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Case Report

Cyto-diagnosis of unilateral adrenal histoplasmosis mimicking a primary adrenal neoplasm in an immunocompetent patient

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ABSTRACT

Histoplasmosis mostly shows bilateral adrenal gland involvement in immunocompromised patients. Our case is of a 43 years old immunocompetent male patient having pain in the left flank for one month. CECT abdomen revealed a well-defined hypodense mass measuring 64×61×56 mm with necrotic areas in right adrenal region. A possibility of primary adrenal neoplasm was suggested. Left side adrenal gland was normal. Microscopic examination of imprint smears from adrenal mass revealed cellular smears revealing histiocytes, plasma cells, lymphocytes and numerous intra-cytoplasmic and extra-cytoplasmic yeast forms with basophilic crescent shaped nucleus with pericellular halo. Background showed RBC's, acellular debris and multinucleate giant cells. Diagnosis of histoplasmosis was suggested which was confirmed on histopathology and culture. Patient recovered with anti-fungal treatment. If Fine needle aspiration (FNA) of the adrenal mass would have been done, adrenalectomy could be prevented. This case highlights the importance of FNA in diagnosing abdominal lumps and avoiding unnecessary surgery.

Keywords: Adrenal histoplasmosis, Immunocompetent, Unilateral involvement

INTRODUCTION

Histoplasmosis is the most common systemic mycosis, characteristically affecting the reticuloendothelial system, blood, and its components. Immunocompromised states like uncontrolled diabetes, AIDS or malignancy results in invasion and dissemination of the histoplasma. Majority of the cases are asymptomatic. Symptomatic patients present with self-limited manifestations like influenza like syndrome and fever. The chronic form of the disease is mainly localized to the lungs and manifests with tuberculosis like picture and sequelae. Disseminated histoplasmosis (1:2000 cases) is quite rare, occurring mostly in acute rather than chronic forms. Adrenal involvement can be either a part of disseminated form in immunosuppressed patients or as a localized adrenal disease.[1] Patients often present with bilateral adrenal masses.[2] Unilateral involvement of adrenal gland in an immunocompetent person which was seen in our case is extremely rare.[3]

CASE REPORT

A 43 years old non-diabetic male patient presented with pain in the left flank for one month. CECT abdomen revealed a well-defined hypodense mass measuring 64×61×56 mm showing moderate heterogenous enhancement and necrotic areas in right adrenal region with prominent periportal and para-aortic lymph nodes. The mass was displacing the kidney, liver and IVC. Adrenal gland was not identified separately. A possibility of primary adrenal neoplasm was suggested. Left side adrenal gland was normal. Serum Na+ levels were 119 mmol/L (low) and serum K+ levels were 5.36 mmol/L

(high). Serum ALP levels were 1228 U/L (high). Serum Cortisol level was 1.20 ug/dl (low). ACTH level was 901 pg/ml (high). Plasma adrenaline was 4 pg/ml and nor-adrenaline were 107.51 pg/ml (both were low). The enzyme-linked immunosorbent assay (ELISA) test for detecting the antibody against HIV1 and HIV2 was nonreactive. The Mantoux test was negative. Right adrenalectomy was performed. Microscopic examination of imprint smears from adrenal mass revealed cellular smears revealing histiocytes, plasma cells, lymphocytes and numerous intra-cytoplasmic and extra-cytoplasmic yeast forms with basophilic crescent shaped nucleus with pericellular halo (Figure 1).

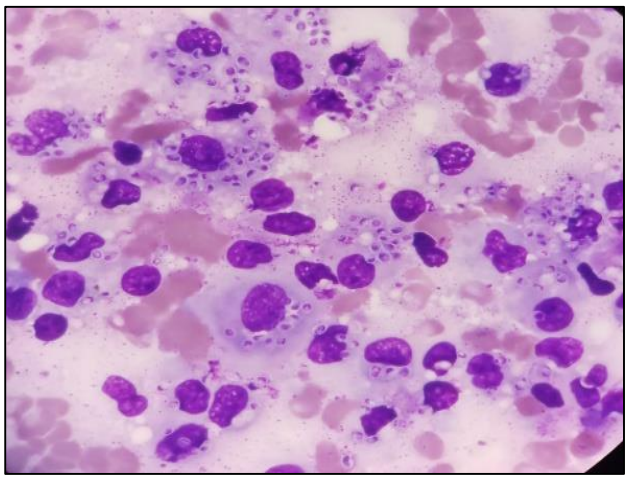

Figure 1: Imprint smears showing numerous histiocytes showing intra-cytoplasmic and extra-cytoplasmic yeast forms with basophilic crescent shaped nucleus and pericellular halo (Giemsa, ×100).

Background showed RBC's, acellular debris and multinucleate giant cells. PAS and GMS staining showed positivity in capsule (Figure 2).

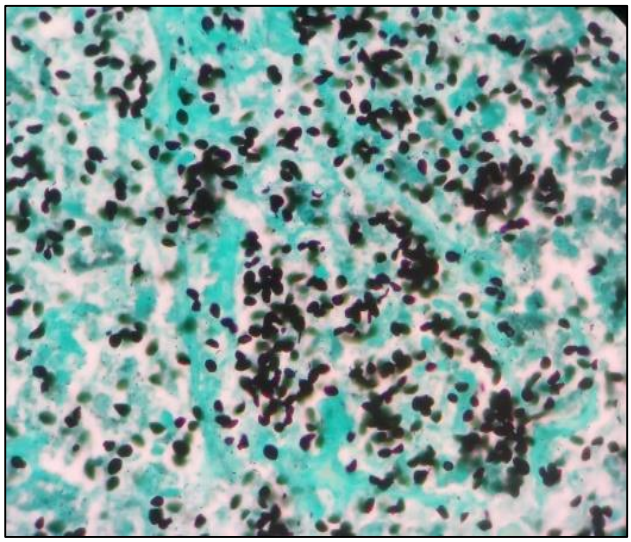

Figure 2: Numerous yeast forms in the necrotic region (GMS, ×100).

Diagnosis of histoplasmosis was suggested. Culture study was advised for confirmation. Grossly, we received a partially encapsulated grey brown to tan brown soft tissue mass measuring 8.5×6.5×3 cm. Cut section revealed predominantly necrotic area and only partially identified normal parenchyma pushed to the periphery. Histopathological examination revealed predominantly necrosis and haemorrhage. Viable area revealed intracytoplasmic and extracytoplasmic yeast forms with crescent shaped nucleus with PAS positive capsule along with chronic inflammatory cells (Figure 3) Grocott-Gomori methenamine silver stain (GMS) also revealed the yeast forms. Diagnosis of histoplasmosis was confirmed on culture. The patient was treated with Amphotericin B. Steroids were given for adrenal insufficiency.

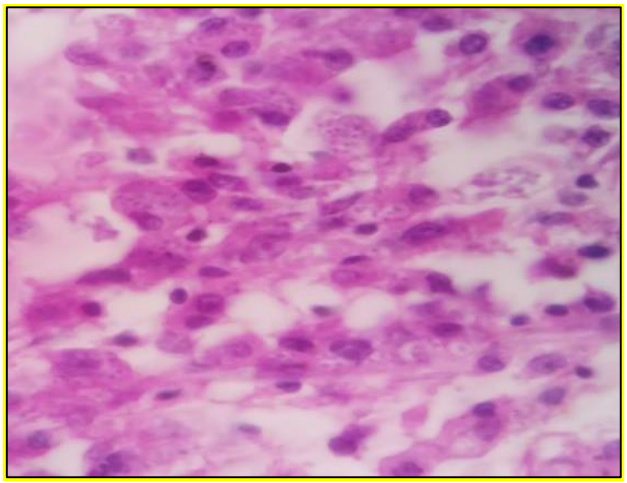

Figure 3: Histopathological sections revealing intra- and extra-cytoplasmic yeast forms (H and E, ×100).

DISCUSSION

Histoplasmosis is caused by the inhalation of spores of dimorphic fungus *H. capsulatum* found in soils contaminated by bird and bat excreta.[4] It occurs temperate and tropical countries in USA, Africa, and Australia. In India, Panja and Sen reported the first case of disseminated histoplasmosis from Calcutta in 1954. Since then, individual cases have been reported from various states, mostly from West Bengal, Andhra Pradesh and Bihar, in immunocompromised patients and showing bilateral involvement of adrenal glands. Unilateral involvement of adrenal gland in an immunocompetent patient is extremely rare.

Histoplasma grows as a mycelium at ambient temperatures especially in moist acidotic soils in river banks and caves and in bat and bird droppings. When the microsporidia are inhaled, it changes its form and grows as a yeast within the alveolar macrophages. Then, it disseminates via reticuloendothelial system to other parts of the body.[5] As mentioned above, it may be asymptomatic, mild influenza-like symptoms, acute, chronic and disseminated disease. It usually affects immunocompromised individuals and

adrenal gland involvement almost always is bilateral. Our case is extremely rare as the patient was immunocompetent and only unilateral adrenal gland was involved.

The differential diagnosis that should be considered includes tuberculosis, blastomycosis, *Penicillium marneffei*, coccidomycosis, cryptococcosis, sarcoidosis, adrenal haemorrhage, primary neoplasm, metastatic carcinoma and lymphoma.[3]

Tuberculosis was kept as one of the differential diagnoses because there was necrosis and numerous multinucleate giant cells. However, it was ruled out because ZN stain and Monteaux test were negative and also because the intracellular and extracellular yeast forms were clearly seen.

Blastomyces dermatitidis has 8-15 um thick-walled spore with broad-based bud and double-contoured cell wall. *Cryptococcus neoformans* has 4-12 um teardrop-shaped buds and spores with distinct mucopolysaccharide rich wide capsule. *Coccidioidomycosis immitis* has 10-80 um thick-walled spores with granular cytoplasm. The larger spores contain endospore.

Penicillium marneffei is another emerging pathogenic dimorphic fungus causing fatal systemic mycosis in immunocompromised patients. *Penicillium marneffei* infection may be considered the homologue of *H. Capsulatum* infection since both exploit the macrophage as a host cell and both can cause acute or persistent pulmonary and disseminated infection and reactivation disease.

Microscopically, they appear as unicellular organisms with round to oval cells of 2-3 um. These cells may divide by cross wall formation within macrophages or alternatively, to form extracellular elongated cells (upto 13 um). These cross wall formations can differentiate yeast cells of *Penicillium marneffei* from *H. Capsulatum*.[6]

Thus, the size of the organism, localization (intracellular or extracellular), cytomorphology and special stains helps us in diagnosis. Histoplasma serum and urine antigen assays, polymerase chain reaction assays, blood cultures, immunoprecipitation antibodies, and complement fixing antibodies also support the diagnosis. But fungal culture is the gold standard confirmatory investigation.

Pheochromocytoma was ruled out because of the absence of epithelial-like aggregates of tumor cells with fine granular relatively abundant cytoplasm. Also, the catecholamine levels which are usually increased in pheochromocytoma were low in our case.

Metastatic carcinoma was ruled out because of the absence of sheets and clusters of malignant tumor epithelial cells.

Lymphoma was ruled out because of the absence of monomorphic population of atypical/malignant lymphoid cells.

This patient was immunocompetent since he was non diabetic, had negative retroviral screening tests and did not have any history of recurrent infections.

CONCLUSION

FNA plays a very important role in diagnosing abdominal lumps and further management of the patient. It not only helps in early diagnosis of the lesion but also in avoiding unnecessary surgeries as was done in this case.

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REFERENCES

1. Kothari D, Chopra S, Bhardwaj M, Ajmani A, Kulshreshtha B. Persistence of histoplasma in adrenals 7 years after antifungal therapy. Indian J Endocrinol Metabol. 2013;7(3):529-31.
2. Kumar N, Singh S, Govil S. Adrenal histoplasmosis: Clinical presentation and imaging features in nine cases. Abdom Imaging. 2003;28(5):703-8.
3. Wahab N, Zainudin R, Kamaruddin N. Adrenal involvement in histoplasmosis. EXCLI J. 2013;12:1-4.
4. Gupta P, Bhardwaj M. Cytodiagnosis of disseminated histoplasmosis in an immunocompetent individual with molluscum contagiosum-like skin lesions and lymphadenopathy. J Cytol. 2016;33(3):163-5.
5. Rit K, Naha A, Saha R. Adrenal histoplasmosis with disseminated cutaneous manifestations in an immunocompetent patient: A case report. Muller J Med Sci Res. 2015;6(1):72-4.
6. Vanittanakom N, Cooper C, Fischer M, Srisanthana T. Penicillium marneffei infection and recent advances in the epidemiology and molecular biology aspects. Clin Microbiol Rev. 2006;19(1):95-110.

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