Case Report

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Pathology Section

Candida Albicans Infection Masquerading as a Soft Tissue Tumour Diagnosed by Fine Needle Aspiration Cytology

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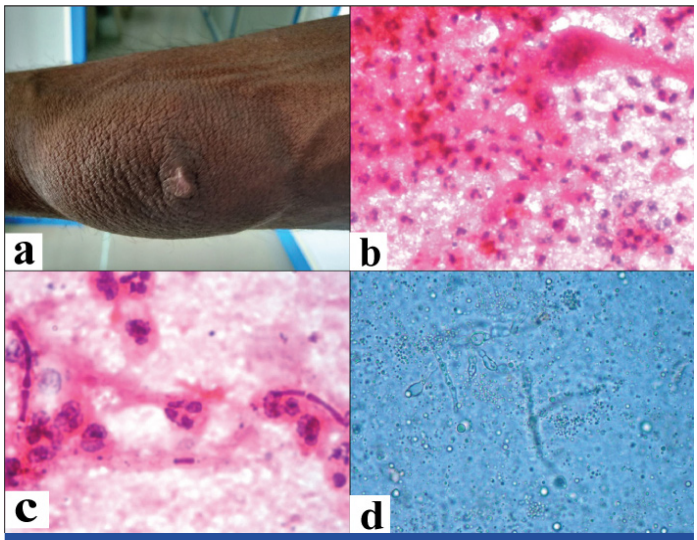
ABSTRACT

A 60-year-old male, diabetic presented with a soft tissue mass over the right forearm of 15 days duration. The swelling was 5 x 3 cm and a clinical diagnosis of neurofibroma was made. Fine Needle Aspiration Cytology (FNAC) was done using standard technique. Smears showed predominantly suppurative inflammation, foreign body giant cells, granulomas and fungal hyphae. KOH mount, culture and germ tube test was positive. Final diagnosis of fungal granuloma was made. Fungal infections should be included in the differential diagnosis of a soft tissue mass lesion. All soft tissue suppurative inflammatory lesions should be diligently screened to look for pathogens if any. Diagnostics in medicine have taken a major leap with advent of molecular technologies. Despite this, simple old traditional methods like FNAC supplemented by other basic laboratory techniques like KOH mount and culture still form the cream of a diagnostic laboratory and can come as a savior for the pathologist, the clinicians and the patients.

Keywords: Fungus, Germ tube test, Granuloma

CASE REPORT

A 60-year-old male subject presented with a soft tissue mass over the right forearm since 15 days [Table/Fig-1]. He was diagnosed with diabetes mellitus eight years back and was on oral hypoglycaemic drugs. However, as per the subject's narration, his diabetes was uncontrolled. He gave a history of minor trauma while blood sample was being drawn from right forearm for investigations three months prior to the development of the mass. The swelling was initially small and gradually increased to the present size of 5x3 cm. There was no history of pain or oozing of pus at the site of swelling. He did not complain of fever, weight loss, loss of appetite or any other systemic manifestations. On examination, the swelling was located on the forearm about 6 cm from the wrist joint, medial aspect, currently measuring 5×3 cm, firm in consistency, non tender and mobile. His random plasma glucose level was 461 mg/dl. His HbA1C level done at the time of presentation was 8.5%. He had a history of tuberculosis three years back, for which he had taken first line of drugs, comprising of four drugs for two months and three drugs for six months. Currently, he did not have any symptoms or signs pertaining to pulmonary or extrapulmonary tuberculosis. Clinical diagnosis of neurofibroma was made. FNAC was done from the site yielded blood mixed material.

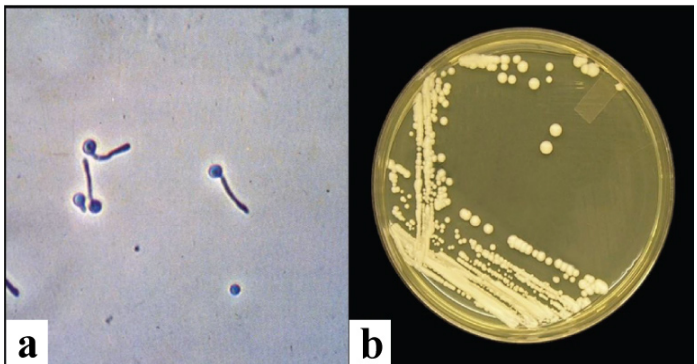


[Table/Fig-1]: a) Soft tissue mass in the right forearm measuring 5x4 cm; b) Cytology smears showing plenty of neutrophils and foreign body giant cell (H&E, 40X); c) Cytology smears pseudo hyphal form of fungus consistent with *Candida* species (H&E, 40X); d) Pseudohyphal form with branching consistent with *Candida albicans*-KOH (H&E, 40X).

Microscopy

FNAC smear evaluation showed plenty of neutrophils along with histiocytes, many foreign body giant cells. Also, few clusters of epithelioid cells forming granulomas [Table/Fig-1b]. Acellular eosinophilic material was observed on H&E, which we interpreted as the Splendore-Hoeppli phenomenon. At places budding yeast and pseudo hyphal forms of fungal organisms belonging to *Candida* species was noted [Table/Fig-1c]. KOH mount showed budding yeast and pseudo hyphal forms with branching consistent with *Candida albicans* [Table/Fig-1d]. Germ tube test and culture showed positive results. Hence, a final diagnosis of granuloma associated with *Candida ablicans* was established [Table/Fig-2a,b].

Patient was treated with Intravenous (IV) antifungal drugs and patient responded well to treatment.



[Table/Fig-2]: a) Germ tube positivity; b) Sabourad's dextrose agar media showing *Candida* colonies.

Authors	Year	Site	Number of cases	Type of fungus identified (number)
Corti M [8]	2015	Chest wall	2	*Candida*
Freedman SI [9]	1986	Lung aspirate	8	Coccidioidomycosis
Sherman ME [10]	1991	Buttock mass Shoulder mass	2	*Coccidioides immitis* Cryptococcosis
Hicks MJ [11]	1994	Neck mass	1	Coccidioidomycosis
Jan IS [12]	2008	Lung, Neck, Sputum	13	*Penicillium marneffei*
Kuruba SL [13]	2011	Orbit	2	*Aspergillus*
Cocker R [14]	2014	Adrenal	1	Cryptococcosis
Gochhait D [15]	2015	-	66	Aspergillosis (36) Mucormycosis (6) Histoplasmosis (3) Cryptococcus (4) Candidiasis (2) Unclassifiable fungal infections (15)

[Table/Fig-3]: Depicts the concise details of the reports describing FNAC in fungal infections [8-15].

DISCUSSION

Fungal infection due to *Candida* species is frequent in immunocompromised patients. The incidence has increased in the past 20 years with *Candida* emerging as the major causative agent [1]. *Candida* exists in a symbiotic relationship in humans. It tops among all the fungus and is linked with highest mortality amongst all other fungal strains causing human infections. In 50% of the cases, *Candida albicans* ranks first for causing Invasive Candidiasis (IC), with *Candida glabrata* being the number two [2]. *Candida* infection presenting as a soft tissue mass lesion is very unusual and can occur either due to haematogenous involvement or trauma [3-5].

Like any other fungus, *Candida* can occur in three forms as superficial, cutaneous and subcutaneous and deep systemic infections. The later is termed as Invasive Candidiasis (IC), which include candidemia and deep seated tissue candidiasis. The disease effects over 25,000 people every year with a mortality rate of 40% [6]. IC is a serious, life threatening condition and early diagnosis is important for initiating appropriate therapy [6].

Any organ can be involved in IC, with predilection for kidney, brain, heart, lung. Muscle involvement which forms an important basis for tenderness and this is accompanied by fever and rash is an important clue to the presumptive diagnosis of invasive candidiasis. Rarely, IC can present as a mass lesion, which in turn can falsely mimic a neoplastic process. Song Z et al., reported a case of localized candidiasis involving renal parenchyma and forming a destructive lesion leading to a false negative diagnosis of renal cell carcinoma [5]. In another such report, Patted SV et al., mentioned the occurrence of a mass like lesion in the right ventricle of a two-month-old immunocompetant child caused due to *Candida krusei* [7]. Despite of adequate medical and surgical intervention, the child died of systemic fungemia and multiorgan failure. *Candida* can form mass lesion in the cerebrum. This attests the inclusion of *Candida* in the differentitial diagnosis of calcified intracranial mass lesions. There are few case reports of subcutaneous abscess formation due to *Candida* infection. Usually, when it occurs, the predisposing factor is the overlying bacterial infection, trauma or intravenous drug abuse. In the case report of Corti M et al., the authors advocate the need for culturing all samples from subcutaneous abscess and maintaining high index of suspicion for a precise diagnosis [8].

A number of predisposing factors predispose to candidiasis and the list continues to lengthen as we further unravel the role of immune mechanism implicated in its pathogenesis. Some of these are an immunocompromised state like Acquired Immunodeficiency Syndrome (AIDS), diabetes mellitus, cancer, anticancer therapy, prolonged use of broad spectrum antibiotics and indwelling intravenous catheter. In our patient, trauma while drawing blood sample for investigations and immune suppression due to uncontrolled diabetes mellitus was the predisposing factor.

FNAC is a widely used tool and has stood test of time for the diagnosis of superficial and deep masses. The main purpose is to delineate the masses as to inflammatory, benign or malignant. Role of FNAC in the diagnosis of mycosis is of paramount importance, as it influences the outcome of the disease. There are very few case reports describing FNAC in fungal infections. The concise details of the reports describing FNAC in fungal infections is shown in [Table/Fig-3] [8-15].

Though culture is a gold standard, growth and characterization requires two weeks. Also, the positivity rate is only 50%, which can be enhanced by lysis centrifugation technique. Serum beta glucan gives positive results in culture negative cases [9]. However, this test is not widely available. Hence, cytology plays a major role in being a simple, fast, easy and cost effective tool in the diagnosis of fungal lesions. Any fungal infection at cytology shows a diverse pattern ranging from the presence of eosinophils, neutrophils, foamy histiocytes, epitheliod granulomas, multinucleate giant cells and necrosis. However, significance and predictive value of these findings vary for different cases based on the host immune response. Also, none of the findings are specific and any one of these can predominate based on the host immune response. A major drawback of FNAC is the inability to differentiate invasive fungal infection from colonization [16].

Fungal infection can present as a mass lesion clinically mimicking a tumour. The cytologic diagnosis of a fungal infection presupposes that the pathologist should maintain a modicum awareness of this entity.

CONCLUSION

Mortality rate associated with invasive fungal infections are very high. All soft tissue suppurative inflammatory lesions should be diligently screened to look for pathogens if any. Diagnostic medicine has taken a major leap with advent of molecular technologies. Despite this simple old traditional methods like FNAC supplemented by other basic laboratory techniques like KOH mount and culture still form the cream of a diagnostic laboratory and can come as a savior for the pathologist, the clinicians and the patients.

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