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Subcutaneous Mycosis Clinically Diagnosed as Lymphoma

KEYWORDS: verrucous , FNAC, mycosis

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ABSTRACT *Diagnosis of certain benign conditions as fungal diseases is frequently missed for many reasons:*

(1) rarity of the lesion (2) requirement of careful search for diagnostic clues which are often sparse in clinical material such as tissue and exudates (3) often they elicit tissue reactions such as verrucous lesion and micro abscesses, misleading the diagnosis (4) lack of 'clinical suspicion'. Here is a case of an eleven-year-old boy who presented with verrucous lesions over nose, back of trunk and leg along with multiple gradually enlarging subcutaneous nodules over neck for last one year. The patient was otherwise healthy. Fine Needle Aspiration Cytology (FNAC) done from subcutaneous nodules showed some faintly stained branching fungal elements (Hematoxylin and Eosin stain). Gomori Methenamine Silver (GMS) stained the branching hyphae and budding yeasts black. Hence the diagnosis of Subcutaneous mycosis was made. The differentials we included were Chromoblastomycosis, sporotrichosis, blastomycosis, histoplasmosis.

Introduction:
The "subcutaneous" mycoses are due to a diverse group of organisms that cause disease when implanted or otherwise introduced into the dermis or subcutis. Sporotrichosis, mycetoma and chromoblastomycosis are common subcutaneous mycoses. Infection slowly evolves as the etiologic agent survives and adapts to the adverse host tissue environment. Diagnosis rests on clinical presentation, histopathology, and culture of the etiologic agents. We have considered sporotrichosis, chromoblastomycosis, blastomycoses and histoplasmosis as the differentials of our case.

Case History:
1. An eleven-year-old boy resident of a hilly area presented with verrucous lesions over the nose (Fig 1) along with multiple progressively enlarging cervical subcutaneous nodules largest measuring 5x4 cm, undergoing cystic changes with the overlying skin partially ulcerated and discharging. The lesions were present for the last one year. His elder sister had a history of similar skin lesions and was on anti-tubercular drugs from another center after a biopsy report showed granulomatous pathology.

The patient was otherwise healthy without any association with pain, trauma, diabetes mellitus, fever, HIV infection or any other chronic illness.

2. Fine Needle Aspiration Cytology (FNAC) from the cervical subcutaneous nodules yielded cellular smears comprising (Fig 2) of large number of histiocytes, lymphocytes, macrophages and polymorphs with multinucleated giant cells lying in a background of blood mixed necrosis and faintly stained branching fungal elements (Hematoxylin and Eosin stain).

3. Ziehl Neelsen staining was negative for acid fast bacilli.

4. Gomori Methenamine Silver (GMS) staining shows (Fig 3) the branching hyphae and budding yeast black, lying in a background of inflammatory cells.

Discussion:
Subcutaneous mycoses include a range of different infections which are characterized by infection of the subcutaneous tissues usually at the point of traumatic inoculation. An inflammatory response develops in the subcutaneous tissue frequently with extension into the epidermis. Sporotrichosis and chromoblastomycosis are common causes of subcutaneous mycoses. Blastomycoses and histoplasmosis cause deep mycoses but may present with subcutaneous lesions and verrucous plaques [1,2].

Chromoblastomycosis is a slow growing chronic granulomatous fungal infection that arises mostly in the tropics affecting mainly males and rural workers[3]. It is characterized by verrucous plaques or nodules attributed to infection by different pigmented fungi which includes *Fonsecaea pedrosoi, Fonsecaea compacta, Fonsecaea monophora* etc. Usually the infection develops after injury, being primarily located on the lower extremities [3,4,5].The clinical presentation and colonial morphologies of each of these fungi are very similar, and differentiation is based on microscopic and conidial characteristics.

Chromoblastomycosis can be easily diagnosed on H and E stained cytological smears when the organisms are in good numbers by demonstrating diagnostic pigmented Sclerotic bodies. It is really challenging for pathologists when (1) the organisms are sparse, (2) the lesion is not fully evolved (as in early ulcer/ plaque stage) and (3) there is no 'clinical suspicion' in the request form.

Sporothrix schenckii commonly occurs in nature as a saprophyte on dead plant material. this dimorphic mold is worldwide in distribution. *Sporothrix schenckii* most commonly gains entrance into the host through traumatic inoculation as a contaminant .The predominant clinical manifestation of the disease is lymphocutaneous sporotrichosis [6]. Diagnosis of *Sporothrix schenckii* depends on demonstration of oval- to elongate-shaped budding yeast-like cells in the tissue

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phase. Given the low numbers fosund in pus, exudates, or aspirates from lesions, Clinical diagnosis is dependent on culture.

Blastomycosis *dermatitidis*, a dimorphic fungus has usually a recent history of occupational or recreational exposure. Chronic pneumonia is recognized in 60-90% of patients with proven blastomycosis. The skin and subcutaneous tissues are the next most common site involved in 38-80% of cases. Two types of skin lesions are seen: verrucous lesions and cutaneous ulcers [7].

Blastomycosis is histologically associated with granulomatous nodules. Definitive diagnosis of blastomycosis requires isolation in culture of *B. dermatitidis* from a clinical specimen. A presumptive diagnosis is made on the basis of histopathology or cytopathology revealing characteristic, broad-based, budding yeasts with a doubly-refractile cell wall demonstrated from a clinical specimen. Once suspected, the diagnosis of blastomycosis can usually be confirmed by demonstration of the characteristic broad based budding organisms in sputum or tissues by KOH prep, cytology, or histology. Commercially available urine antigen testing appears to be quite sensitive in suggesting the diagnosis in cases where the organism is not readily detected.

Histoplasmosis is caused by the *Histoplasma capsulatum* found throughout the world. Symptoms of this infection vary greatly, but the disease affects primarily the lungs. Occasionally, other organs are affected; this is called disseminated histoplasmosis, and it can be fatal if left untreated.

Histoplasmosis is common among AIDS patients. Histoplasmosis is found in soil, often associated with bird droppings. Contact with such soil aerosolizes the microconidia, which can infect humans

Histoplasmosis can be diagnosed by samples containing the fungus taken from sputum, blood or infected organs. It can also be diagnosed by detection of antigens or antibodies in blood or urine samples by ELISA or PCR. Formal histoplasmosis diagnoses are often confirmed only by culturing the fungus directly [8]. Cutaneous manifestations of disseminated disease are diverse and often present as a nondescript rash with systemic complaints. Diagnosis is best established by urine antigen testing. Blood cultures may take up to 6 weeks for diagnostic growth to occur and serum antigen testing often comes back with a false negative before 4 weeks of disseminated infection [9].

In the present case, clinical suspicion for lymphoma was strong and the diagnosis was incidental in cytopathology. The only clue that made us search for organisms were numerous multinucleated giant cell in a background of dense mixed inflammatory infiltrate

In conclusion, It is well known that many cases are missed cytologically (as well as histologically) due to lack of 'clinical suspicion'. Clinician should include fungal causes in the differential diagnosis whenever they encounter above lesions and should send the unfixed extra sample for mycological culture studies. also whenever pathologists encounter warty, verrucous lesions they should make every effort for complete search for fungal elements.

Fig 1- Clinical picture showing the verrucous lesion over nose and neck

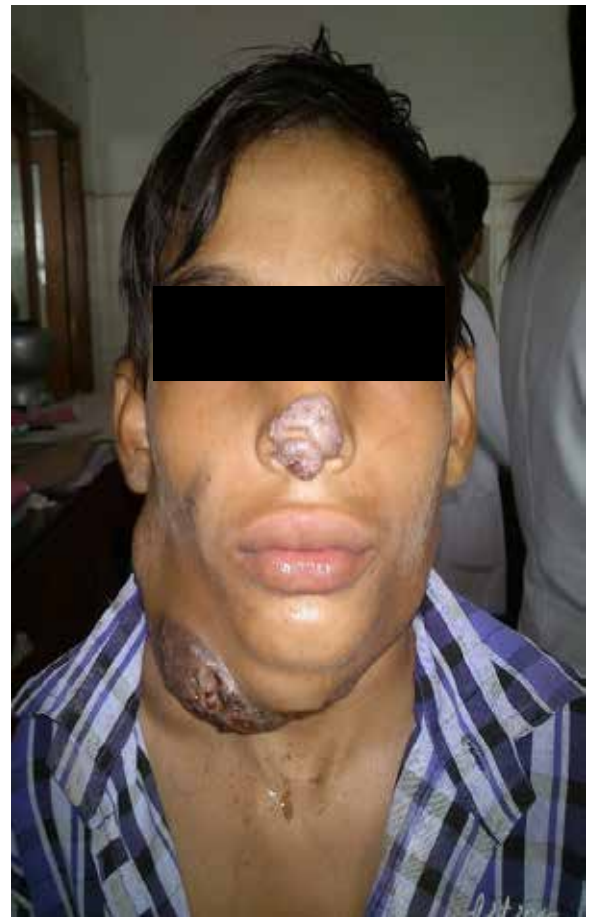
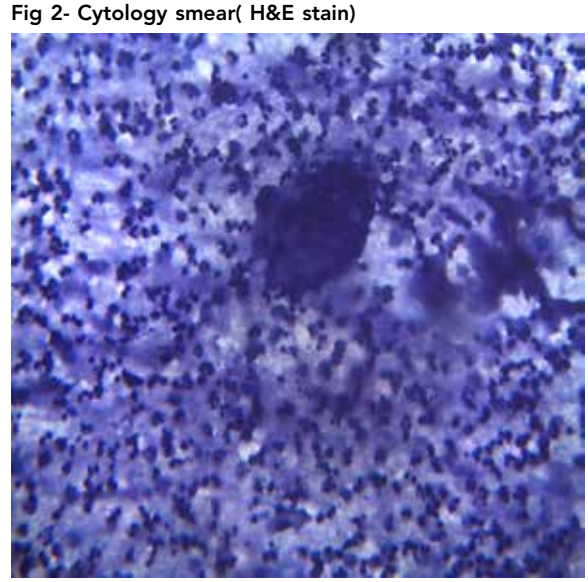


Fig 2- Cytology smear(H&E stain)



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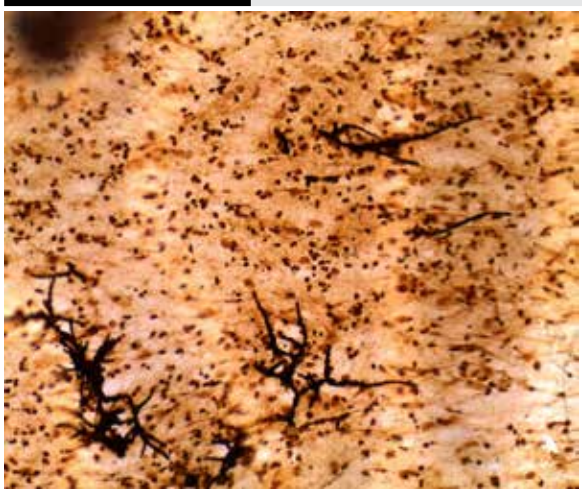

Fig 3- Smear in GMS stain

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