CASE REPORT

Extrapulmonary disseminated tuberculosis with tuberculous adrenalitis: a stitch in time saves nine

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SUMMARY

A 40-year-old manual labourer presented with easy fatiguability, recurrent vomiting and loss of weight of 3 months, duration. Upon examination, there was significant axillary and cervical lymphadenopathy. No pallor, icterus or clubbing was evident. There was generalised hyperpigmentation and multiple oral ulcers. The blood pressure 90/60 mm Hg in the right upper limb in the supine position. Investigations showed a low serum cortisol. Mantoux test was strongly positive (20 mm). A fine needle aspiration biopsy of the cervical lymph node revealed reactive changes. Bone marrow aspiration and biopsy were normal. Cervical lymph node biopsy showed caseating granulomas suggestive of tuberculous lymphadenitis. A CT scan of the abdomen showed bilaterally enlarged adrenal glands with hypodense areas suggestive of necrosis. He was diagnosed with extrapulmonary disseminated tuberculosis with tuberculous adrenalitis. He was started on directly observed therapy (DOTS) for disseminated tuberculosis and 40 mg of prednisolone. He is improving with treatment.

BACKGROUND

India has the highest burden of tuberculosis in the world.¹ Tuberculosis is known to present with diverse clinical features, but involvement of the adrenal glands in tuberculosis is rare. Here, we report a patient with primary adrenal insufficiency, due to adrenal tuberculosis as part of a disseminated infection. The case is being reported for its unusual presentation and rarity. A high index of suspicion is required for early diagnosis of the disease so as to avoid delay in initiation of treatment and minimise high mortality associated with the illness.

CASE PRESENTATION

A 40-year-old manual labourer presented with easy fatiguability, recurrent vomiting and loss of weight of 3 months duration. He had no history of fever, headache, seizures, abdominal pain, loose stools, syncope or sexual dysfunction. Nor was there a history of diabetes, hypertension, pulmonary tuberculosis or bronchial asthma in the family. Until 3 years previously, he had smoked about 10 cigarettes a day for 10 years but then abandoned the habit. He had no other addictions/high-risk behaviour. Upon examination, significant axillary and cervical lymph node enlargements were present. No pallor, icterus, cyanosis or clubbing was evident. Generalised hyperpigmentation and multiple oral ulcers were present (figure 1A–D). The pulse rate was 78/min, regular and the blood pressure was 80/60 mm Hg in the right upper limb in the supine

position. Gastrointestinal examination revealed no hepatosplenomegaly and the external genitalia was normal. The cardiovascular, respiratory and central nervous systems were normal after examination.

INVESTIGATIONS

Investigations revealed that the patients haemoglobin was 14 g%. The total white cell count was 8080/mm³ and the differential count showed neutrophils 60%, lymphocyte 40% and platelet count 290×10³/mm³. The erythrocyte sedimentation rate was 15 mm/h. Urine routine examination was normal. The blood urea was 35 mg/dl, serum creatinine 0.9 mg/dl, serum sodium 124 meq/l and potassium 4.2 mm eq/l. Repeated values of sodium/potassium were 120/4.2, 130/4.1, respectively. Random blood sugar was 92 mg/dl. Urine/serum creatinine ratio was 32/0.9. Liver function showed a serum bilirubin of 0.9 mg/dl with direct being 0.2 mg/dl. Total proteins 6.8, albumin 4 g%, serum glutamate oxalate transaminase 76 IU/l and serum glutamate pyruvate transaminase 44, alkaline phosphatase 142. Serum fasting cortisol 2 ng/dl (15–60) (rechecked), plasma adrenocorticotrophic hormone (ACTH) 438.3 (20–100 pg/ml) (rechecked) S Ferritin 200 (27–670 pmol/l), free T4 was 1.35 ng/dl (0.81–1.8 ng/dl), antithyroxine antibodies were negative, serum calcium was 9.2 mg/dl, and phosphorus 4 mg/dl. The chest radiograph and electrocardiogram were normal. Oesophagogastrroduodenoscopy and colonoscopy were normal. Mantoux test was strongly positive (20 mm). ACT scan of the abdomen showed bilaterally enlarged adrenal glands with hypodense areas suggestive of necrosis (figure 2A). A contrast-enhanced CT scan of the abdomen showed bilaterally enlarged adrenal glands with adrenal masses showing central low-attenuation areas (figure 2B). A fine needle aspiration biopsy of the cervical lymph node revealed reactive changes node. Bone marrow aspiration and biopsy were normal. Cervical lymph node biopsy showed caseating granulomas suggestive of tuberculous lymphadenitis (figure 3A–C).

He was diagnosed to have adrenal tuberculosis due to disseminated tuberculosis resulting in adrenocortical insufficiency: Addison's disease.

DIFFERENTIAL DIAGNOSIS

Haemochromatosis, polyglandular syndrome, upper gastrointestinal malignancy, histoplasmosis, blastomycosis, adrenal metastases, primary adrenal tumours and opportunistic infections related to HIV/AIDS.²

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Figure 1 (A) Generalised hyperpigmentation; (B) multiple oral ulcers pigmentation of both hands; (C) hyperpigmentation of the palms; (D) hyperpigmentation of the dorsal aspect of the hand.

TREATMENT

He was started on directly observed therapy category I antituberculous along with prednisolone 40 mg, which was tapered off to 5 mg over 4 weeks.

OUTCOME AND FOLLOW-UP

At the first review, he is gaining weight and is asymptomatic.

DISCUSSION

The prevalence of chronic primary adrenal insufficiency (Addison's disease) has been reported to be 39–60 per million population.² The mean age at diagnosis in adult patients is 40 years (range, 17–72).² The most common cause was formerly tuberculous adrenalitis, but now it is autoimmune adrenalitis (slow destruction of

the adrenal cortex by cytotoxic lymphocytes).² The most commonly involved endocrine organ in tuberculosis is the adrenal gland.³ Adrenal glands may be directly or indirectly affected by tuberculosis. Tuberculous Addison's disease is still an important cause of primary adrenocortical insufficiency, particularly in the developing countries.³ The prevalence of permanent adrenal insufficiency is 5 in 10 000. A hypothalamic-pituitary origin of disease is most frequent, with a prevalence of 3 in 10 000, whereas primary adrenal insufficiency has a prevalence of 2 in 10 000. Adrenal insufficiency arising from suppression of the hypothalamo-pituitary axis as a consequence of glucocorticoid treatment occurs in 0.5–2% of the population in developed countries.⁴

Primary adrenal insufficiency is most commonly caused by autoimmune adrenalitis. Isolated autoimmune adrenalitis

Figure 2 Panel (A) CT abdomen—axial section showing bilaterally enlarged adrenal glands with hypodense areas suggestive of necrosis (white arrows); (B) coronal section demonstrates bilaterally enlarged adrenal glands with adrenal masses showing central low-attenuation areas (white arrows).

Figure 3 (A, B) Low-power view of the histopathology showing caseating necrosis of the lymph node; (C) histopathology of a lymph node high-power view showing Langhans giant cells.

accounts for 30–40%, whereas 60–70% of adrenal deficiency occurs as a part of polyglandular syndromes.⁴ Rarer causes of adrenal insufficiency involve destruction of the adrenal gland, such as a consequence of infection, haemorrhage or infiltration. Tuberculous adrenalitis is still a frequent cause of the disease in developing countries.⁴ Other infections responsible may be HIV, cytomegalovirus, cryptococcosis, histoplasmosis and coccidioidomycosis.⁴ Chronic adrenal insufficiency manifests with relatively non-specific symptoms such as fatigue and loss of energy, often resulting in delayed or missed diagnosis. A distinguishing factor of primary adrenal insufficiency is hyperpigmentation, which is caused by excess ACTH stimulation of the melanocyte. Hyperpigmentation is most pronounced in skin areas exposed to increased friction or sheer stress and is increased by sunlight. Conversely, in secondary adrenal insufficiency, the skin has a labaster-like paleness due to lack of ACTH secretion.⁴ Adrenal tuberculosis, a manifestation of disseminated disease, presents rarely as adrenal insufficiency.⁵ Adrenal tuberculosis was seen in 6% of the 871 patients with active tuberculosis at autopsy and in 3 patients at adrenalectomy. The adrenal gland was the only organ involved by active tuberculosis in 14 of these 55 patients (25%; 35 men, 20 women).⁶ Addison's disease results when >90% of the glands are involved. In early series, tuberculosis was responsible for 70–90% of cases, but the most frequent cause now is idiopathic atrophy and an autoimmune mechanism is probably responsible.⁷

A contrast-enhanced computed scan of the abdomen with the suggestive features is confirmative.⁸ Fine needle aspiration cytology was not useful for diagnosing adrenal tuberculosis.⁶ CT may be helpful in diagnosing adrenal tuberculosis when it is clinically suspected, and CT features are correlated to the clinical duration of Addison's disease.⁸ The CT signs of active tuberculous adrenalitis are bilaterally enlarged glands associated with large, hypo-attenuating necrotic areas, with or without dot-like calcification. The imaging features are helpful in differentiating tuberculous adrenalitis from adrenal neoplasm. Bilateral adrenal enlargement, contour of the gland preserved and peripheral rim enhancement+ often showed calcification, whereas in adrenal neoplasm, which is usually unilateral, calcification is not usual, with peripheral rim enhancement being less conspicuous and the contour of the gland not being preserved.⁹ When CT features in 42 patients with documented adrenal tuberculosis were evaluated retrospectively by Guo *et al* for the location, size, morphology and enhancement patterns shown on CT images, the clinical duration was correlated with the CT features. Of the 42 patients with untreated adrenal tuberculosis, 91% (38) had bilaterally enlarged adrenals and 51% (21) had enlarged glands

with preservation of the contours. As the duration of Addison's disease increased, the presence of calcification and contour preservation increased concomitantly, whereas peripheral rim enhancement and mass-like enlargement decreased concomitantly on CT images.⁸ Notwithstanding the low incidence of symptomatic Addison's disease even in disseminated tuberculosis, it remains an important condition to be considered in India, where the burden of tuberculosis is the highest in the world¹ as the absolute number of patients suffering from this condition—which adds to the morbidity of disseminated tuberculosis—is still high.

CONCLUSION

Adrenal tuberculosis, a manifestation of disseminated disease, presenting as adrenal insufficiency, is rare. Tuberculous Addison's disease is still an important cause of primary adrenocortical insufficiency, particularly in developing countries. A high index of suspicion is required for early diagnosis of the disease so as to avoid delay in initiation of treatment and to minimise high mortality associated with the illness.

Learning points

- ▶ Tuberculosis is known to present with diverse clinical features, but involvement of the adrenal glands by tuberculosis is rare.
- ▶ A high index of suspicion is required for early diagnosis of the disease so as to avoid delay in initiation of treatment and to minimise high mortality associated with the illness.
- ▶ Addison's disease remains an important condition for consideration in India, where the burden of tuberculosis is the highest in the world,⁶ as the absolute number of patients suffering from this condition adds to the morbidity of disseminated tuberculosis.

Contributors CR was the primary clinician under whom the patient was admitted, investigated and treated. RP who presented the case and edited and formatted images and significantly contributed in collecting all the references. All the authors had equal role in writing, editing and formatting the manuscript.

Competing interests None.

Patient consent Obtained.

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