Primary adrenal insufficiency due to adrenal tuberculosis: a case report

Jie Yu, Yingli Lu and Bing Han

Abstract
We report a case of primary adrenal insufficiency (PAI) due to adrenal tuberculosis with no findings of active tuberculosis in the lung of a 51-year-old female patient. The patient was admitted with a 10-year history of skin hyperpigmentation and was diagnosed with PAI. The primary cause was adrenal tuberculosis. An adrenocorticotropic hormone stimulation test, T-Spot test and adrenal computed tomography scan were used to confirm the diagnosis. The patient’s status improved, and the hyperpigmentation subsided after 15 months of treatment with anti-tuberculosis drugs and cortisol replacement therapy.

Keywords
Primary adrenal insufficiency, adrenal tuberculosis, hyperpigmentation, autoimmune adrenal disease, cortisol replacement therapy, extra-pulmonary tuberculosis

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Introduction
Primary adrenal insufficiency (PAI), also known as Addison’s disease, is a rare disease with an incidence of 4:1,000,000 cases per year in Western countries and can lead to life-threatening consequences. The symptoms are related to the extent of insufficiency in glucocorticoid and mineralocorticoid hormone. The primary cause of PAI in Western countries is autoimmune adrenal disease, which is characterized by the presence of 21-hydroxylase autoantibodies. Tuberculosis (TB) was the most common cause of adrenal insufficiency. However,
because the incidence of TB has decreased, there have been fewer identified cases of PAI caused by TB, resulting in possible delays in the diagnosis and treatment of these patients. Here, we report a rare case of PAI due to adrenal TB with no findings of active TB in the lung.

Case report

A 51-year-old woman was admitted to our hospital for skin hyperpigmentation. In 2010, she gradually developed hyperpigmentation in her face, lips and nails. Physical examination at admission indicated hyperpigmentation in her hands (Figure 1a). Her blood pressure was 123/66 mmHg, and hormone tests showed significantly elevated adrenocorticotropic hormone (ACTH) (>1250 pg/mL, normal range: 0–46 pg/mL) and decreased cortisol (4.66 μg/dL, normal range: 5–25 μg/dL) levels at 8 am. The results of an ACTH stimulation test showed a slight decrease in serum cortisol levels within 30 minutes (4.2 μg/dL). She had normal serum supine aldosterone (65.92 pg/mL, normal range: 29.4–161.5 pg/mL). Her supine renin level was 0.10 ng/mL/hour (normal range: 0.05–0.79 ng/mL/hour). Serum sodium was 137 mmol/L (normal range: 135–147 mmol/L), and potassium was 4.19 mmol/L (normal range: 3.5–5.1 mmol/L). The fasting glucose level was 4.6 mmol/L (normal range: 3.9–6.1 mmol/L). Autoimmune antibodies, including anti-mitochondrial antibody, anti-nucleosome antibody, anti-histone antibody and anti-ds-DNA, were all negative. Her T-SPOT.TB test was positive. A lung computed tomography (CT) scan showed no findings of active TB, and an adrenal CT scan showed bilateral adrenal

![Figure 1](image_url)

Figure 1. Clinical manifestation of the 51-year-old female patient reported in this case. Hyperpigmentation in the hands and nails (a) of the patient before and (b) after treatment with anti-tuberculosis drugs [isoniazid (0.3 g/day, orally) and rifampin (0.6 g/day, orally)] and cortisol replacement therapy [hydrocortisone (12.5 mg twice a day, orally)]. Computed tomography images of the adrenal gland (c) before and (d) after treatment.
hyperplasia (Figure 1c). As a result, the patient was diagnosed with PAI induced by TB. She was treated with anti-TB drugs [isoniazid (0.3 g/day, orally) and rifampin (0.6 g/day, orally)] and cortisol replacement therapy [hydrocortisone (12.5 mg twice a day, orally)]. Fifteen months later, the adrenal hyperplasia improved (Figure 1d), and her hyperpigmentation subsided (Figure 1b). The patient is currently taking hydrocortisone at a dose of 12.5 mg twice a day (orally). No secondary osteoporosis or cardiovascular complications have been observed to date.

Discussion

We report a patient with TB-induced PAI who presented with typical hyperpigmentation but without abnormal electrolytes, abnormal glucose levels or hypotension. The diagnosis was based on clinical manifestations and laboratory tests. The T-SPOT test was used to confirm the diagnosis of TB. Measuring interferon gamma release by sensitized T-cells in response to highly specific *Mycobacterium tuberculosis* antigens has been shown to have a high sensitivity and specificity in pivotal clinical trials.²,³ Although QuantiFERON was reported to have a higher sensitivity than T-SPOT,⁴ T-SPOT is widely used in most parts of China.⁵,⁶

The primary cause of PAI in Western countries is autoimmune adrenal disease, which is characterized by the presence of 21-hydroxylase autoantibodies. TB is another common cause of PAI. In China, although the incidence of TB has decreased between the years 2000 (more than 100 cases/100,000 people) and 2018 (61/100,000), the country still shares a significant part of the global burden of TB cases (9%).⁷ The patient reported in this case lives in Zhejiang Province in China. It was reported that the residents in this Province exhibit low levels of TB awareness, especially of its suspicious symptoms,³ leading to a delay in seeking care. This enables the potential development of PAI. Thus, TB remains a primary factor contributing to PAI in China and should be considered an indicator when hyperpigmentation and weakness are observed. The patient presented with TB in the adrenal gland as the only site of infection. In a survey of adrenal TB, the adrenal gland was the only extra-pulmonary organ affected by TB in 25% of patients.⁹ Therefore, the significance of extra-pulmonary TB should be considered in patients with PAI.

Conclusion

We report a case of PAI due to adrenal TB. The patient had no active findings in the lung, and the results of electrolyte and glucose tests were normal. She was successfully treated with anti-TB drugs and cortisol replacement therapy. Given the current status of TB in China, attention should be paid to the awareness of TB among residents and the role of TB in inducing PAI. Extra-pulmonary TB should also be considered when PAI is found.

Ethics statement and informed consent

Ethics approval was not obtained because this manuscript is a case report. Written informed consent was obtained from the patient.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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