Malignant otitis externa (MOE)

INTRODUCTION:

- In 1959, Meltzer & Kelemen presented the first case
- In 1974, Chandler presented Malignant otitis externa (13 cases from 1968 to 1974)
- Invasive infection of the external auditory canal and skull base
- Typically occurs in elderly patients with diabetes mellitus
- Increasing reports in patients with immunodepression state, e.g. AIDS, hematological disorder (Leukemia, anemia, granulocytopenia, during cytotic or immunosuppressive therapy)

EPIDEMIOLOGY:

- Mean age: 65-70 years old, Male: female: 1.8:1~18:1
- Elderly diabetic patients are overwhelmingly the population at risk for malignant external otitis.
- >90 percent of adults with MOE have glucose intolerance
  Susceptibility to MOE has not been correlated with a level of glucose intolerance
- Hypotheses to explain predisposition in diabetics including:
  1. Microangiopathy in the ear canal
  2. Increased pH in diabetic cerumen → reduce concentration of lysozyme
- Rare in children, fewer than 20 cases in the literature
  → immunocompromised (malignancy or malnutrition)
  → more toxic than adult (fever, leucocytosis and bacteremia), but no mortality case
  → Facial nerve paralysis more frequently and rapidly, usually complete and permanent
    1. Mastoid process is undeveloped
    2. The facial nerve is located closer to the EAC

MICROBIOLOGY:

- P. aeruginosa in more than 95 percent of cases
- Other organisms in case report: Aspergillus species, Staphylococcus aureus, Proteus mirabilis, Klebsiella oxytoca, P. cepacia, and Candida parapsilosis
- Among 7 cases reported in HIV-infected patients, for example, Aspergillus fumigatus was isolated in 3.
PATHOGENESIS:

- P. aeruginosa → ubiquitous G(-) bacterium, capable of growing in distilled water
- Not a normal component of ear canal flora even in diabetics, its recovery indicates the presence of a pathogen
- Aural water exposure contributed to the development of malignant external otitis
- In the study, 2/3 of patients with the disease had an antecedent history of ear irrigation (generally for the purposes of removing cerumen) compared with matched controls

CLINICAL MANIFESTATIONS:

- Exquisite otalgia (>90% case) → lancinating and throbbing pain, nocturnal pain and extend into the temporomandibular joint, aggravated by chewing, not responsive to topical drugs
- Purulent fetid otorrhea in 45%~100% case
- Fever: rare
- Physical examination → granulation tissue in the inferior portion of the external auditory canal at the bone-cartilage junction (at the site of Santorini's fissures). However, this finding may be absent in atypical patients (eg, HIV-infected and children)
- Infection route: epithelial barrier of EAC osteo-cartilaginous junction → anterior into parotid compartment or downward along tympanomastoid fissure → stylomastoid foramen of jugular foramen → vascular channel and cone surface of the pyramid → Posterior fossa, middle fossa and petrous apex → Clivus and sphenoid sinus → Contralateral temporal bone
- Cranial nerve palsy in over 40% of patient, especially facial nerve dysfunction
- Children with malignant external otitis → Higher incidence of facial palsy → Relatively undeveloped mastoid process and the more medial location of the fissures of Santorini, which places the facial nerve in closer proximity to the ear canal.
- Other CNS complications are rare, but fatal → meningitis, brain abscess and dural sinus thrombophlebitis
DIAGNOSIS:

- Absence of a single pathognomonic criterion, the diagnosis is based upon a constellation of clinical, laboratory and radiographic findings.
- Laboratory: Elevated erythrocyte sedimentation rate (ESR). Although nonspecific, a strikingly elevated ESR is the most characteristic laboratory abnormality and is a useful way of monitoring disease activity.
- Anatomic imaging modalities (CT and MRI) allow for both anatomic localization of disease as well as the assessment of disease resolution.
- CT: useful for assessing both soft tissue and bone involvement, reveal inflammation in the soft tissue of tympanic cavity, mastoid infratemporal fossa, parapharyngeal space and nasopharynx, but little use when assessing therapy response.
- In a prospective study, the presence of bone erosion and/or soft tissue abnormalities in the infratemporal fossa was helpful in making the diagnosis of malignant external otitis. Although bone did not remineralize, resolution of the soft tissue component did correlate with disease activity.
- MRI: useful in evaluation of involvement of intracranial soft tissue, slightly better at medial skull base disease due to its ability to delineate changes in the fat content of the marrow, but little use when assessing therapy response.
Subtemporal soft tissue abnormalities were better appreciated with MRI and had low signal intensity on T1- & T2-weight image, unlike normal inflammation, indicating a fibrotic, necrotizing pathologic process.

Bone scanning with technetium Tc-99m accumulates at sites of osteoblastic activity positive in acute or chronic osteomyelitis, primary or secondary neoplasm, arthritic disorders and surgical or trauma zone.

Tc-99m bone scan was very sensitive in making the diagnosis, but not a specific study since there are reports of positive bone scans in simple external otitis, and bone scans are not suitable for following response to treatment since they do not normalize (9 months to several years).

Quantitative bone scanning and Ga-67 scintigraphy:
- distinguish simple from malignant external otitis
- lesion to non-lesion ratio greater than 1.5 on bone scan and 1.3 on Ga-67 scan

Gallium-67 citrate scanning more specific, incorporated into granulocytes and bacteria
- Active osteomyelitis → Tc-99m(+), Ga-67(+)
- Non-active osteomyelitis → Tc-99m(+), Ga-67(-)

Although several studies have reported that gallium scanning can be used to follow disease activity, others have noted that normal scans can be found in patients with recurrent disease.

Combination of Ga-67 single photon emission computerized tomography (SPECT) scanning is useful in the diagnosis and follow-up examination of these patients.

Integrated evaluation:
- CT: evaluate exact the bone site involved
- MRI: evaluate soft tissue
- Tc-99m bone scan: reveal as early as possible any osteomyelitic involvement
- Ga-67 scan: obtain first image for comparison with later ones while monitoring therapy

Squamous cell carcinoma of the temporal bone can also present as a painful draining ear canal. Since radiographic studies cannot differentiate tumor from necrotizing infection, biopsy is the only definitive method to distinguish.
Nosological criteria

Table I. Nosological criteria

Corey et al., 1985 (15)
At least 3 of 5 of the following signs and symptoms:
1) Persistent external otitis;
2) Granulation tissue in the EAC;
3) Evidence of mastoiditis or osteomyelitis of the skull base by radiograph or biopsy;
4) Cranial nerve paralysis;
5) Isolation of *P. aeruginosa* from the EAC or deeper skull site.

Cohen et al., 1987 (11)
Major (obligatory) signs:
1) Pain;
2) Exudate;
3) Edema;
4) Granulations;
5) Microabscesses;
6) Positive Tc99 scan or failure of local treatment after more than 1 week;
7) (*Pseudomonas*)
Minor (occasional) signs:
7) *Pseudomonas*;
8) Positive radiograph;
9) Diabetes mellitus;
10) Cranial nerve involvement;
11) Debilitating conditions;
12) Old age.

Babiatzki, Sadé *et al.*, 1987 (5)
1) Severe external otitis which does not improve after 8 days of conservative treatment;
2) Pain, especially at night;
3) Granulation tissue, mostly at the base of the EAC;
4) Culture of *P. aeruginosa*, usually;
5) Positive temporal bone scanning;
6) Diabetes (in most patients).

Sadé *et al.*, 1989 (6)
1) Severe external otitis unresponsive to at least 10 days of conservative treatment;
2) Increasingly agonizing pain exacerbated at night;
3) Typical granulation tissue, usually in the base of EAC;
4) Repeated isolation from the EAC of a Gram-pathogen, predominantly *P. aeruginosa*.

Levenson *et al.*, 1991 (10)—Ceruse *et al.*, 1993 (9)
1) Refractory otitis externa;
2) Severe otalgia, worse at night;
3) Purulent exudate;
4) Granulation tissue;
5) Recovery of *P. aeruginosa*;
6) Diabetes mellitus or other immune state compromise;
7) Positive Tc99 bone scan of the temporal bone.
The radiographic appearance of malignant external otitis
TREATMENT:

- Antipseudomonal antimicrobials are the mainstay of therapy
- Prior to the development of systemic agents, 50 percent mortality with frequent recurrence
  - Parenteral semisynthetic penicillins → 20 percent mortality
  - Oral fluoroquinolones → 10 percent mortality, with few adverse effects reported
- Ciprofloxacin (750 mg PO twice daily) → antibiotic of choice, although no comparative trials have been reported.
  1. Low toxicity profile
  2. Excellent penetration to bone
  3. Do not require adjustment in the elderly patient with renal dysfunction
- Initial with intravenous ciprofloxacin (400 mg every eight hours) until subjective clinical response or a decrease in ESR → then oral ciprofloxacin
- Prolonged treatment for 6~8 weeks is generally recommended, as indicated for osteomyelitis
- With widespread use of both oral and topical quinolones, there are increasing reports of a less severe clinical presentation of malignant external otitis and the emergence of ciprofloxacin resistance
- Patients with resistant P. aeruginosa require hospitalization for biopsy, debridement and parenteral antibiotics (>12 weeks antipseudomonal beta-lactam with/without aminoglycoside)
- Aspergillus species → Prolonged treatment (>12 weeks) with amphotericin B
  - Liposomal amphotericin B → lower the incidence of nephrotoxicity
- No role for topical antibiotics. Instillation of antipseudomonal topical agents may only increase the difficulty in isolating the organism from the ear canal.
- Surgical excision plays no role in the current treatment. Debridement and/or biopsy to rule out cancer are the only indicated surgical procedures.
- Hyperbaric oxygen (HBO) has been used on occasion with mixed results and may be considered as an adjuvant treatment for refractory cases. However, a Cochrane review found no randomised controlled trials comparing HBO to treatment with antibiotics and/or surgery and concluded that there was no clear evidence to demonstrate the efficacy of HBO treatment
REFERENCES


