



External Ear infections in diabetics- Challenges in management

¹ Vadisha Srinivas Bhat, ² Shubha P Bhat, ¹ Harish Rao, ¹ Satheesh Kumar Bhandary

¹ K S Hegde Medical Academy, Mangalore-575018 Karnataka, India

² Kasturbha Medical College, Mangalore

ABSTRACT

Infections tend to occur more commonly and with more severity in people with diabetes than in non diabetics. Local and systemic immunological defects are likely to be responsible for high infection rates in diabetics. Hyperglycaemia in poorly controlled diabetes provides a good environment for vast number of microorganisms including bacteria, virus and fungi. Moreover, active infection in diabetes poses difficulty in controlling diabetes, hence causing a vicious cycle of infection and hyperglycaemia. An infection, which is easily manageable in non diabetics may turn out to be of a severity out of proportion than expected in diabetics.

Incidence of certain ear infections like malignant otitis externa is disproportionately higher in diabetics and so is the difficulty encountered in managing these conditions. Also, as some infections in diabetics present in a subtle and atypical manner, prompt recognition of infection followed by appropriate medical or surgical intervention is necessary.

Introduction:

Diabetes Mellitus is a common health problem worldwide. India is a country with largest population of diabetics, with nearly 60 million people diagnosed with diabetes. The number is expected to increase to 87 million by 2030¹. Diabetes is widely believed to predispose to serious infections and there are literatures supporting the association between diabetes and infection.^{2,3} Infection is associated with impaired carbohydrate tolerance, and in uncontrolled diabetes, mortality due to certain infections like Mucormycosis, Malignant otitis externa, necrotizing soft tissue infections, and gram negative and staphylococcal pneumonia was very high in spite of treatment.⁴

Diabetes and altered immunity:

Individuals with diabetes are at higher risk of infection, caused by altered defence mechanisms including the effect of hyperglycaemia, effect of neuropathy, impaired perfusion and delayed wound healing.² In a given infection, morbidity and mortality is higher in an individual with diabetics than non diabetics. Although good control of diabetes can prevent life threatening infections, the enhanced susceptibility to infections has been attributed to defects in cell mediated and humoral immunity.^{5,6} Also, in elderly diabetics, immune senescence due to aging affecting the cell mediated immunity, results in increased risk of bacterial, mycobacterial, fungal and viral infections.^{7,8}

Common external ear infections in diabetics, acute otitis externa, malignant otitis externa and Otomycosis are discussed under.

Acute Otitis externa:

Acute otitis externa is an inflammatory condition in the external auditory canal, involving the skin and subdermis. This will be associated with oedema in the external auditory canal. A localized form of this is furuncle, which is a staphylococcal infection of the hair follicle in the cartilaginous portion, the lateral one third of the external auditory canal. People with poorly controlled diabetes are more susceptible for acute otitis externa.^{9,10}

Acute otitis externa is more common in warmer and humid climates and there is increased risk of infection after water exposure like swimming. Wax in the ear canal creates a slightly acidic pH that inhibits pathogenic organisms like pseudomonas. But this acidic pH can be altered by removal of wax and water exposure. Minor abrasions caused while cleaning the ear wax is one of the triggering factors for acute otitis externa. Also, congenital anomalies of ear canal, wearing of hearing aid, excessive sweating and stress are considered the predisposing factors for Acute Otitis externa.¹¹ Annual incidences of acute otitis externa range from 1:100 to 1:250 of the population.¹⁰ The disease has a rapid onset, with severe otalgia, fullness in canal and hearing loss of variable degree. The earache may be worsened by jaw movement. The hallmark sign of diffuse acute otitis externa is tenderness of the tragus that is often intense. The canal wall is oedematous with localized or diffuse erythema (Fig 1). Purulent discharge can be seen, though this is not always a feature. Tympanic membrane is intact but may be congested.

Treatment of furuncle of ear includes local heat, Icthamol glycerine pack, incision and drainage, analgesics and antibiotics against *Staphylococcus aureus*. The response to treatment is although dramatic in most cases, there is a need for longer duration of treatment in diabetics.

Topical preparations are recommended as initial therapy for diffuse uncomplicated acute otitis externa. Topical treatments used are acetic acid, boric acid, aluminium acetate and silver nitrate. Topical steroids are also used either alone or in combination with acetic acid, or topical antifungal agents. Topical preparations produce very high concentration of drug to infected tissue, often 100 to 1000 times higher than can be achieved with systemic therapy.¹⁰ In the presence of a tympanic membrane perforation, care is taken while using ototoxic antibacterial ear drops like aminoglycosides, as antibiotics placed into the middle ear can reach the inner ear causing hearing loss. But, tympanic membrane cannot be visualized in all patients of acute otitis externa. A perforation may be suspected if the patient has a history of ear discharge in the recent past. Ear drops containing quinolones are considered safer for use in middle ear. Patients being treated with topical neomycin should be under close clinical observation.

Patients are advised to avoid manipulation of the ear to minimize ear and avoid entry of water into the ear canal. The insertion of earplugs or cotton with petroleum jelly or edible oil while taking bath can reduce the entry of moisture into the ear. Patients with AOE should preferably avoid swimming for 7 to 10 days during treatment.

Patients with hearing aids should limit insertion until pain and/or discharge have subsided.¹⁰ Acute otitis externa may exist together with acute otitis media, either the former being secondary to acute otitis media, or both developing independently. In such situation, otitis media should be treated as an independent disease process.

Systemic treatment is indicated in diabetics, immunocompromised patients, inability of topical therapy. Failure to distinguish acute otitis externa from other causes of otorrhea like malignant otitis externa or middle ear infections may prolong the morbidity or cause complications.¹⁰

Malignant Otitis externa:

Malignant Otitis externa is a rare but potentially fatal disease of external auditory canal, most frequently occurring in diabetics. The condition was first reported by Toulmouche in 1838.¹² Meltzer and Kelemen in 1959 reported *Pseudomonas osteomyelitis* of temporal bone, mandible and zygoma.¹³ Chandler published a report on this condition in 1968, and he named the condition as Malignant Otitis externa.¹⁴ The condition is also referred as necrotizing otitis externa. As the disease spread to involve skull base, it is also called skull base osteomyelitis. However, it is popularly known by the less precise name, malignant otitis externa, as the condition behaves aggressively, like a malignant condition.¹⁵

Deficient cell mediated immunity and hypo perfusion secondary to micro angiopathy predisposes to this condition in diabetics.¹⁶ Also, cerumen in diabetic patients have a higher pH and less lysozymes, which impair local immunity.¹⁷

This invasive granulomatous form of otitis externa is seen commonly in diabetics, and the mortality used to be as high as 75% in some reported series.¹⁸ It can also be seen in any condition causing immunosuppression like AIDS, individuals on immunosuppressive therapy after organ transplantation, patients with leukaemia, lymphoma and patients undergoing chemotherapy. In 46 cases of malignant otitis externa reported by Franco- Vidal V et al, the prevalence of diabetes was 65%.¹⁹ But Chandler, Berenholz et al reported 90% to 100% prevalence of diabetes in patient with malignant otitis externa.^{20,21}

The organism isolated in this dreaded infection is mainly *Pseudomonas aeruginosa*. This is a gram negative obligate aerobe which is a commensal in the external auditory canal. In the presence of lowered host immunity, any trauma in the external auditory canal, ignite this aggressive infection, which once started progresses relentlessly. The 2, 6 and 11 strains of *Pseudomonas aeruginosa* are associated with aggressive type of disease.²² They produce lytic enzymes including endotoxin, collagenase and elastase causing necrotizing vasculitis and endarteritis, facilitating the spread of inflammatory process to the neighbouring tissues.

Apart from *pseudomonas*, *Staphylococcus aureus*, *S epidermidis*, *Proteus mirabilis*, *Klebsiella oxytoca* and *P cepatica* have been isolated in malignant otitis externa. However the true pathogenicity of these organisms has not been confirmed.¹⁵

In a few cases of malignant otitis externa, fungus have been isolated, including *Aspergillus fumigatus*, *Aspergillus flavus*, *Aspergillus niger*²³, *Mucor*²⁴ and *Scedosporium spp.*²⁵ Fungal infection need to be considered in an immunocompromised patient with a disease mimicking malignant otitis externa, but unresponsive to appropriate antibacterial treatment for adequate duration. However a high index of suspicion is needed in such cases, as early diagnosis improves survival and limits morbidity.

The disease process in malignant otitis externa originates at the junction of cartilaginous and bony external auditory canal. Later the infection spreads to the preauricular tissues, necrosis of adjacent cartilage and osteomyelitis of the temporal bone and the skull base.¹² Facial nerve palsy is common in this form of otitis externa, due to the proximity of the stylomastoid foramen, through which the facial nerve exits the cranial cavity. When the infection spreads to the skull base, there may be involvement of Jugular foramen, IX, X and XI cranial nerves. The disease may also spread to the parotid gland through the fissures of Santorini. The thrombosed jugular vein may give way to cavernous sinus thrombophlebitis and very rarely meningitis.¹² Involvement of Middle ear occurs later and otic capsule is generally not involved even in advanced disease.^{14,26} Intracranial involvement increases the mortality rate. In the earlier report of Chandler, 7 out of the 13 cases succumbed to the disease process.¹⁴ However with aggressive medical therapy, the fatality is significantly reduced now.

The chief complaints of malignant otitis externa include severe earache, purulent and sometimes blood stained otorrhea and hard of hearing with the effected ear. Earache will be worse in the night. Later in the disease there may be swelling in the preauricular region, pain over the temporomandibular joint area and trismus.¹⁵ Typically an elderly diabetic presents with severe earache and purulent discharge from the ear canal, which persists in spite of conservative management. There will be history of disturbed sleep because of pain. On examination, affected ear will be tender with inflammatory oedema of the ear canal with purulent discharge. Extensive granulations are seen in the canal, at the osseocartilaginous junction and the floor, with necrosis of the cartilage as well as bone. Tympanic membrane will be hidden because of canal wall oedema, but when visualized will be healthy. In advanced disease, there will be preauricular swelling and lymphadenopathy. Skull base involvement leads to cranial nerve palsy, the facial nerve being most commonly affected, as common as in 25% of patients, because of the proximity of the stylomastoid foramen to the ear canal. In one of the series of Chandler, the incidence of Facial palsy was 32%.²⁰ As facial palsy can also be seen as a result of diabetic mononeuropathy, it is essential to differentiate this entity and the palsy due to malignant otitis externa.

Haematological investigations in malignant otitis externa show leucocytosis, which is not the case in malignancies. This should provide a clue to the clinician in the diagnosis. Blood sugar levels should be estimated, and it is critical to control the diabetes for better control of the disease. Even in those people with malignant otitis externa, without history of diabetes, blood sugar level estimation is mandatory.¹² Culture and sensitivity of ear discharge should be done, and the microbiologist should be provided with detailed clinical findings, which is useful for isolating the organism.

Cultures should be taken for aerobes, anaerobes, fungal elements. Sensitivity of the isolated bacteria for antimicrobials should be tested. Biopsy of the granulations is taken to rule out malignancy. This will also help in diagnosing any fungal pathogens.

Imaging is important to determine the extension of the disease and to know the response to the treatment. CT scan and MRI are useful to know the bone erosion and soft tissue extension respectively. CT scan is sensitive in diagnosing abscess formation, extension into temporomandibular joint and mastoid (Fig 2). However, this is not useful in early disease, as CT scan can detect the changes after 30% demineralization.

Technetium-99m bone scan is a more sensitive investigation, as this is positive in all cases of malignant otitis externa. But this is not specific to infection, as the test is based on binding to osteoblasts, which are also seen in neoplasm and trauma. Gallium-67 scan will be positive in soft tissue and bone infections via binding to lactoferrin. The uptake returns to normal after infection is cleared. Hence this is more useful than Technetium-99m in diagnosis, for monitoring the response to treatment as well as detecting recurrence.¹⁵

Treatment of malignant otitis externa is multidisciplinary. Aggressive control of diabetes is critical for improvement. In the past, surgical treatment was the mainstay of treatment, but now it is effectively treated with hospitalization and intravenous antibacterial agents.

Minor surgical debridement of the necrotic tissue is helpful. Culture directed antibacterial therapy is recommended. Antipseudomonal penicillins like carbenicillin; cephalosporins like ceftazidime and aminoglycosides are widely used. However nephrotoxicity and ototoxicity need to be monitored, as diabetics per se are at risk of compromised renal function.^{15,21} Oral administration of ciprofloxacin for long duration has been recommended for selected mild cases.^{27,28} All patients should be treated medically for as long as improvement continues, reserving surgical intervention only if symptoms and signs become worse under treatment. Six to eight weeks of antibacterial treatment is required for complete remission. With or without a major surgical debridement, it is advised to continue treatment for at least seven days after apparent cure in order to avoid recurrence.²⁰ Amphoterecin B or the safer liposomal Amphoterecin B are used for fungal malignant otitis externa.²³ Itraconazole is the alternative administered orally, which can be started after a course of amphoterecin B.²⁹

With the advantage of investigation modalities for early diagnosis, and better and safer antibiotics, the mortality because of malignant otitis externa is reduced from 50% in the earlier report of Chandler¹⁴ to 21% in a review of 19 cases by Shaun Loh³⁰. Recurrence is not uncommon, and the recurrence rates of 15% to 20% are reported.³¹ Earlier beliefs that Facial nerve involvement as a poor prognostic factor has not been supported by the recent reports.³²

Malignant otitis externa should be suspected and evaluated in very diabetic patient who presents with otitis externa, which is not responding to conventional antibiotic therapy.

Otomycosis:

Otomycosis is a superficial fungal infection of the external auditory canal. It can also affect the middle ear and sometimes open mastoid cavity. Almost 10% of otitis externa are caused by fungus.³³ It is common in tropical countries owing to the greater humidity. It is seen more frequently in diabetics, immunocompromised states and due to prolonged use of topical antibiotic use.³⁴ In a study by H S Satish et al, 16% of patients were diabetics among the 30% of the patients who were immunocompromised. The fungal species responsible for Otomycosis are *Aspergillus* species and *Candida* in immunocompetent hosts. *Candida* is the commonest fungus in immunocompromised state.³⁵ The altered cellular immunity in people with diabetes mellitus seems to be the cause of Otomycosis in these people. Although this is not a serious condition, resistance to treatment requiring long duration of treatment and recurrence after treatment, makes the condition frustrating to the treating physician.

Otomycosis presents with pruritus, ear block, discharge from the ear, earache, and occasionally with reduced hearing. The diagnosis of Otomycosis is mainly by history and clinical examination. Candidal otitis externa results in white debris in the ear canal when examined with an otoscope. *Aspergillus Niger* appears as a moist white plug dotted with black debris giving an appearance of a "wet newspaper".

³⁶

Fungal cultures confirm the diagnosis and isolate the species. The treatment of Otomycosis is suction clearance of the fungal debris, followed by topical antifungal medication. Clotrimazole is the widely used topical antifungal agent for Otomycosis. Fluconazole can be the alternative in patients who do not respond to clotrimazole.³⁵ Antibacterial ear drops should be avoided, or discontinued if the patient is already using them.³³ Diabetic patients require treatment for longer duration up to 3 weeks, and the recurrence rate is high in these patients. The role of systemic antifungal agents in superficial fungal infections is uncertain. Oral antifungal agents are prescribed for immunocompromised patients with Otomycosis. However, in the absence of local treatment, systemic antifungal treatment is not beneficial.³⁷ The complications like tympanic membrane perforations are more common in immunocompromised patients than immunocompetent. Kumar KR in his series found tympanic membrane perforation in 11% of patients with Otomycosis, and the perforation was more common with *Candida albicans*.³⁸ However whether the perforation is caused by the fungus or the Otomycosis was secondary to suppurative otitis media was not definite. In a series of 200 patients of Otomycosis, HS Satish et al found tympanic membrane perforation in 6 patients, and all of these were immunocompromised.³⁵ The perforation of tympanic membrane is likely to be due to avascular necrosis of part of tympanic membrane due to thrombosis of blood vessels of tympanic membrane.³⁹ Smaller perforations heal spontaneously, but larger perforations require tympanoplasty.

Invasive fungal infections of the Ear:

Aggressive invasive fungal infection involving the temporal bone is seen in diabetics with malignant otitis externa.⁴⁰ Tuzcu A et al reported a case of aggressive rapidly progressing invasive Mucormycosis of external auditory canal in a 17 year old girl with diabetic ketoacidosis²⁴.

Aspergillus and *Mucor* can cause vasculitis in uncontrolled diabetes, leading to infarction and tissue necrosis. Invasive fungal infection of temporal bone can extend into the cranial cavity leading to meningoencephalitis.⁴¹ Invasive fungal infections necessitate parenteral antifungal treatment. Amphoterecin is the drug used for first line treatment of invasive Mucormycosis.⁴² Since it is a nephrotoxic drug its use should be guarded in uncontrolled diabetic patients, who also likely to have compromised renal function. Lipid formulations of Amphoterecin B are less nephrotoxic and they are safe even when used for longer duration and at higher dose. The liposomal amphoterecin B is associated with better survival rate compared to conventional amphoterecin B.⁴² The survival is better if the treatment is started within 5 days of presentation, so establishing an early diagnosis is critical.⁴³ CT scan is useful to detect bone erosion and extension into soft tissue, and should be performed in diabetic patients with otitis externa, which is resistant to topical and systemic antibacterial agents. Presence of necrotic tissue results in poor penetration of drug, so these necrotic tissues need to be debrided for better penetration of the drug. Diabetes should be treated aggressively to maintain euglycemia and normal acid-base status in such patients.⁴²



Fig 1: Acute otitis externa of left ear of a female with diabetes, with oedema of ear canal and tragus

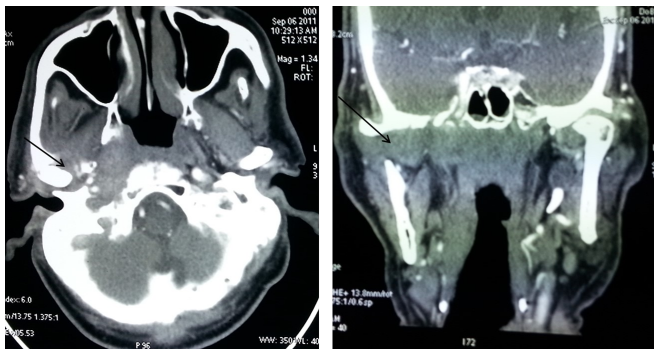


Fig 2: CT scan Axial and Coronal cuts of an elderly male diabetic with Right Malignant Otitis Externa. There is extension of the disease into temporomandibular joint and into parapharyngeal space

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