion of aldosterone).

Imaging usually shows bilateral involvement⁸ and adrenal calcifications in more than 50% of cases,⁵ usually in late disease. In our case, the disease was still active so hypertrophic hyperplastic glands were seen.

As TB progresses, gland destruction usually occurs, and most patients become dependent on long-term corticosteroids, throughout their lives.⁵

Urogenital TB is the second most common form of EPTB in high-incidence countries (10% to 14% of EPTB)^{7 9 10} and the third most common in low-incidence countries.^{9 11 12} TB can affect virtually any organ—the kidney in 74% of cases⁹ (haematogenous spread) followed by epididymis, testis, bladder, ureter and prostate gland.¹¹ These other organs are normally infected

Figure 2 Adrenal nodules, seen in right adrenal gland.

Figure 3 Heterogeneity and a nodule in the prostatic parenchyma.

by contiguity, descending infection and sexual contact.^{12 13} Prostatic TB is a very rare condition and only a few cases have been reported in immunocompetent individuals.¹⁰ Clinical features are variable and include perineal pain, dysuria, haematospermia and frequent urination.^{7 11 14} Digital rectal examination can be normal or a peripheral nodule may be identified, with or without a raised prostate specific antigen titre.¹⁰ Urinalysis is altered in 80% of cases (classic sterile pyuria 44–75%).^{9 11} An acidic urine with pyuria and negative urinary culture is extremely suggestive of TB.⁷

A useful aid in diagnosing urogenital TB may be the ‘three-glass test’.^{9 11} In this test, specimens grown from the first urine collected correspond to urethral infection, the midstream to bladder or upper urinary tract and, finally, the last urine sample (when the external bladder sphincter contracts) is equivalent to a sample obtained after prostatic massage and correlates to prostatic pathogens.¹¹ The cultural examination of the ejaculate can also identify the microorganism. Prostatic ultrasound usually shows a peripheral irregular hyperechoic lesion.

Both the EPTB forms of disease discussed have non-specific clinical features, being extremely rarely seen together at presentation. A high level of clinical suspicion is required in order to

allow for early diagnosis and timely initiation of adequate treatment.

Contributors MCM, SR and RD were the main doctors caring for this patient. MCM and SCR elaborated the manuscript; SR and RD reviewed the final draft.

Competing interests None declared.

Patient consent Obtained.

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Learning points

- ▶ Tuberculosis (TB) is a major public health problem, and raised awareness is necessary, including being alert to rare extrapulmonary forms of the disease.
- ▶ Clinical suspicion is still the most important diagnostic tool, as the disease can easily mimic other pathologies.
- ▶ Extrapulmonary TB is more frequent in immunocompromised patients, but rare forms of the disease can appear in immunocompetent individuals.

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