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Case report

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A 41-year-old male with generalized hyperpigmentation and weakness: "Histoplasmosis- a mimic of tuberculosis"

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Abstract

A 41-year-old man with diabetes mellitus and smoking history was initially treated for tuberculosis (TB) based on clinical and radiological findings despite a negative sputum test. However, his treatment was interrupted by jaundice and an adrenal crisis. Further testing revealed that he had disseminated histoplasmosis involving the liver and adrenal glands. He was partially improved with antifungal and steroid therapy. This case highlights the difficulties in distinguishing between these two diseases and the need for a high index of suspicion and cytological confirmation for accurate diagnosis and treatment. *[J Assoc Clin Endocrinol Diabetol Bangladesh,* July 2025;4(2)*: 85-89]*

Keywords: Adrenal histoplasmosis, Tuberculosis, Adrenal CT scan, Itraconazole, Generalized hyperpigmentation

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Introduction

Histoplasmosis is an endemic mycosis in most of the world, including Southeast Asia. It commonly causes lung infection. Disseminated and extrapulmonary histoplasmosis are rare but have been reported from endemic areas, mainly in immune-compromised patients.[1] Adrenal histoplasmosis and tuberculosis (TB) have similar clinical and imaging features. In an endemic region like Bangladesh, histoplasmosis should be excluded when the initial diagnosis of TB is questioned or non-responsive to a standard anti-TB regimen in a patient with bilateral adrenomegaly.[2] Untreated adrenal histoplasmosis may lead to a fatal adrenal crisis, whereas proper treatment started on time might be life-saving.[3] Here, we report a case of disseminated histoplasmosis with primary adrenal insufficiency who was initially diagnosed and treated as a case of pulmonary TB.

Case report

A 41-year-old male farmer sought medical attention due to a year-long progression of darkening skin, beginning on his face and spreading to his hands, feet, mouth, and tongue. Over the past eight months, he also experienced significant weight loss (5-6 kg), increasing fatigue, poor appetite, nausea, general discomfort, and occasional low-grade fevers. He had a history of diabetes, smoking, and previous TB exposure.

The patient's condition deteriorated despite initial treatment. Further testing, including chest X-ray (Figure 1A) and contrast-enhanced CT scan (CECT), revealed a possible granuloma (?tuberculoma) in his right lung. A positive tuberculin skin test (MT) led to the start of category I anti-TB medication. However, he developed jaundice within a week, requiring discontinuation of the medication. His health continued to decline, resulting in severe symptoms like postural dizziness, nausea, vomiting, and immobility.

On admission into our unit, he was dehydrated and mildly anemic, with generalized pigmentation and the absence of lymphadenopathy. He exhibited hypotension (80/60 mm of Hg) with a postural drop (supine: 90/70 mm of Hg, standing: 70/60 mm of Hg), and his pulse rate was 106 beats per minute, having low volume. Other examinations revealed no abnormalities. Based on initial routine investigations (Table-I) and low (12.40

Table-I: Biochemical and hormonal profile of the patient before and after treatment

Tests	Component	Before treatment	At 6 months of treatment	Reference values
Complete	Hemoglobin, gm/dL	11.0	12.7	13.0 - 17.0
blood count	ESR in 1st hour, mm	77	20	0 – 10
	Total leukocyte count, (/µL)	8,000	11,500	4,000 - 11,000
	Neutrophils, %	61	73	40 – 75
	Lymphocytes, %	29	23	20 – 50
	Monocytes, %	6	2	1 – 6
	Eosinophils, %	4	2	0 – 1
Electrolytes	Sodium, mmol/L	136	137	136 – 145
	Potassium, mmol/L	4.2	4.1	3.5 - 5.5
	Chloride, mmol/L	107	99	98 – 107
	T-CO_2, mmol/L	22.7	24	20 – 31
Glycemic status	Fasting glucose, mmol/L	4.2	13.0	< 7.0
	2 hours after breakfast, mmol/L	11.3	15.2	<10.0
	HbA1c, %	5.7	6.0	<6.5
Renal &	Creatinine, mg/dl	1.20	1.10	0.6-1.4
Liver function test	Total bilirubin, mg/dl	0.89		0.3-1.0
	Albumin, mg/dl	38		35-50
	ALT, U/L	30	38	Up to 40
	Mantoux test, mm	11	9	
Immuno-logical	AntiHIV1 & HIV2	Negative		
	HBsAg	Negative		
	Rheumatoid factor	Negative		
	pANCA	Negative		
	cANCA	Negative		
	Urine C/S	No growth		
Others	Blood C/S	No growth		
	Gene Xpert for MTB	Negative		
	Plasma ACTH, pg/ml	618.80	189	5.0- 46.0
Hormonal profile	Basal Cortisol, nmol/L	4	10	
	24hr Urinary Metanephrine, nmol/day	1320.85		<1775.0
	Plasma renin, pg/ml	25.6		1.63-95.56
	Plasma aldosterone, pg/ml	31.6		12.87-358.5
	DHEAS, µg/dl	13.70		70-495

nmol/l) random serum cortisol, he was diagnosed with a case of adrenal crisis and treated with a major stress dose of injectable hydrocortisone along with IV fluid. His general condition improved after 3 days, and then IV hydrocortisone was switched to oral hydrocortisone.

After the clinical condition had been settled, further investigations were done to find out the etiology of the adrenal crisis. Hormonal investigation revealed primary adrenocortical insufficiency (Table-I). USG of the abdomen showed bilateral adrenal enlargement as a well-circumscribed, hypoechoic mass. CT-guided FNAC was done from a solitary pulmonary nodule that showed an inconclusive inflammatory lesion. CECT of the abdomen showed bilateral adrenomegaly with mixed density and a space-occupying lesion (SOL) in the 6th segment of the right lobe of the liver (Figure-1C). Then CT-guided FNAC from the adrenal gland revealed an admixture of blood with a small number of lymphocytes and polymorphs, interestingly a few yeasts of *Histoplasma capsulatum* with budding (Figure-2). Then, itraconazole 400 mg/day was started in two divided doses. A few days later, the patient was discharged on a hydrocortisone and itraconazole maintenance dose.

After six months, the patient showed positive progress in general condition. He gained 3 kg, his appetite improved, and his skin discoloration slightly lessened. His blood pressure was stable (110/80 mm-Hg without postural drop), though his cortisol remained low (Table-I). Additionally, the tuberculosis test remained positive, and a lung nodule, although smaller, persisted

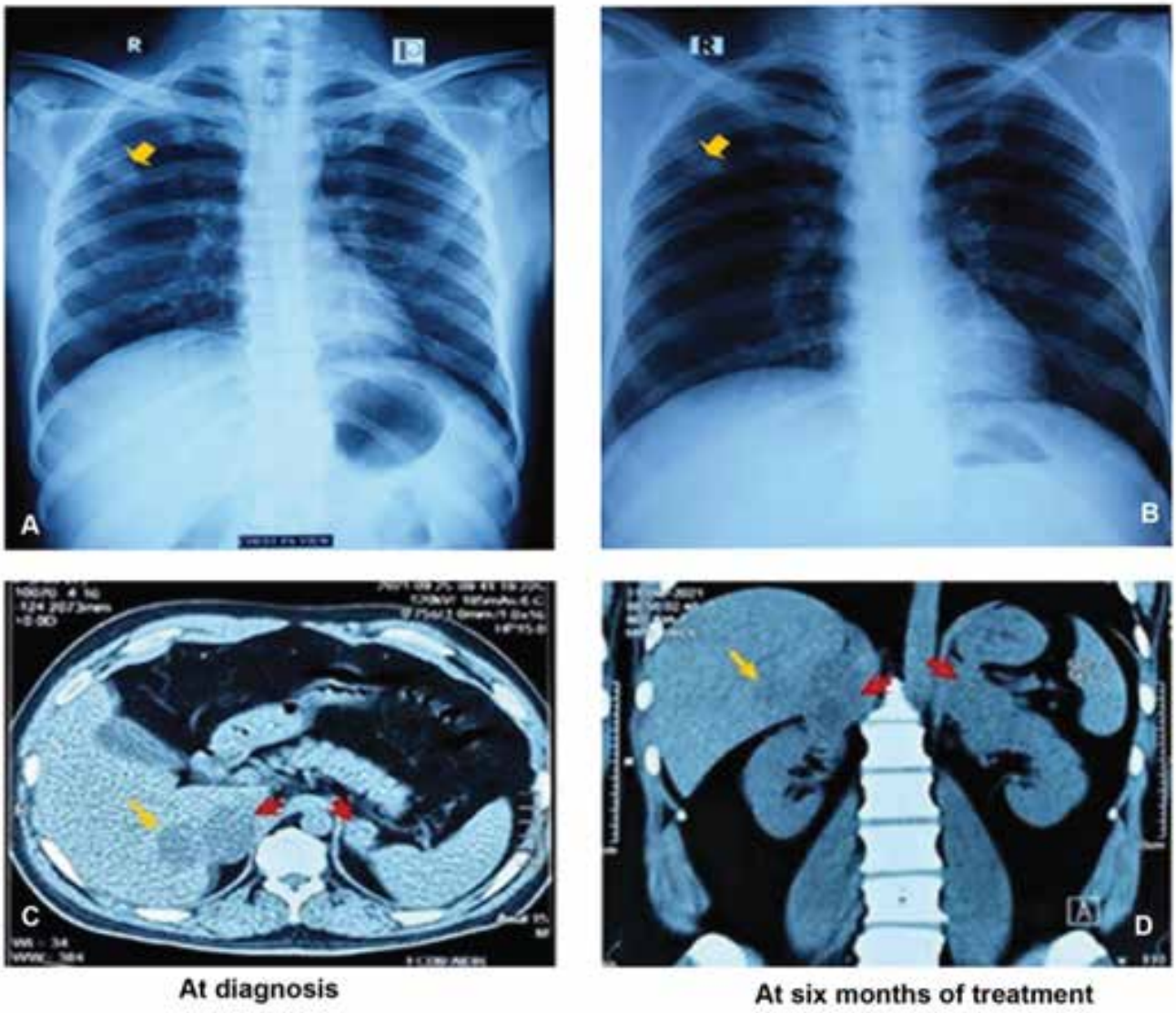

Figure-1: Chest X-ray PA view showing solitary pulmonary nodule at the right upper zone of the chest (yellow arrow) before (A) and after treatment (B). CT scan of the abdomen showed bilateral adrenomegaly (orange dotted arrow) with a space occupying lesion in the right lobe of the liver (yellow arrow) at diagnosis (C) and six months of therapy (D).

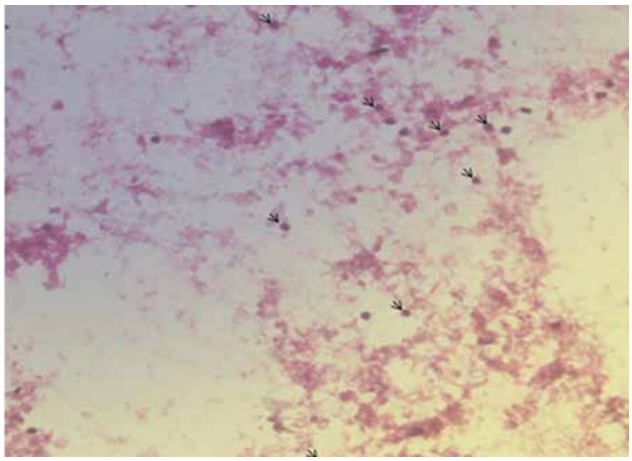

Figure-2: Periodic acid-Schiff's stain for *H. capsulatum* showing budding (black arrow)

(Figure-1B). While his ACTH dropped significantly, imaging still revealed enlarged adrenomegalies and the previous liver lesion without size decrement (Figure-1D).

Discussion

Disseminated adrenal histoplasmosis can cause adrenal insufficiency, which shares symptoms with TB. Both conditions may manifest with fatigue, weight loss, loss of appetite, and fever. When histoplasmosis damages both adrenal glands, it can result in an adrenal crisis characterized by weakness, low blood pressure upon standing, nausea, vomiting, and skin darkening, as seen in the described case.[4, 5, 6, 7] Furthermore, our patient had typical biochemical abnormalities found in

histoplasmosis.[8-10] However, imaging findings of the abdomen overlap with TB, malignancies, and other infections, making definitive diagnosis crucial.[11-13]

A confirmed diagnosis can be made by cytopathological (showing fungal elements), i.e., ultrasonography or CT-guided fine-needle aspiration, and using periodic acid-Schiff (PAS) or Grocott's methenamine silver (GMS) stain.[4] Diagnosis of adrenal histoplasmosis by cytopathological examination might be difficult. This occurs in our case due to technical challenges like deviation of a needle to other tissue, inadequate sample, or sample having only necrotic tissue. In those scenarios, multiple reviews of slides or other methods should be used to aid in diagnosis.

Treatment depends on the symptoms and severity of the disease.[14] Acute adrenal crisis requires fluid resuscitation and corticosteroids, followed by antifungal therapy. Currently, for moderately severe to severe cases, amphotericin B is advised for one to two weeks, followed by itraconazole, and for mild to moderate cases, itraconazole is prescribed. Although the recommended treatment is amphotericin B, itraconazole is also effective in severe form, as seen in the reported case. However, adrenal size remained unchanged in CECT during follow-up. It is seen that even after treatment for 7 years, there is no reduction in the size of the adrenal glands, so size reduction of the adrenal gland should not be the main focus during follow-up of adrenal histoplasmosis.[15,16]

Positive MT and the presence of pulmonary nodules were the initial deceiving factors leading to the start of anti-TB medications. People can be exposed to tubercular bacilli remain asymptomatic in an endemic area, and non-specific tests like MT can be positive. A nodule on the Chest X-ray might be consistent with old-healed TB.[15] In our case, FNAC from the nodule showed an inconclusive inflammatory lesion, and after 6 months of treatment, the nodule did not resolve. It might be an old healed tuberculoma, granulomatous histoplasmosis, or non-specific inflammatory lesion; thus, further evaluation might be needed.

Conclusion

If a patient's diagnosis is uncertain or doesn't improve with TB treatment, doctors should consider testing for histoplasmosis. Based on symptoms and imaging alone, these two infections can be difficult to tell apart. It's crucial to identify the root cause of hypoadrenalism because, without treatment, patients are at risk of a life-threatening adrenal crisis. Fortunately, effective treatment is readily available and affordable.

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Disclosure

The authors declare that no conflict of interest could be perceived as prejudicing the impartiality of the research reported.

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Data Availability

Any inquiries regarding supporting data availability of this study should be directed to the corresponding author and are available from the corresponding author on reasonable request.

Ethical Approval and Consent to Participate

Written informed consent was obtained from the patient. All methods were performed in accordance with the relevant guidelines and regulations.

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