

## Case Reports

### A Child with Chronic Fungal Infection in Bangladesh that Mimicked Malignancy: Disseminated Histoplasmosis

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#### Summary:

*Histoplasma capsulatum* is a dimorphic fungus, which primarily causes a pulmonary disease. It is found throughout the world with the soil being the environmental reservoir. In infants and toddlers, disseminated histoplasmosis is the commonest presentation. In this age group, 60-80% patients has acute disseminated progressive disease. Disseminated histoplasmosis may also cause bone involvement with osteolytic lesion. Here, we have described a rare and unusual disseminated histoplasmosis, a 3 and half year old boy from Bangladesh with multiple abscess like soft tissue lesions, along with multiple osteolytic bone lesions.

**Key words:** Disseminated histoplasmosis, Child, Abscess, Osteolytic lesion

#### Introduction:

Histoplasmosis was first described a little over a century ago by an American physician, Samuel Darling, who was working in the Canal Zone in Panama. He described the disseminated form of the disease in a fatal case.<sup>1</sup> It took decades to prove that *Histoplasma capsulatum* is a dimorphic fungus residing in soil, which primarily causes a pulmonary disease.<sup>2, 3</sup> Exposure to *H. capsulatum* is very common for persons living within areas of endemicity, but symptomatic infection is uncommon. Incidence of histoplasmosis in USA is 6.4 per million population in adults.<sup>4</sup>

*Histoplasma capsulatum* is found throughout the world. It is endemic in certain areas of the United States. Bird and bat droppings in soil promote growth of *Histoplasma*. Contact with such soil aerosolizes the microconidia, which can infect humans. It is also common in many parts of Africa.<sup>5</sup> In India, the

Gangetic West Bengal is the site of most frequent infections, with 9.4 percent of the population testing positive.<sup>6</sup> *Histoplasma capsulatum* was isolated from the local soil proving endemicity of histoplasmosis in West Bengal.<sup>7</sup>

The usual case of acute pulmonary histoplasmosis is a self-limited illness occurring mostly in children exposed to the organism for the first time. Symptoms include fever, headache, sub-sternal chest discomfort and dry cough.<sup>8</sup> In infants and toddlers, disseminated histoplasmosis is the commonest presentation, occurring in 60-80% of patients. Sixty to seventy percent of them may also have bone marrow involvement, which is manifested as pancytopenia and coagulopathy.<sup>9, 10</sup>

In an acutely ill patient, tissue biopsy should be done as soon as possible to look for *H. capsulatum*. Finding the distinctive 2 to 4  $\mu$ m, oval, narrow-based budding yeasts allows a tentative diagnosis of histoplasmosis.<sup>11</sup> Chronic pulmonary and progressive disseminated histoplasmosis were often fatal if not treated.<sup>12</sup> All patients with disseminated histoplasmosis should be treated with an antifungal agent.<sup>13</sup>

#### Case Report:

A 3½-year old boy from southern Dhaka, Bangladesh, was presented to the Bangabandhu Sheikh Mujib Medical University (BSMMU) of Dhaka, with recurrent, multiple abscess like swelling over body for the last 2 years.

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**Received:** 08 March 2018    **Accepted:** 21 June 2018

The initial swelling was over the right side of chest at the age of 1½ years. It was soft, painful, associated with irregular fever and was partially improved with antibiotic and surgical drainage. At 2 year of age, the child was admitted in a medical college hospital for irregular fever. There, physicians noticed nodular swellings (lymph nodes) over the sides of his neck and axilla and advised a biopsy. The histopathology of axillary lymph node found caseation granuloma, most likely due to Tuberculosis. So Anti-TB medication was started and was continued for 9 months. In the meanwhile, the child developed more and more abscess like swellings over scalp, forehead, eyelids, forearms, hands and feet. Fever was low grade and occasionally high grade in nature. X ray of skull that showed osteolytic lesion. Then the patient was referred to BSMMU.

There was no H/O prolong cough, recurrent pneumonia or diarrhea, polyuria, polydipsia, seborrheic dermatitis or contact with TB patient. The

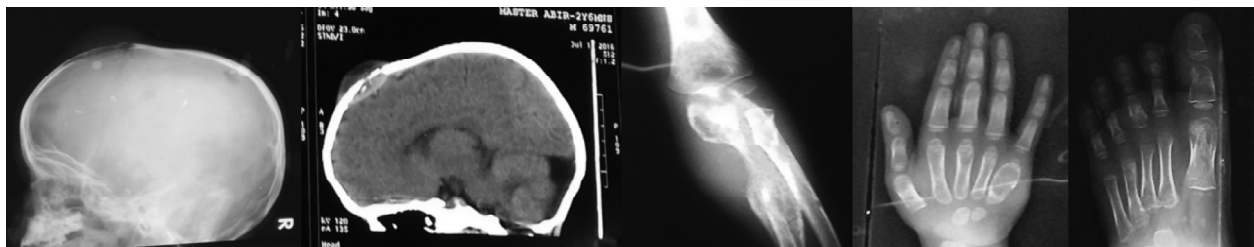
child lives in a village with plenty of birds and chicken in the surroundings.

On admission, the child was ill looking, fretful, moderately pale, had generalized lymphadenopathy, multiple tender swellings over scalp, forehead, eyelids, forearms, hands and feet, some are soft and nodular and some are ulcerated with whitish discharge. He had hepatomegaly, 4 cm, and firm in consistency. Movements of both elbows were restricted due to pain. All other systemic examination revealed no abnormality.

The child was found anemic (Hb 7.2 gm/dl), had high ESR (106 mm in 1<sup>st</sup> hour), neutrophilic leucocytosis (20,000/cumm, N- 52%), thrombocytosis (platelet-520,000/cumm), serum ALT was 22 U/L, serum creatinine was 0.62 mg/dl, serum electrolytes were normal. Mantoux test was negative, serum Ig E was high (240 U/L), Ig G, Ig M and Ig A were in the normal range. There was no growth in blood culture. X ray showed osteolytic lesion in skull, forearm, hands and feet. CT scan of brain showed osteolytic lesion of skull with intracranial extensions.



**Fig.-1:** Swellings all over body, some with ulcerations



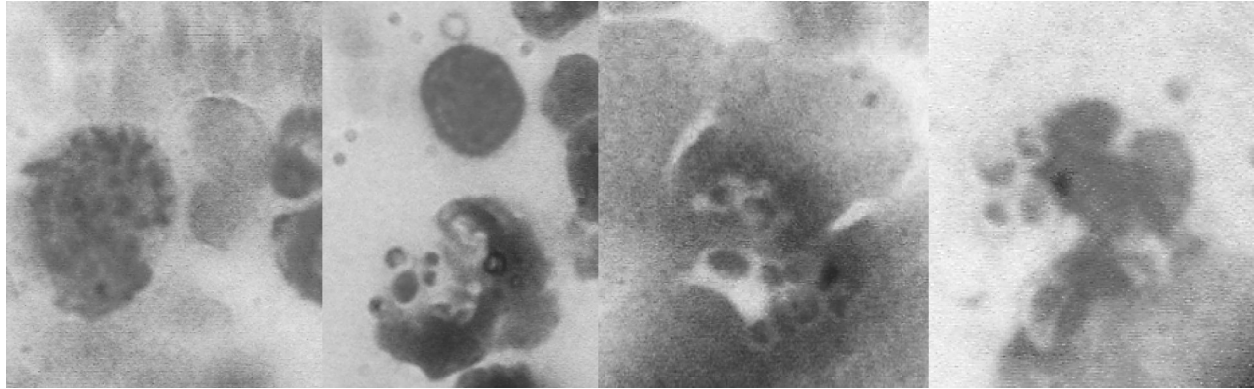
**Fig 2:** Osteolytic lesions



**Fig 3:** Normal chest Xray

Soft tissue biopsy from scalp was done. There were dense infiltration of acute and chronic inflammatory cells and histiocytes with many intra and extracellular round to ovoid bodies, resembling *Histoplasma capsulatum*, suggestive of *Histoplasmosis*. The report was reviewed and reconfirmed by 3 different laboratories. Bone marrow aspiration was done. It also revealed intracellular *Histoplasma capsulatum*.

The child was started with intravenous Amphotericin deoxycholate along with ceftriaxon and amikacin. But the response to treatment was poor for initial 14 days.



**Fig 4:** Direct microscopic identification of *Histoplasma capsulatum*

Then surgical drainage of the abscesses was done. Since then, the patient began to show clinical improvement in terms of fever, pain and general condition. Systemic amphotericin was continued for 82 days. Then he was advised to continue daily oral itraconazole prophylaxis.

At the end of treatment, the child was asymptomatic, afebrile, all the swellings disappeared with no lymphadenopathy or organomegaly. His blood counts and biochemistry were also normal. So far, this is the first case of completely treated Disseminated Histoplasmosis in Bangladesh. All pictures were captured with permission from parents, with an intention for dissemination of knowledge only.



**Fig 5:** Clinical improvement after systemic anti-fungal treatment

#### **Discussion:**

Here, we have described a 3½-year old child from Bangladesh with multiple bony and soft tissue lesions, initially resembling the diagnosis of Langerhans cell histiocytosis; but at the end was diagnosed as disseminated histoplasmosis.

Our patient's initial presentation was recurrent multiple abscess with generalized lymphadenopathy, for which his initial diagnosis was Tuberculosis. But, even after 9 months of anti-tubercular treatment his disease was still progressing. On re-evaluation, multiple osteolytic lesions were found. Our patient was then diagnosed with the help of direct microbiological study. The diagnostic samples were tissue from scalp abscess, lymph node biopsy sample and bone marrow aspirates. Direct microscopy revealed many intra and extracellular round to ovoid micro-organisms, which were characteristic of *Histoplasma Capsulatum*. His response to treatment with systemic antifungal was also supporting his diagnosis.

Multifocal osteolytic lesions in children are often due to Langerhans cell histiocytosis (LCH), leukemia, neuroblastoma, multifocal osteomyelitis.<sup>14</sup> But, it may also occur in patients with disseminated histoplasmosis. African histoplasmosis presents with tender subcutaneous abscesses and osteolytic lesions of skull, vertebrae, ribs and long bones.<sup>15</sup> It may also be asymptomatic, as in a case of histoplasmosis of bone manifested by a single punched-out lesion in the humerus in a man with mild chronic disseminated histoplasmosis.<sup>16</sup> In the north-eastern India, a 13-year-old immunocompetent child presented with florid bone involvement with *Histoplasma capsulatum*, who had chronic exposure to pigeon droppings.<sup>17</sup>

Our patient was from sub-urban areas of Bangladesh, where there is adequate exposure to soil containing birds and bat excreta. As histoplasmosis is not very common in this part of the world, his diagnosis was much delayed. Here direct microscopic identification of fungus was done, which was not expensive, but requires professional experience of the department of pathology and microbiology. This case emphasizes the need for considering fungus as an etiology in any chronic, antibiotic refractory infection.

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