ORIGINAL RESEARCH PAPER

Radiology

KEY WORDS: : Adrenal histoplasmosis, ultrasound, FNAC

Adrenal Histoplasmosis: Clinical, Imaging and Pathological Correlation

Dr.Rakesh Mehra Department of Radiology, Patna Medical College and Hospital Patna Bihar

Dr(Prof.)G.N.Singh Professor and Head, Department of Radiology, Patna Medical College and Hospital, Patna Bihar

Dr.Pallavi Agrawal Assistant Professor, Department of Pathology, Patna Medical College and Hospital, Patna Bihar

ABSTRACT

Background Histoplasmosis is a restricted form of fungal infection caused by histoplasma capsulatum. We describe the clinical, radiological and pathological features of adrenal histoplasmosis .

Method An analysis of 10 cases of adrenal histoplasmosis was done with elaboration of clinical, radiological and histopathological findings during 2014-2017

Results The mean age was 65 years with M:F ratio of 4:1. Most of them presented with complaints of fever, weight loss and chronic fatigue. Adrenal insufficiency was noted in 4 cases. 6 cases had bilateral involvement with 4 cases having unilateral involvement. Ultrasound revealed hypoechoic, homogenous and heterogenous lesions All the cases were confirmed on FNAC and histopathology.

Conclusion Bilateral adrenal enlargement in a nonimmunocompramised patient with variable clinical presentation should always raise the suspicion of histoplasmosis and which subsequently should be confirmed by FNAC.

Introduction

Histoplasmosis is a fungal infection caused by Histoplasma capsulatum. It is endemic in certain parts of the world including Asia. Spores containing H. capsulatum can be found in soils contaminated by droppings from birds and bats. Patients are infected via inhalation of these spores. Around 80 % of them are skin test positive with histoplasmin. Most infected patients are asymptomatic or self-limiting.1 It usually presents in 2 forms; pulmonary and extrapulmonary, which is also known as disseminated histoplasmosis (DH). Disseminated histoplasmosis is uncommon but frequently (80 %) affects the adrenal glands generally presenting as bilateral adrenal masses. 2 A high index of suspicion should always be considered as the presentation may mimic other chronic infections or malignancy especially in the elderly or the immunosuppressed host. Herein we discuss the various clinical, imaging features of adrenal histoplasmosis which were finally confirmed on fine needle aspiration cytology (FNAC) and histopathology.

Materials and Methods

It is an analysis of ten cases of histoplasmosis involving the adrenals who were investigated in a tertiary teaching hospital in Bihar. All cases were seronegative for human immunodeficiency virus (HIV). All of them had cytopathological and histopathological evidence of histoplasmosis with adrenal involvement. Information obtained from the medical records included age, gender, underlying predisposing risk factors for the disease, clinical manifestations, preoperative adrenal function and microbiologic studies.

RESULTS

Of the ten cases identified as having adrenal histoplasmosis, the mean age was 65years with male:female ratio of 4:1. Majority presented with chronic fatigue, weight loss, anorexia, and fever. The history of symptoms ranged from one to six months. Four cases were considered to have primary adrenal insufficiency and underwent adrenocortical function testing. All cases were investigated for adrenal lesion and underwent imaging followed by FNAC to make a final diagnosis. 6 cases had bilateral adrenal mass however 4 cases presented with a unilateral mass followed by bilateral involvement later. The adrenal masses were 1 to 4.2 cm in diameter. All cases were eventually diagnosed by needle biopsy or adrenalectomy. In 5 cases Ultrasound revealed enlarged hypoechoic homogenous lesion in the adrenals while other 5 revealed hetroechoic lesion. (Figure1) FNAC was performed under USG guidance from adrenal gland, which revealed cluster of macrophages with abundant cytoplasm containing yeast form of histoplasma capsulatum.(Figure2)

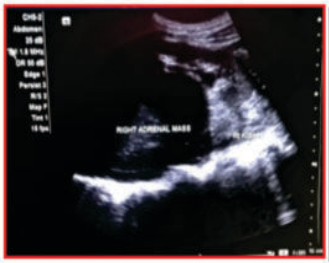

Figure 1 Utrasonography showing hypoechoeic adrenal mass

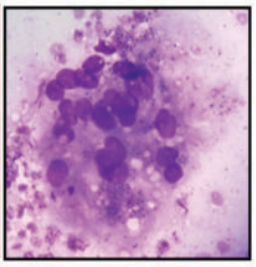

Figure 2 FNAC showing histoplasma in macrophages (Giemsa Stain 40x)

The histopathology showed granulomatous inflammation with giant cell reaction. The sections of the adrenal glands showed oval hyaline granules 2 to 4 µm in diameter, and uninuclate intracellular and extracellular yeast. The yeast had single buds attached by a relatively narrow base and were often clustered. Culture of adrenal tissue obtained in two patients revealed Histoplasma capsulatum. Serum Histoplasma antibodies were positive in four cases. In one case, the patient had systemic histoplasmosis involving the gastrointestinal tract, bone marrow, and spleen. Clinical management depended on the clinical situation of the individual cases. Antifungal drugs itraconazole, and/ or amphotericin B were given to majority of cases. One case was treated with adrenalectomy besides antifungal medication. The treatment resulted in cure in all the cases. These patients were followed up for 2years. All of them showed marked clinical improvement. These cases are illustrated and summarized in Table1

Table 1 Clinical, Radiological and Pathological Features of Adrenal Histoplasmosis

S No.	Age (yr)	Sex	Clinical Presentation	Adrenal insufficiency	Adrenal involvement	Ultrasound findings	FNAC/ HP	Serum histoplasma antibody	Clinical Outcome
1	78	M	Fever,Fatigue	+	U/L later B/L	heteroechoeic lesion	Histoplasmosis	+	Good
2	56	M	Fever,wt loss	_	B/L	Hypoechoeic heterogenous	Histoplasmosis	+	Good
3	52	M	Fever,wt loss	+	B/L	Homogenous hypoechoic	Histoplasmosis	NA	Good

4	45	F	Fever,anorexia	_	B/L	Homogenous hypoechoiec	Histoplasmosis	NA	Good
5	37	M	Wt loss	+	B/L	heteroechoeic lesion	Histoplasmosis	+	Good
6	48	M	Fever,wt loss	_	U/L later B/L	Homogenous hypoechoiec	Histoplasmosis	NA	Good
7	42	F	Fatigue wt loss	+	B/L	Homogenous hypoechoiec	Histoplasmosis	NA	Good
8	39	M	Fever,wt loss	_	B/L	Homogenous hypoechoiec	Histoplasmosis	NA	Good
9	62	M	Fever fatigue wt loss	_	U/L later B/L	heteroechoeic lesion	Histoplasmosis	+	Good
10	65	M	Fever, wt loss	_	U/L later B/L	heteroechoeic lesion	Histoplasmosis	+	Good

Note: U/L Unilateral,B/L Bilateral, HP histopathology

DISCUSSION

Histoplasmosis is a self-limiting pulmonary infection, which is usually asymptomatic. There are three major clinical presentations: 1) Pulmonary 2) Progressive disseminated and 3) Primary cutaneous histoplasmosis. Progressive disseminated form of the disease is rare and occurs in the immunocompromised patients in the endemic areas. Progressive disseminated disease may manifest as chronic disease in immunocompetent host or acute progressive disease in immunosuppressed hosts. In the patients with disseminated histoplasmosis, abdominal imaging usually reveals mild to moderate hepatomegaly with or without splenomegaly. Abdominal lymphadenopathy and focal hypodense lesions in the spleen are also been described. [3]

The patients of adrenal histoplasmosis usually reveal bilateral adrenal masses of varied imaging features. On ultrasonography, they may show uniformly hypoechoic to heterogenous echopattern. Bilateral symmetrical adrenomegaly with preservation of the contour of the gland, central hypodensity with peripheral enhancement and presence of calcification has been typically described in CT. The adrenal glands tend to maintain their normal configuration.4 The differential diagnosis of bilateral adrenal masses with fever, loss of weight, malaise, fatigue, and generalized weakness include tuberculosis, histoplasmosis, metastatic carcinoma, lymphoma,sarcoidosis, amyloidosis, aspergillosis, cryptococcosis, blastomycosis, and penicillosis.5,6 Rarely, longstanding untreated congenital adrenal hyperplasia and macronodular adrenal hyperplasia may also be associated with bilateral adrenal masses. Hence, the diagnosis of adrenal histoplasmosis cannot be made radiologically. Therefore, a high index of suspicion is essential. Characteristic histopathology demonstrates fungal elements and tissue reactivity. Histoplasmosis typically results in a localized mononuclear cell infiltrate developing granulomatous reaction with multinucleated giant cells. Yeast in tissue sections show uninuclate hyaline spherules or ovules 2 to 4 µm in diameter. Using special stains like Periodic acid Schiff stain and Gomori methamine silver stain, yeast may be detected in necrotic areas. Other laboratory tests, such as serology, complement fixation, a precipitation test, latex particle agglutination test, agar-gel double immunodiffusion test and radioimmunoassay have also been used. However, the gold standard for a definite diagnosis of histoplasmosis is tissue culture.7 FDG-PET is a useful modality for distinguishing malignant from benign adrenal lesions in patients with incidentally detected adrenal tumors on CT or MRI. There is increased uptake of FDG by malignant adrenal lesions, with a reported sensitivity of 100% and specificity of 80–100%.[8]

Adrenal infection is most frequently caused by haematological spread. Most patients had symptoms, clinical signs, laboratory and radiological features resembling adrenal neoplasms. So ultrasound proves to be a cheap, quick, effective and non-invasive tool in early diagnosis of such cases. Mycobacterium tuberculosis is the most common bacterial pathogen associated with adrenal destruction. Fungal infection is an uncommon disease of the adrenal gland. Most reported cases have involved Histoplasma species. Adrenal histoplasmosis has a wide spectrum of clinical manifestations, including chronic fatigue, weight loss, anorexia, and fever. Duration of the presenting symptoms is highly variable, ranging from one to six months. Patients with adrenal histoplasmosis exhibit fever, malaise, orthostatic hypotension, nausea, and vomiting. Hyperkalemia, hyponatremia and eosinophilia are present. Addison disease typically occurs with extensive destruction of both adrenal glands by infection. In early stages of destruction, it typically presents as chronic fatigue syndrome.9,10 The majority of individuals with histoplasmosis recover spontaneously and do not require specific therapy. Supportive treatment is often recommended for symptomatic acute histoplasmosis. However, chronic and severe acute infections must be treated. Adrenal histoplasmosis should be treated like disseminated histoplasmosis. Patients who are not severely ill can be treated with oral itraconazole. Patients with severe infection should be treated initially with amphotericin B or the lipid formulation of amphotericin B.[11]

This study elaborates the clinical, pathological and radiological findings of adrenal histoplasmosis and emphasizes the importance of imaging and image guided FNAC in the early diagnosis and treatment of such cases. Bilateral adrenal enlargement in a nonimmunocompramised and non-tubercular patient with variable clinical presentation should always raised the suspicion of histoplasmosis and which subsequently should be confirmed by FNAC. Our paper demonstrates that adrenal histoplasmosis does occur in immunocompetent persons living in areas not endemic for the disease and the imaging features are variable. In the regions where endemic, possibility of histoplasmosis should always kept in a patient with enlarged, hypoattenuating bilateral adrenal glands with peripheral rim enhancement and enhancing internal septations. Image guided FNAC will demonstrate the disease and should be performed without delay as a great number of patients with adrenal histoplasmosis may develop life-threatening adrenal insufficiency if untreated.There is limited description in the literature of the initial diagnosis of adrenal histoplasmosis so further larger case studies are recommended to know the behaviour and clinical outcome.

References

1) Goswami R, Pramanik N, Banerjee D, Raza M, Guha S, Maiti P. Histoplasmosis in eastern India: the tip of the iceberg? Transactions of the Royal Society of Tropical Medicine and Hygiene 1999;93:540-542.
2) Kumar N, Singh S, Govil S. Adrenal histoplasmosis: clinical presentation and imaging features in nine cases. Abdominal Imaging 2003;28:703-708.
3) Radin DR. Disseminated histoplasmosis: Abdominal CT findings in 16 patients. AJR Am J Roentgenol. 1991;157:955–8.
4) Levine E. CT evaluation of active adrenal histoplasmosis. Urol Radiol 1991;13:103–6.
5) Rozenblit AM, Kim A, Tuvia J, Wenig BM. Adrenal histoplasmosis manifested as Addison's disease: unusual CT features with magnetic resonance imaging correlation. Clin Radiol. 2001;56:682–4.
6) Schonfield AD, Jackson JA, Smith DJ, Hurley DL. Disseminated histoplasmosis with bilateral adrenal enlargement: diagnosis by computed tomography directed needle biopsy. Tex Med. 1991;87:88–90.
7) Kawashima A, Sandler CM, Fishman EK, Charnsangavej C, Yasumori K, Honda H, et al. Spectrum of CT findings in non-malignant disease of the adrenal gland. Radiographics. 1998;18:393–412.
8) Yun M, Kim W, Alnafisi N, Lacorte L, Jang S, Alavi A. 18FFDG PET in characterizing adrenal lesions detected on CT or MRI. J Nucl Med 2001;42:1795–9.
9) Rozenblit AM, Kim A, Tuvia J, Wenig BM. Adrenal histoplasmosis manifested as Addison's disease: unusual CT features with magnetic resonance imaging correlation. Clin Radiol 2001; 56: 682-4.
10) Sarosi GA, Voth DW, Dahl BA, Doto IL, Tosh FE. Disseminated histoplasmosis: results of long-term follow-up. A center for disease control cooperative mycoses study. Ann Intern Med 1971; 75: 511-6
11) Wheat J. Histoplasmosis: experience during outbreaks in Indianapolis and review of the literature. Medicine 1997; 76: 339-54.