

FUNGAL OSTEOMYELITIS OF ZYGOMATICO-MAXILLARY COMPLEX: A CASE REPORT HIGHLIGHTING CLINICO-PATHOLOGICAL APPROACH TO DIABETIC PATIENTS

Ghulam Saqulain¹, Muhammad Mumtaz Khan², Sabeen Nasir², Sardar Muhammad², Muhammad Haris Ramzan³

¹Department of ENT and Head & Neck Surgery, Capital Hospital, Islamabad

²Department of Pathology, Peshawar Medical College, Riphah International University, Islamabad

³Department of Physiology, KMU Institute of Medical Sciences, Kohat, Pakistan

ABSTRACT

Osteomyelitis of zygomatico-maxillary complex is rare. We present a diabetic patient who initially reported a small cystic swelling on lower orbital margin which on exploration came out to be a subperiosteal cold abscess. No bone erosion could be detected on routine x-rays. The cytology and initial biopsy revealed chronic nonspecific inflammation. Repeated bacterial cultures and staining for AFB were negative. Later a discharging sinus was formed. CT scan suggested osteomyelitis. Conservative surgery with sequestrectomy and debridement was performed. The biopsy revealed necrotic bony fragments along with fungal hyphae and spores. On fungal culture a growth of *Aspergillus flavus* was obtained. A final diagnosis of fungal osteomyelitis of lateral part of lower orbital margin involving zygomatico-maxillary complex was made. Patient responded to conservative treatment with oral antifungal agents and minimal surgical intervention. The possibility of fungal etiology must be considered in a diabetic patient even at unusual sites.

KEY WORDS: Aspergillus; Diabetes complications; Osteomyelitis.

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INTRODUCTION

Osteomyelitis is an inflammatory process of bone that usually begins as an infection of the medullary cavity, rapidly involves the Haversian system and quickly extends to the periosteum. The infection establishes in the calcified portion of the bone.¹ It may be a complication of any systemic infection but frequently manifests as a primary solitary focus of disease and may have a bacterial, viral, parasitic or fungal etiology.^{2,3} The predisposing factors include radiation, malignancy, odontogenic causes, chronic sinusitis, diabetes mellitus and trauma. Immunosuppression and corticosteroid therapy are also important risk factors.^{4,5}

Over the last 50 years, incidence of osteomyelitis of the jaws has decreased dramatically due to

the availability of bactericidal antimicrobial therapy.⁶ Fungal osteomyelitis presenting as cold abscess is rare in the facial bones. Unusual organisms causing osteomyelitis in the cranio-facial region may include *Pseudomonas*, *Actinomyces*, *Candida*, *Mucormycosis*, *Mycobacterium tuberculosis*, *Alternaria* and *Aspergillus*.⁷⁻¹³

Aspergillus is usually a harmless saprophyte but capable of opportunistic infections and therefore found in immunosuppressed or compromised patients,⁵ IV drug abusers, patients on chemotherapy, transplant recipients and uncontrolled diabetics who are known for altered immune defense mechanisms. Fungal osteomyelitis of jaws is more likely to be invasive as compared to bacterial, if not diagnosed early and treated with appropriate anti-fungal agents.¹⁰

Histology is helpful in making a provisional diagnosis. The specific diagnosis is made by culture and sensitivity for fungi. Magnetic resonance imaging (MRI) and technetium scans are useful adjuncts in assessing and gauging the extent of the bone involvement and soft tissue infection.

Corresponding Author:

Dr. Muhammad Mumtaz Khan

Associate Professor

Department of Pathology,

Peshawar Medical College, Peshawar, Pakistan

E-mail: mmumtazkhan@gmail.com

Surgical debridement and removal of sequestrum, if present is essential before starting antibiotic and antifungal therapy. Invasive aspergillosis may be treated with voriconazole, amphotericin B and itraconazole.

The aim of this study is to create alertness among clinicians and pathologists about the possibility of fungal infections around the orbit and maxilla even if the sinuses and nasopharynx are normal especially in diabetics.

CASE REPORT

A 55 years old diabetic male was admitted, to the ENT Department of Capital Hospital, Islamabad, Pakistan, with a small painless infra-orbital swelling on the right side for 5 months. Examination revealed



Figure 1: Right infra-orbital swelling: a close view.



Figure 2: Formation of discharging sinus at the site of lesion.

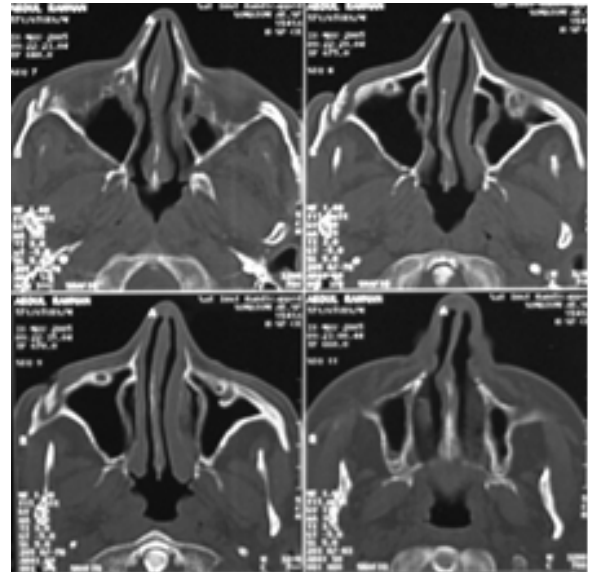


Figure 3: CT scan showing destruction of zygomatic arch and anterior maxillary wall on the right side.



Figure 4: Fungal spores, hyphae and necrotic bony fragments. H&E stain (x40).

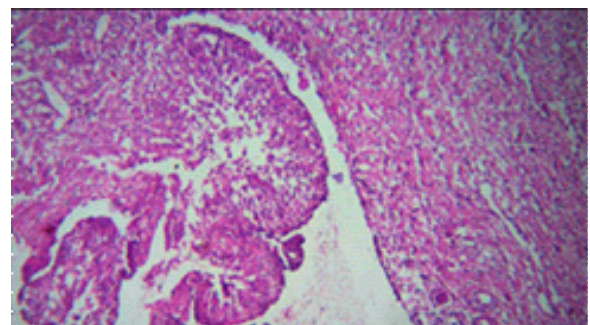


Figure 5: Ill-defined granulomas. (H&E stain x20).

a cystic swelling measuring 1.5x1 cm on lateral part of the right infra-orbital margin extending to the floor of the orbit. The margins were poorly delineated. The swelling lacked signs of acute inflammation. (Fig. 1)

The systemic examination was unremarkable. Routine investigations were normal except for a raised fasting and random blood sugar of 151 mg/dl and 197 mg/dl respectively. Mantoux test was negative. No bone erosion was seen on plain radiographs and a provisional clinical diagnosis of an infra-orbital cyst was made. On exposure through a horizontal incision on lower orbital margin, a collection of pus was found under the periosteum. The pus was drained along with curettage of bone underneath. A biopsy was taken. The cytology of pus revealed numerous polymorphs and histiocytes in a background of karyorrhectic material and necrotic cellular debris, findings consistent with acute inflammation / abscess formation. Although the culture of pus revealed growth of no organisms and the Ziehl-Neelsen stain for acid fast bacilli was negative, prophylactically the patient was put on broad spectrum antibiotics which provided only temporary relief. The biopsy showed fibrovascular tissue densely infiltrated by lymphocytes, histiocytes, plasma cells and polymorphs in a background of focal necrosis. A diagnosis of acute on chronic nonspecific inflammation was made. Two months later another culture of the pus was performed giving growth of *Staphylococcus aureus* coagulase negative suspected to be skin flora. The pus was cultured third time after about 06 months which again yielded no growth.

After more than a year from initial presentation, the patient reported with the formation of a sinus discharging pus off and on. (Fig. 2) Suspecting chronic osteomyelitis, a CT scan was performed which showed destruction of zygomatic arch and part of anterior wall of maxilla on the right side. Maxillary antrum, Infra-temporal fossa, peri-orbital fat and muscles appeared normal. (Fig. 3)

Surgery was planned. The sinus was opened through an elliptical infra-orbital bone deep incision around the margins. A sequestrum was identified measuring 2 cm in diameter. It was removed and bone was curetted. Wound was closed with Bismuth Iodine Paraffin Paste pack.

Sinus was aspirated and pus was sent for microbial and fungal culture. Biopsy was taken. Grossly it consisted of skin and bony fragments collectively measuring 1.5x1x0.3 cm. Microscopy showed skin and necrotic bony fragments. The skin with underlying dermis revealed marked infiltration by lymphocytes, histiocytes, plasma cells and polymorphs. The necrotic bony fragments showed invasion by fungal hyphae and spores. (Fig. 4)

Histological opinion was of chronic fungal osteomyelitis with superadded acute inflammation. Pus for fungal culture revealed *Aspergillus flavus*. Post-operatively the patient was kept on Ketoconazole 100 mg Orally TDS which fully cured him.

DISCUSSION

The above case highlighted problems related to our approach to the patient. We take many things for granted in dealing with patients routinely and in our approach to diagnosing and treating patients we tend to be fixed and consequently the tangential possibilities do not cross our minds.

The fungus was seen in the second biopsy when bone had been involved so the first question that arose in our minds was the possible route of entry of the organism. In such cases most of the time odontogenic microorganisms,⁶ infections in the paranasal sinuses or pharynx are involved.¹⁴ The maxillary antrum, paranasal sinuses, Infra temporal fossa, pharynx, peri-orbital fat and muscles were found to be normal on examination in our patient. The next possibility was that the fungus might have been introduced accidentally during the first surgery about a year before because candida and aspergillus are the most common fungal infections in surgical patients who are treated with invasive devices or procedures, broad-spectrum antibiotics, or have some form of immunosuppression.¹⁵ For this we reviewed the sterilization and disinfection protocol carried out before and during the procedure in which we routinely eliminate all the possible sources of infection.

This left us with a single possibility that the fungus might have been there from the beginning. Superficial bacterial infections especially folliculitis is common in diabetes. Poor glycemic control in diabetic patients is likely to end up as altered immunity favoring infection by saprophytic fungi and other opportunistic organisms.¹⁶ In our patient this appears to be the likely etiology and the possible route of entry.

A provisional diagnosis of cold abscess was considered initially and Ziehl-Neelsen stain was performed to rule out the presence of AFB but the possible mycotic etiology was not considered. Although common in diabetics but there is always a likelihood of missing fungal infections at unusual places. Superficial fungal abscesses are quite common in uncontrolled diabetics though infra-orbital region and zygomatico-maxillary complex are uncommon sites for them.^{9,14}

Up to the final diagnosis culture for bacterial organisms were performed four times besides one pus sample for identification of AFB all of which were consistently negative. On review the deeper levels of the first biopsy revealed occasional ill-defined

epithelioid granulomas although no fungal spores or hyphae could be identified. (Fig. 5) Clinically the patient gave the impression of a cold abscess but in the absence of signs of acute inflammation it can be misleading. Analyzing patient's data retrospectively a negative Mantoux test in an adult diabetic signifies deranged immunity attracting fungal infections.^{5,17}

Among other infections diabetics are at higher risk for acquiring fungal infections of skin and mucus membranes and with advanced age the risk of infection increases further. With poor glycemic control there are defects in the function of lymphocytes, neutrophils and monocytes especially their phagocytic activity which may lead to the formation of ill-defined granulomas.¹⁸ In this case the final biopsy helped in the diagnosis in which we saw invasion of the necrotic bony fragments by fungal hyphae and spores confirmed as *Aspergillus flavus* on culture.

CONCLUSION

A high index of suspicion must be maintained for infection by saprophytic fungi in diabetic patients with no growth on bacterial culture, AFB negativity, ill-defined granulomas on microscopy and no response to antibacterial therapy even in rare sites like face and orbital region.

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CONFLICT OF INTEREST

Authors declare no conflict of interest.

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None declared.