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Addison's disease caused by adrenal tuberculosis may lead to misdiagnosis of major depressive disorder: a case report

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Abstract:

BACKGROUND

Addison's disease (AD) is a rare disease in Western countries and has fatal consequences. The symptoms of the disease can easily be misdiagnosed at an early stage. Severe adrenal tuberculosis (TB) infection may lead to depression in patients.

CASE SUMMARY

We report a case of primary adrenal insufficiency secondary to adrenal tuberculosis with tuberculosis in the lungs and skin of a 48-year-old female patient. The patient was misdiagnosed with depression because of depressed mood. She had hyperpigmentation of skin, nails, mouth, and lips. The final diagnosis was adrenal tuberculosis resulting in insufficient secretion of adrenocortical hormone. Adrenocortical hormone test, skin biopsy, T cell spot test of tuberculosis infection (T-Spot.TB), and adrenal computed tomography scan were used to confirm the diagnosis. The patient's status improved after hormone replacement therapy and antituberculosis treatment.

CONCLUSION

Given the current status of TB in high burden countries, outpatient doctors should pay attention to the awareness of TB and understand the early symptoms of AD.

Keywords: primary adrenal insufficiency; adrenal tuberculosis; fatigue; hypotension; hyperkalemia; hyponatremia; depression

Core Tip: 1. Addison's disease induced by adrenal tuberculosis should be considered for early onset of depressed mood and skin pigmentation symptoms in developing countries.

2. Diagnostic antituberculosis therapy is not recommended as a diagnostic measure because of the potential for adrenal crisis with rifampicin.

3. T-SPOT negativity cannot be used as a basis for excluding TB infection, especially in immunocompromised patients or those with hematogenous disseminated pulmonary tuberculosis.

4. Adrenal function does difficult to recover from AD caused by adrenal tuberculosis, most cases require lifelong hormone replacement therapy.

INTRODUCTION

Primary adrenal insufficiency, or Addison's disease, is characterized by damage to the adrenal gland, resulting in insufficient production of cortisol, aldosterone, and sex hormones. It is a rare disease with an incidence of 4:1,000,000 cases per year in Western countries and has fatal consequences[1]. This disorder can lead to depressed mood and depression[2].

Autoimmune adrenalitis is the leading cause of AD in developed countries, whereas in developing countries, adrenal tuberculosis remains an important cause of morbidity. Nonspecific symptoms of AD and a low frequency of non-TB epidemic countries often lead to

neglect or a delay in diagnosing diseases. Less experience in diagnosis was noted for nonrelated professional doctors, resulting in a higher frequency of misdiagnosis in recent years[3].

CASE PRESENTATION

Chief complaints

A 48-year-old female patient was admitted to Shaanxi Tuberculosis Hospital with a complaint of skin pigmentation for 1 year.

History of present illness

She complained of nausea, depression, fatigue, decreased appetite, hyperpigmentation of skin, nails, mouth, and mucous membranes of the lips. Symptoms started 1 year before presentation with depressed mood.

History of past illness

Her skin pigmentation symptoms lasted for 1 year, she was diagnosed with depression according to the ICD-10 at other hospitals, the treatment protocol was as follows: duloxetine hydrochloride 60mg once daily, clonazepam 0.25mg once daily, after 1 month of treatment, there was no improvement in depressive symptoms. She was presented with a skin ulcer on her back, pathological biopsy findings of dorsal skin lesions showed hyperkeratosis and tuberculoid granulomatous inflammation. (Fig. 2 A.B)

Personal and family history

The patient denied of genetic or mental illness, no did she have a history of smoking or pulmonary tuberculosis.

Physical examination

On physical examination, the vital signs were as follows: Body temperature, 37.4℃; blood pressure, 63/40 mmHg; heart rate, 114 beats per min; respiratory rate, 21 breaths per min. Hyperpigmentation on the skin, nails, mouth, and mucous membranes of the lips, without fading after pressing and wiping. (Fig. 1) Two skin lesions were found on the left back, no secretion was found. (Fig. 2 C)

Laboratory examinations

Laboratory tests showed elevated inflammatory parameters (erythrocyte sedimentation rate = 42 mm/h, C-reactive protein = 52.2 mg/L, procalcitonin = 0.65 ng/mL). She also had hyperkalemia and hyponatremia (potassium ion = 5.6 mmol/L, sodium ion = 111.8 mmol/L, and chloride = 81.1 mmol/L). Further, persistent hypotension (80/40 mmHg) was observed. T-SPOT.TB was positive.

Imaging examinations

Chest computed tomography (CT) showed infectious lesions of both lungs (Fig. 3). Fiberoptic bronchoscopy was recommended; however, the patient refused.

FURTHER DIAGNOSTIC WORK-UP

Refractory hyperkalemia and hyponatremia, persistent hypotension (80/40 mmHg) was observed. However, correction of electrolyte imbalance, rehydration, and use of vasoactive drugs were ineffective. A diagnosis of adrenal hormone secretion deficiency was considered based on her symptoms and laboratory tests. Cortisol and adrenocorticotropic hormone (ACTH) hormones were detected (cortisol < 1.31 μg/dL, ACTH > 2000 pg/mL). Meanwhile, adrenal CT showed that calcification and giant masses were observed in the adrenal glands bilaterally (Fig. 4).

FINAL DIAGNOSIS

Combined with the patient's medical history, the final diagnosis was Addison's disease, caused by adrenal tuberculosis.

TREATMENT

The treatment protocol was as follows: Prednisone (PAT) 5 mg once daily at 8 am, isoniazid 0.3 g once daily, rifampicin 0.6 g once daily, pyrazinamide 0.5 g three times daily, and ethambutol hydrochloride 1.0 g once daily. During the combined treatment of prednisone and antitubercular therapy, the patient had no adverse drug reactions.

OUTCOME AND FOLLOW-UP

After 2 weeks of combined treatment, the symptoms of depression were significantly improved, blood pressure and serum electrolyte levels were normalized(Fig. 5). After 1 month of combined treatment, chest CT showed improvement in inflammation（Fig. 6 C.D）, and after 6 months, the patient's pigmentation improved(Fig. 7).

3. Discussion

At present, the prevention and treatment of tuberculosis remains grim. In 2020, approximately 1.5 million deaths worldwide were attributable to TB, with a TB case fatality rate of 15% (up from 14% in 2019). The number of TB deaths among HIV-negative patients increased from 1.21 million to 1.28 million in 2019[4]. Primary adrenal insufficiency was discovered by Thomas Addison in 1855. When he first described his patients with adrenocortical insufficiency, 6 of 11 cases were caused by the destruction of adrenal cortex by mycobacterium tuberculosis[6]. In 1930, Guttman reported 566 patients with AD, of whom 70% had AD caused by tuberculous adrenalitis[7]. By 1956, the number dropped to 25%. A meta-analysis performed by Italian scholars in 2011 showed a decrease in the incidence of adrenal failure secondary to tuberculous in 615 patients with AD. Only 9% of the cases were caused by

tuberculosis[8]. Tuberculosis is no longer the most common cause of Addison's disease (AD) in developed countries. Recent data suggest a continuation of this trend with a further increasing prevalence of AD particularly in women[5]. Today, in western societies, 80% of AD is caused by autoimmune adrenalitis followed by tuberculosis or other infectious diseases and malignant diseases in about 10% of cases. But the most common cause of AD in developing countries remains infection with mycobacterium tuberculosis that spreads to the adrenal glands via blood[6]. The current treatment is hormone therapy, and most patients require lifelong replacement therapy, hydrocortisone is the drug of choice for the replacement of glucocorticoids. As an alternative to hydrocortisone, 3–5mg/d prednisolone as a single dose or in 2 divided oral doses is suggested.

Many patients have no obvious early symptoms. Changes in sleep habits, mood, and behavior can sometimes be the first symptoms. Severely ill patients seek medical attention with fatal adrenal crisis. AD becomes apparent only when more than 90% of the adrenal glands are destroyed by tuberculosis. Most active or recently active (<2 years) patients with TB have bilateral adrenal enlargement, calcifications, and atrophy that is typical of longstanding infections caused by tuberculosis[9].

In our case, AD was misdiagnosed in the outpatient clinic of the patient with depression due to long-term skin pigmentation. At the time of admission to our hospital, her chest CT showed manifestations of a pulmonary infection, and skin biopsy revealed a pathological diagnosis of tuberculosis granuloma. The adrenal gland CT showed enlargement and calcification. Given the signs and symptoms of this patient, high suspicion for tuberculous adrenalitis, cortisol and ACTH were tested, resulting in a diagnosis of AD secondary to adrenal tuberculosis. After 1 month of anti tuberculosis and hormone replacement therapy, chest CT showed improvement in inflammation, and after 6 months, the pigmentation was partially reversed.

This paper aimed to show our experience in the diagnosis and treatment of AD. First, it was important that the physician made the correct diagnosis in the outpatient at an early stage. AD involves multiple organs, including the brain. This patient was diagnosed with depression at another hospital, where the signs of skin hyperpigmentation, hypotension, and electrolyte disorder were ignored. Thus, AD should be considered when multiple mucosal hyperpigmentation and depression are observed in countries with a high burden of TB. Second, hormone secretion changes in AD induced by adrenal TB are extremely difficult to recover after long-term anti-TB treatment. Most patients require lifelong hormone replacement therapy. Additionally, we do not recommend diagnostic anti-TB therapy as a diagnostic measure because it is also worth noting that rifampicin has the potential to cause adrenal crisis. This can interfere with the diagnosis of AD and needs to be carefully differentiated[10]. Third, t cell spot test of tuberculosis infection positivity can be used as a reference indicator for TB infection, but T-SPOT negativity cannot be used as a basis for excluding TB infection, especially in immunocompromised patients or those with hematogenous disseminated pulmonary tuberculosis[11]. In terms of treatment, once AD induced by adrenal TB is diagnosed, lifelong hormone replacement therapy and a course of anti-TB treatment are required. In summary, AD symptoms caused by tuberculosis are insidious and easily misdiagnosed in the early stage.

CONCLUSION

Given the current status of TB in high burden countries, outpatient doctors should pay attention to the early symptoms of AD and consider the possibility of tuberculosis infection. In addition, adrenal function does difficult to recover from AD caused by adrenal tuberculosis, most cases require lifelong hormone replacement therapy.

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