Quiz Case

Frontal swelling in adult male: Cytological consideration of an uncommon diagnosis

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A 53-year-old male presented with a complaint of swelling on the forehead extending up to the left supraorbital region for 1 year. There was past history history of trauma 1 year back. There was no history of pain, fever, weight loss, or tuberculosis. Local examination revealed a well-defined, non tender swelling, soft in consistency, with limited mobility measuring 2 cm × 2 cm [Figure 1a-c] shows the cytomorphological features of the fine-needle aspiration (FNA) in Giemsa stained smears.

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Figure 1: (a) Frontal swelling extending up to the left supraorbital region. (b) Osteoclastic giant cells with dense inflammatory infiltrate and fungal hyphae (Pap, ×100). (c) Dense inflammatory cells with fungal hyphae (Giemsa stain, ×400).

Q1. What is your interpretation?
   a. Microfilaria
   b. Fungal infection
   c. Malignancy
   d. Inflammatory cystic lesion.
ANSWER

Q1. b.

The correct cytopathological interpretation is (b) fungal infection. Fungal infection of the bones is unusual and generally presents in an indolent fashion. It usually occurs in immunocompromised patients. Fungal infection is devastating to patients if it is invasive in nature. Fungal osteomyelitis is an opportunistic infection which frequently enters the body due to decrease in host defense or through an invasive gateway, such as dental extraction.[1] Candidal infection is more often encountered when compared to other fungal infections, i.e., mucormycosis and aspergillosis.[1] Osteomyelitis mostly results from bacterial infection. However, fungi, parasites, and viruses can also affect bone and bone marrow.[1]

In the present case, noncontrast computed tomography (NCCT) brain revealed soft tissue density lesion showing CT attenuation in the left frontal scalp region extending to frontal sinus with erosive destruction [Figure 2a]. Contrast-enhanced CT paranasal sinuses showed evidence of a large heterogeneous enhancing soft tissue mass measuring 6 cm × 5 cm × 3 cm in the forehead with expansile lytic destruction of the frontal bone [Figure 2b]. FNA of the swelling yielded clear fluid. Dry and wet-fixed smears prepared from the aspirate were routinely stained with Giemsa and Pap stain, respectively. Additional wet-fixed smears were retained for special stains. Smears consisted of dense inflammatory infiltrate, osteoclastic giant cells, and osteoblasts along with granuloma with interspersed numerous fungal hyphae, which were slender, septate, with acute angle branching possibly Aspergillus. Following this observation, special stain periodic acid–Schiff (PAS) was used on the wet-fixed smear. The fungal hyphae were positive on PAS stain [Figure 2c]. A provisional diagnosis of fungal infection due to Aspergillus species was made, and a repeat FNA was advised for fungal culture. Culture of the sample produced Aspergillus fumigatus.

On follow-up, the patient was put on antifungal therapy and repeat cultures of the lesion 3 weeks later were free from fungal elements.

ADDITIONAL QUIZ QUESTIONS

Q2. Which of the following fungus have septate hyphae with acute angle branching?
   a. Candida albicans
   b. Aspergillus niger
   c. Nocardia asteroides
   d. Rhizomucor sp.

Q3. Each of the following statements concerning mucormycosis is correct except –
   a. The fungi that cause mucormycosis are transmitted by airborne asexual spores
   b. Cytology smears from a patient with mucormycosis show budding yeasts
   c. Ketoacidosis in diabetic patients is a predisposing factor to mucormycosis
   d. Hyphae typically invade blood vessels and cause necrosis of tissue.

Q4. Which are the reliable diagnostic modalities for fungal osteomyelitis?
   a. Raised erythrocyte sedimentation rate (ESR), elevated leukocyte count
   b. Culture on pus aspirate
   c. Direct evidence on FNA cytology smears
   d. All of the above.

Q5. Which of the following special stain combination can be used to diagnose fungal infection?
   a. PAS and Ziehl–Neelsen (ZN) stain
   b. PAS and Grocott's stain
   c. PAS and Alcian blue
   d. PAS and mucicarmine.

ANSWERS TO THE ADDITIONAL QUIZ QUESTIONS

Q2. b; Q3. b; Q4. d; Q5. b

Q2. b Hyphae in aspergillosis are quite characteristic showing narrow septate hyphae of 3-6 μm in size having dichotomous branching at 45° and 90°.

Q3. b Mucormycosis which belongs to Zygomycetes family typically shows broad aseptate hyphae of size 6–20 μm with branching at >90°.

Q4. d Blood cultures should be obtained in all patients with osteomyelitis, but it is especially important in those patients where hematologic spread is a concern. Other useful laboratory values include elevated white blood cell count and positive fungal cultures.
count, certainly in the acute stages. Elevated ESR and elevated C-reactive protein may also be useful markers in the diagnosis and treatment of osteomyelitis. In case of fungal osteomyelitis, direct evidence of fungus on cytology smears allows rapid diagnosis.

Q5. b PAS and Grocott’s stains are the standard histological stains used to highlight the fungi. Alcian blue stains mucins but does not stain neutral mucins and mucicarmine is very specific for epithelial mucins. ZN stain used to identify acid-fast organisms.

BRIEF REVIEW OF THE TOPIC

Osteomyelitis mostly results from bacterial infection. However, fungi, parasites, and viruses can also affect bone and bone marrow. Since fungal infections involving bone occur infrequently, it can pose a diagnostic and therapeutic dilemma for those who are not familiar with its clinical presentation, thus leading to ineffective treatment or resolution. The clinical presentation of fungal osteomyelitis would be similar to the bacterial osteomyelitis. Candidal infection is the most often encountered fungal infection followed by aspergillosis. Aspergillosis is usually invasive in nature though noninvasive forms have also been reported and do not cause bone destruction when compared to mucormycosis. Aspergillus species are ubiquitous saprophytic organisms. More than 300 species are known, but only a few of them are of importance regarding opportunistic infection. Invasive aspergillosis usually involves the sinopulmonary tract, with the lung being the most common site of infection, while osteomyelitis due to Aspergillus species is rare. Hyphae in aspergillosis are quite characteristic showing narrow septate hyphae of 36 μm in size having dichotomous branching between 45° and 90°. Mucormycosis which belongs to Zygomycetes family typically shows broad aseptate hyphae of size 620 μm with branching at >90°. The diagnostic workup is of paramount importance to differentiate between bacterial and fungal osteomyelitis. Culture and sensitivity should be followed in all cases, irrespective of its nature.

FNA is a reliable, simple, and quick technique for its diagnosis. The search for fungal profiles should be more aggressive in smears rich in inflammatory and foreign body giant cells or in cases with a strong clinical or radiological suspicion. In most cases, differentiation between the two most common offending fungi, i.e., Aspergillus and Mucor, can be made on cytology with the help of special stains such as PAS and Grocott’s stains. Thus, preoperative FNA diagnosis obviates the need for a diagnostic biopsy, allows rapid diagnosis as cultures take time, and helps to plan proper treatment to suit individual patients. The present case assesses the role of preoperative FNA for this purpose.

SUMMARY

Osteomyelitis of the facial bones is a complex problem which needs to be investigated thoroughly as there is no difference in clinical presentation between bacterial and fungal osteomyelitis unless accompanied by sinusitis. Fungal osteomyelitis is very rare, and appropriate treatment with antifungal regimen and timely surgical intervention, i.e., debridement, curettage, and sequestrectomy, will lead to successful resolution of the disease process. Failure to do so can result in a host of complications and consequences. Cytology, being an easily available, minimally invasive, and inexpensive procedure, can be used as initial diagnostic modality in cases of osteomyelitis.

COMPETING INTERESTS STATEMENT BY ALL AUTHORS

The authors declare that they have no competing interests.

AUTHORSHIP STATEMENT BY ALL AUTHORS

Each author has participated sufficiently in the work and takes public responsibility for appropriate portions of the content of this article.

All authors read and approved the final manuscript.

Each author acknowledges that this final version was read and approved.

ETHICS STATEMENT BY ALL AUTHORS

As this is case without identifiers, our institution does not require approval from Institutional Review Board (IRB) (or its equivalent).

LIST OF ABBREVIATIONS (IN ALPHABETIC ORDER)

CECT - Contrast-enhanced computed tomography
CRP - C-reactive protein
CT - Computed tomography
ESR - Erythrocyte sedimentation rate
FNA - Fine-needle aspiration
FNAC - Fine-needle aspiration cytology
PAS - Periodic acid–Schiff
ZN - Ziehl–Neelsen.

EDITORIAL/PEER-REVIEW STATEMENT

To ensure the integrity and highest quality of CytoJournal publications, the review process of this manuscript was conducted under a double-blind model (authors are blinded for reviewers and vice versa) through automatic online system.
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