

# Otogenic skull base osteomyelitis caused by invasive fungal infection

## Case report and literature review

Dominik Stodulski · Bożena Kowalska ·  
Czesław Stankiewicz

Received: 21 November 2005 / Accepted: 15 June 2006 / Published online: 9 August 2006  
© Springer-Verlag 2006

**Abstract** Otogenic skull base osteomyelitis (SBO) of fungal etiology is a very rare but life-threatening complication of inflammatory processes of the ear. The authors present a case of otogenic SBO caused by *Aspergillus flavus* in a 65-year-old man with a fatal course. Because of the encountered difficulties with the proper diagnosis and treatment, the authors reviewed the literature on the subject.

**Keywords** Otitis · Skull base · Osteomyelitis · Fungus · *Aspergillus*

## Introduction

Otogenic skull base osteomyelitis (SBO) is a rare but serious complication of inflammatory processes of the ear, posing great diagnostic and therapeutic difficulties. Otogenic SBO was first described in 1959 by Meltzer and Kelemen [25]. In 1968, Chandler introduced a term of malignant otitis externa referring to the aggressive, destructive inflammatory process caused by *Pseudomonas aeruginosa*, originating in the external auditory canal and having a tendency to spread to the skull base.

The disease manifests itself in cranial nerves palsies and often leads to death [7]. The etiological factor is in 99.2% *P. aeruginosa* [2, 10], and in the remaining cases other microorganisms such as *Staphylococcus aureus*, *Proteus mirabilis*, *Klebsiella oxytocyta* and fungi [15, 21, 27, 29, 38]. Typical otogenic SBO of bacterial etiology is a result of the inflammatory process of the external ear and generally develops in people over 60 with uncontrolled diabetes. The points of entry of mycotic infections may be both the external ear and the middle ear (acute or chronic otitis media), and the predisposing factors are immunodeficiency (most often AIDS and blood proliferative diseases) [29, 38]. Petrak et al. were the first to describe a case of SBO in the course of invasive, mycotic (*Aspergillus*) otitis externa in 1985 [30]. Since then only 38 cases of invasive mycotic inflammation of the temporal bone with or without the involvement of the skull base have been described in the English-language literature. Having in mind the above described diagnostic and therapeutic difficulties the authors present their case of this severe disease together with the literature review.

## Case report

A 65-year-old man was admitted to hospital having suffered from acute headaches of the left side accompanied by vertigo, disturbed balance, nausea, difficulty in swallowing and choking for 3 months. He had also been suffering from periodic otorrhea from the left ear and some loss of hearing for about 3 years. He had been hospitalized twice in the previous 2 months in other ENT department where recurrent acute otitis media had been diagnosed and conservative treatment had

---

D. Stodulski (✉) · B. Kowalska · C. Stankiewicz  
Department of Otolaryngology,  
Medical University of Gdańsk, ul. Dębinki 7,  
80 211 Gdańsk, Poland  
e-mail: dstodulski@amg.gda.pl

B. Kowalska  
e-mail: bkowalska@amg.gda.pl

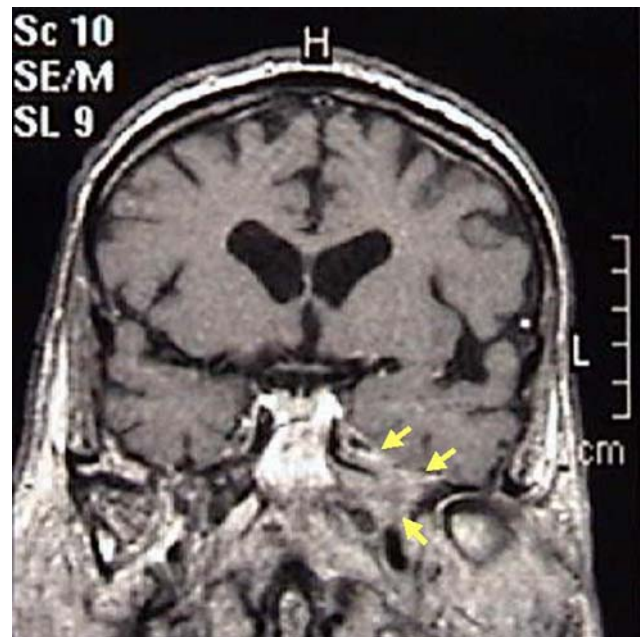
C. Stankiewicz  
e-mail: stank@amg.gda.pl

been ordered (intravenous antibiotics and paracentesis). The case history revealed chronic alcohol abuse, type 2 diabetes mellitus (treated with oral hypoglycemic drugs for several years) and arterial hypertension. On admission his general condition was medium severe, the patient was afebrile. On ORL examination left external auditory canal showed no signs of inflammation or granulation. Tympanic membrane was thickened, without visible anatomic structure, movable. Fistulous test was negative. His right ear was without any deviation. Tuning fork tests were consistent with a left conductive hearing loss, which was confirmed by 40- to 55-dB hearing loss on pure tone audiometry. Additionally, a sensorineural hearing loss up to 40 dB for 4 kHz in the right ear was revealed. The examination showed a peripheral nerve VII palsy (4/6 in House-Brackmann scale) and palsy of cranial nerves IX, X, XI, XII on the right side. Meningeal symptoms were negative. Laboratory tests showed increased values of C-reactive protein of 84 mg/l. The level of serum glucose was 187 mg%. Diagnostic paracentesis was performed and plethoric secretion was sucked out. However, pathogens were cultured neither from this secretion nor from the left auditory canal smears (examination repeated three times). The patient was tested for tuberculosis, Wegener's granuloma and HIV, and the results were negative.

Scintigraphic examination of bones showed an increased marker uptake in the left temporal bone projection. MRI detected extensive infiltration within the pyramid of the temporal bone and middle skull base fossa, in the vicinity of the clivus, extrameningeally. It was spreading to the right side and got more intense with contrast medium. The image showed an inflammatory process (Fig. 1).

Both clinical and additional examination results led to the diagnosis of otogenic SBO. Taking into consideration bad condition of the patient, further invasive diagnostic procedures (mastoidectomy) were abandoned. Empiric therapy with intravenous antibiotics aimed at *P. aeruginosa* was employed: ceftazidime (Fortum<sup>®</sup>), dose  $2 \times 1.0$  g; ciprofloxacin (Ciprinol<sup>®</sup>), dose  $2 \times 0.2$  g. Hyperbaric oxygenation (HBO, altogether 16 exposures) in the National Center of Hyperbaric Medicine in Gdynia was ordered too. Antibiotic treatment was supplemented with intensive insulinotherapy and antifungal protection (ketoconazole 0.2 g/24 h).

Despite the applied therapy, the patient's condition did not improve and after 18 days there was a violent progression of the disease—nerves III, IV and VI palsies on the left side together with quantitative disorder of consciousness and worsening of patient's general condition. Repeated MRI examination dis-



**Fig. 1** Coronal MRI. An extensive infiltration of the left temporal bone and middle cranial fossa enhanced with gadolinium contrast

closed significant progression of the disease with infiltration caused by the inflammatory process in the left cavernous sinus, bulb of the interior jugular vein, parapharyngeal space and penetration to the nasopharynx as well as contraction and loss of flow in the internal carotid artery. The infiltration got more intense with contrast medium, with visible dura enhancement in the area of the temporal lobe and ponto-cerebellar angle. There were no signs of increased intracranial pressure (Fig. 2).

Lumbar puncture disclosed reactive cerebrospinal fluid with no pleocytosis. First, in repeated bacteriological tests (smears from the left auditory canal) isolated colonies of *Aspergillus* spp. were cultured. Next examination revealed presence of *Aspergillus flavus*. Suspected systemic mycosis was confirmed serologically (titer of antibodies against *A. flavus* 1:320, *Aspergillus* antigen negative). Because of patient's severe condition (very high risk of surgery) and the isolation of the etiological factor confirmed by serological examination, the previously planned diagnostic mastoidectomy was abandoned again.

Liposomal Amphotericin B (Ambisome<sup>®</sup>) was administered intravenously, in increasing dose from 1 to 3 mg/kg/24 h and orally—itraconazole (Orungal<sup>®</sup>)  $2 \times 0.2$  g. Despite the applied therapy lasting 30 days, further worsening of patient's general condition was observed—respiratory failure demanding mechanical ventilation, rises of systolic blood pressure to



**Fig. 2** Axial MRI. Progression of the disease—inflammatory infiltration of the left cavernous sinus, internal carotid artery with penetration to the nasopharynx. Meningeal enhancement around the left temporal lobe

250 mmHg, arrhythmia, heavy electrolytic disturbances and changes in neurologic status—deep coma, right-sided hemiparesis and right nerve VI palsy. The patient died on the 53rd day of hospitalization.

Post-mortem examination confirmed the clinical diagnosis of fungal (*Aspergillus*), invasive, otogenic SBO of the left side. The left temporal bone and lateral skull base were completely destroyed by infiltration containing large amounts of yellowish, thick pus, which on histological examination revealed numerous septate branching fungal hyphae, consistent with *Aspergillus*. It disclosed fungal meningitis in the region of the left temporal lobe with some infiltration of cavernous sinus and the spread of the inflammatory process to the cerebral tissue. The autopsy also showed some features of endosepsis with the presence of fungal pulmonary embolism as well as changes characteristic of alcoholic liver disease.

## Discussion

There are four potential routs of infection for invasive temporal bone and lateral SBO: from the external ear or, in the course of acute or chronic otitis media, via tympanic cavity (tympanogenic), meningogenic (in fungal meningitis, via internal auditory canal), from the Eustachian tube and hematogenic [17, 34, 39].

Extremely rare lateral SBO follows paranasal sinus infections [24]. Fungal infection usually develops primarily within the middle ear (tympanic cavity or mastoid process of the temporal bone) [37–39, 42]. In our patient the rout of entry of aspergillosis was most probably this area (recurrent acute otitis media treated with wide-spectral antibiotics) [31–33].

Table 1 presents a comparison of 40 cases of invasive mycoses of the temporal bone and lateral skull base. The dominant pathogen was *Aspergillus fumigatus*—19 pts, then *A. flavus*—10 pts, and significantly less frequent other fungi (*Aspergillus niger*, *Aspergillus without determination of species*, *Pseudallescheria boydii*, *Scedosporium apiospermum*, *Malassezia sym-podialis*, *Lecythophora hoffmannii*, *Candida ciferri*). We found it odd that no *Mucor* infection was found in this group.

The predisposing factors in invasive fungal mycoses are found to be primary and acquired immunodeficiency (AIDS, neutropenia, leukemias), malignant neoplasms and their treatment (irradiation, chemotherapy), the use of steroids and wide-spectral antibiotics, “graft versus host” disease, systemic diseases and microflora disorders in the ear [26, 27, 35, 38, 42]. The comparison of invasive mycoses of the temporal bone and skull base presented in Table 1 shows that by far the most frequent risk factor was AIDS—15 patients, then—the disorder of leukocyte system (acute or chronic leukemia, neutropenia). Diabetes occurred in nine patients (in seven of them as the only risk factor). Chronic otitis media was found in four patients, secretory otitis media in one and recurrent acute otitis media in the described case. In one case, systemic lupus erythematosus (SLE) and immunosuppressive treatment led to fungal invasive infection. No risk factor was found in five patients. In our case, apart from uncompensated diabetes, the major factor affecting the course of the disease seems to be alcoholism, since the suppressive influence of ethanol on the immunological system is generally known [19]. The age of the patient, unlike in the bacterial SBO, seems to be of secondary importance. In the 40 described cases, the age fluctuated from 6 to 85 years.

Many authors stress the need for prompt identification of the microorganisms involved in otogenic SBO [2, 3, 22, 24, 26, 37]. Cunningham et al. [10] are of the opinion that empiric treatment (directed against *P. aeruginosa*) of malignant otitis externa is unfounded, and prolonged antibiotic therapy should always be preceded by bacteriological examination. In case of mycoses, there are two problems: first, positive cultures are obtained only in 40% of aspergilloses (histopathologically confirmed) [3], and additionally,

**Table 1** Comparison of 40 cases of invasive mycoses of temporal bone and lateral skull base

Case	Author (year)	Organism	Risk factors	Treatment (antimycotic)	Results of treatment
1.	Petrak et al. (1985) [30]	<i>A. fumigatus</i>	AML	A	Recovery
2.	Stanley et al. (1988) [39]	<i>A. fumigatus</i>	CLL	A, F	Recovery/dead of other cause
3.	Cunningham et al. (1988) [10]	<i>A. fumigatus</i>	Aged/none	A	Recovery/dead of other cause
4.	Bickley et al. (1988) [3]	<i>A. species</i>	Myelodysplasia	A	Recovery/dead of other cause
5.	Menachof and Jackler (1990) [26]	<i>A. flavus</i>	AML, COM	A	Recovery/dead of other cause
6.		<i>A. fumigatus</i>	COM	None	Unrecovery/dead of other cause
7.	Granstroem et al. (1990) [16]	<i>P. boydii</i>	DM	I + HBO	Recovery
8.	Phillips et al. (1990) [31]	<i>A. species</i>	AML, DM	A, I	Recovery/dead of other cause
9.	Strauss and Fine (1991) [40]	<i>A. fumigatus</i>	AIDS	A, I	Dead of disease
10.	Reiss et al. (1991) [32]	<i>A. fumigatus</i>	AIDS	A, I	Recovery
11.		<i>A. fumigatus</i>	AIDS	A, I	Recovery/dead of other cause
12.	Hall and Farrior (1993) [17]	<i>A. fumigatus</i>	AIDS, COM	A	Recovery/no follow up
13.		<i>A. fumigatus</i>	COM	A	Recovery
14.	Hanna et al. (1993) [18]	<i>A. flavus, C. ciferri</i>	DM	A	Recovery
15.	Gordon and Giddings (1994) [14]	<i>A. flavus</i>	DM	A, I	Recovery
16.		<i>A. flavus</i>	Aged/none?	A, I	Recovery
17.	Harley et al. (1995) [20]	<i>A. flavus</i>	ALL	A	Dead of disease
18.	Bryce et al. (1997) [4]	<i>A. fumigatus</i>	AIDS	A, I	Recovery
19.	Ress et al. (1997) [33]	<i>A. fumigatus</i>	AIDS	None	Dead of disease
20.	Busaba and Poulin (1997) [5]	<i>P. boydii</i>	AIDS	A, I	Recovery
21.	Kountakis et al. (1997) [22]	<i>A. flavus</i>	DM, CRI	A + MA	Recovery
22.	Yates et al. (1997) [43]	<i>A. fumigatus</i>	AIDS, hemophilia	MA + I	Recovery/dead of other cause
23.	Munoz and Martinez-Chamorro (1998) [27]	<i>A. fumigatus</i>	AIDS	I, A	Dead of disease
24.	Diop et al. (1998) [12]	<i>A. fumigatus</i>	AIDS	A	Dead of disease
25.	Slack et al. (1999) [37]	<i>A. flavus, fumigatus, niger</i>	ALL	A, I	Dead of disease
26.		<i>S. apiospermum</i>	AIDS	A, I	Unrecovery
27.	Chen et al. (1999) [9]	<i>A. fumigatus</i>	AIDS	MA + A, I	Recovery
28.		<i>A. fumigatus</i>	AIDS	I + MA + A	Recovery
29.		<i>A. fumigatus</i>	AIDS, SOM	MA	Dead of unknown cause
30.	Chai et al. (2000) [6]	<i>M. sympodialis</i>	DM	A	Recovery
31.	Ohki et al. (2001) [28]	<i>A. flavus</i>	No	MA + FL	Recovery
32.	Yao and Messner (2001) [42]	<i>S. apiospermum</i>	AIDS	A, I, K, M	Dead of disease
33.	Finer et al. (2002) [13]	<i>A. flavus</i>	Neutropenia	I	Recovery
34.	Shelton et al. (2002) [35]	<i>A. niger</i>	No	I, C	Recovery
35.	Bellini et al. (2003) [2]	<i>A. niger</i>	DM	A, I	Recovery
37.	Chang et al. (2005) [8]	<i>L. hoffmannii</i>	No	MA + PHMB	Recovery
38.	Amonoo-Kuofi et al. (2005) [1]	<i>A. fumigatus</i>	SLE, immunosuppression	MA + V	Recovery
39.	Kuruvilla et al. (2006) [23]	<i>A. species</i>	DM	I	No follow up
40.	This report	<i>A. flavus</i>	rAOM, DM, ALC	K, A, I + HBO	Dead of disease

*A.* Aspergillus, *C.* Candida, *L.* Lecythophora, *M.* Malassezia, *P.* Pseudallescheria, *S.* Scedosporium, *ALC* alcoholism, *ALL* acute lymphocytic leukaemia, *AML* acute myeloid leukaemia, *CLL* chronic lymphocytic leukaemia, *COM* chronic otitis media, *CRI* chronic renal insufficiency, *DM* diabetes mellitus, *rAOM* recurrent acute otitis media, *SOM* secretory otitis media, *SLE* systemic lupus erythematosus, *A* amphotericin B, *C* clotrimazole, *F* flucytosine, *FL* fluconazole, *HBO* hyperbaric oxygenation, *I* itraconazole, *K* ketokonazole, *M* miconazole, *V* voriconazole, *MA* mastoidectomy, *PHMB* polyhexamethylene biguanide

the value may be decreased by the prolonged use of antibiotic ear drops [15, 26]. Second, due to the frequent occurrence of saprophytic fungi in the external auditory canal, cultivation of *Aspergillus* does not justify the diagnosis of invasive mycosis. However, such examination result should not be disregarded and repeated smears and histopathological examination should be carried out [2, 17, 22]. Serological diagnostics of systemic mycoses is of limited value in immuno-

compromised patients since seroconversion occurs only in 35% of such patients [3].

To correctly diagnose and establish the proper antifungal treatment in case of non-diagnostic cultures and lack of improvement or progression of the disease, it is necessary to obtain material for histopathological and microbiological examination that may be acquired by mastoidectomy [10, 26]. Histopathological material obtained by mastoidectomy allows not only to confirm



**Table 2** Classification of fungal infections of the ear and temporal bone by Chen et al. [9]

Type	Extension of the disease	Characteristics	Treatment
I	Limited otitis externa	Localized infection; no tissue invasion	Cleaning, topical anti-fungal agents
II	Otitis externa with extension into mastoid cavity/mastoiditis	Bone invasion, granulomatous response, fibrosis	Topical and systemic anti-fungals. Surgery for consideration (if no improvement)
III	Invasive mastoiditis with nerve VII palsy	Aggressive tissue invasion. Can occur in immunocompetent patients	Amphotericin B; itraconazole; surgical debridement
IV	Invasive mastoiditis, nerve VII palsy, SBO	Angioinvasion. Mild tissue granulomatous response (especially in immunocompromised patients)	Amphotericin B; itraconazole; surgical debridement

invasive mycosis but also to rule out the neoplastic growth or granuloma [15, 22, 29, 38, 41]. On the other hand, Kountakis et al. recommend performing a diagnostic mastoidectomy after 4 weeks, if the applied treatment does not bring any improvement [22]. Considering the described case and difficulties to discover the etiology of lateral skull base osteomyelitis, the authors state, that diagnostic mastoidectomy should not be postponed longer than 2 weeks, if empiric therapy is not effective. In case of very extensive osteomyelitis and bad general condition of a patient, thus with high risk of rapid progression of the disease, initial “aggressive” diagnostics could be considered.

Classic invasive (caused by *P. aeruginosa*) otitis externa was divided into three stages (I—the process limited to the soft tissues and cartilage of the external auditory canal, II—limited SBO, III—diffuse infiltration of the skull base) [29]. However, this division has no practical use in case of mycoses because of frequently occurring involvement of the middle ear area. Chen et al. [9] proposed an interesting classification of fungal infections of the ear and temporal bone infections on the base of classification of paranasal sinuses mycoses. They divided mycotic infections into four types depending on the extension of the inflammation process and the presence of facial nerve palsy including their proper treatment (Table 2).

Once the diagnosis is confirmed, treatment of invasive fungal infections of the temporal bone and skull base consists of three parts: compensation of immunological deficiency and/or predisposing disease (AIDS, diabetes), administration of anti-fungal agents and aggressive surgical debridement [1, 2, 39, 42]. Grandis et al. [15] recommend prolonged (above 12 weeks) administration of Amfotericin B, best in a liposomal form, since it is less nephrotoxic (which is important for a diabetic patient). According to the data from Table 1 most of the cases were treated with Amfotericin B intravenously with a positive response in 21 of 40 patients and with a failure in 8 and itraconazole was administered as an additional agent or in a

prolonged therapy. In three cases, itraconazole was used as the only antifungal drug (in one case together with HBO) and the result in two patients was full recovery (the follow up in the third patient was unavailable) [13, 16, 39]. One case of *Aspergillus* mastoiditis was successfully treated with new broad spectrum antifungal agent—voriconazole [1]. Therapeutic mastoidectomy is recommended, according to Finer et al. [13], when persistent mycosis (despite intravenous and/or oral treatment) is suspected. Other authors reported, that only a wide cortical mastoidectomy with opening and clearing of the mastoid antrum allows for local control of the disease [9, 28]. HBO against invasive mycosis of the temporal bone and skull base is not a generally accepted method of treatment, unlike in malignant otitis externa of *P. aeruginosa* etiology. Apart from our patient, this method was applied only in one case [16]. It was proved (mainly by in vitro tests) that hyperbaric oxygen had at least an inhibiting effect on fungi [16]. HBO, as an adjuvant method, is generally accepted in cases of osteomyelitis and the indication for its use are stages II and III of malignant otitis externa [11, 36]. According to the classification proposed by Chen et al. [9], in case of invasive mycoses of temporal bone and skull base, HBO should be used in stages III and IV and its use should be considered in stage II.

Involvement of cranial nerves in malignant, bacterial external otitis testifies to the extension of the process and is an unfavorable prognostic factor [24, 29, 34, 38]. Similar to *P. aeruginosa*, one of the endotoxins produced by *Aspergillus* shows neurotoxic activity [26]. Additionally, in mycoses of the temporal bone there is a great risk of sensorinervous deafness [28]. Among 40 cases of invasive mycoses of the temporal bone and skull base, isolated paresis/palsy of the facial nerve was dominant (about 70%). In four patients, other cranial nerves (IX–XII) were also involved. However, because of too small group of patients it is impossible to determine if the cranial nerves involvement is a significant prognostic factor

[1–6, 8–10, 12–14, 16–18, 20, 22, 23, 26–28, 30–33, 35, 37, 39, 40, 42, 43].

According to Table 1 mortality due to invasive mycosis of the temporal bone and lateral skull base was about 27%. It should be mentioned that prognosis seems to depend more on the state of the immunity system than on the treatment applied [2, 27, 37, 42].

To summarize, invasive, fungal temporal bone and SBO occurs usually in immunocompromised patients (AIDS, blood diseases). Diabetes and age are of significantly less importance. The route of entry may be both the middle ear (tympanic cavity and mastoid process) and the external auditory canal. Prognosis depends not only on early, sometimes “aggressive” diagnosis (with obligatory microbiological and histopathological confirmation) and the therapy applied, but also (and perhaps mainly) on the condition of the immunological system of a patient. Fungal infection should be always considered part of the differential diagnosis of patients with lateral SBO, who are relatively immunocompromised and who do not respond to antibiotic treatment (in our opinion not longer than 2 weeks) regardless of cranial nerves involvement.

## References

- Amonoo-Kuofi K, Tostevin P, Knight JR (2005) *Aspergillus* mastoiditis in a patient with systemic lupus erythematosus: a case report. *Skull Base* 15(2):109–112
- Bellini C, Antonini P, Ermanni S, Dolina M, Passera E, Bernasconi E (2003) Malignant otitis externa due to *Aspergillus niger*. *Scand J Infect Dis* 35:284–288
- Bickley LS, Betts RF, Parkins CW (1988) Atypical invasive external otitis from *Aspergillus*. *Arch Otolaryngol Head Neck Surg* 114:1024–1028
- Bryce GE, Phillips P, Lepawsky M, Grible MJ (1997) Invasive *Aspergillus* tympanomastoiditis in an immunocompetent patient. *J Otolaryngol* 26:266–269
- Busaba NY, Poulin M (1997) Invasive *Pseudallescheria boydii* fungal infection of the temporal bone. *Otolaryngol Head Neck Surg* 17:S91–S94
- Chai FC, Auret K, Christiansen K, Yuen PW, Gardam D (2000) Malignant otitis externa caused by *Malassezia sympodialis*. *Head Neck* 22:87–89
- Chandler JR (1968) Malignant external otitis. *Laryngoscope* 78(8):1257–1294
- Chang CY, Schell WA, Perfect JR, Hulka GF (2005) Novel use of a swimming pool biocide in the treatment of a rare fungal mastoiditis. *Laryngoscope* 115(6):1065–1069
- Chen D, Lalwani AK, House JW, Choo D (1999) *Aspergillus* mastoiditis in acquired immunodeficiency syndrome. *Am J Otol* 20:561–567
- Cunningham M, Yu VL, Turner J, Curtin H (1988) Necrotizing otitis externa due to *Aspergillus* in an immunocompetent patient. *Arch Otolaryngol Head Neck Surg* 114:554–556
- Davis JC, Gates GA, Lerner C, Davis MG Jr, Mader JT, Dinesman A (1992) Adjuvant hyperbaric oxygen in malignant external otitis. *Arch Otolaryngol Head Neck Surg* 118:89–93
- Diop EM, Schachern PA, Paparella MM (1998) Acquired immunodeficiency syndrome with massive *Aspergillus fumigatus* infection. *Otolaryngol Head Neck Surg* 118:283–285
- Finer G, Greenberg D, Leibovitz E, Leiberman A, Shelef I, Kapelushnik J (2002) Conservative treatment of malignant (invasive) external otitis caused by *Aspergillus flavus* with oral itraconazole solution in neutropenic patient. *Scan J Infect Dis* 34:227–229
- Gordon G, Giddings NA (1994) Invasive otitis externa due to *Aspergillus* species: case report and review. *Clin Infect Dis* 19:866–870
- Grandis JR, Branstetter BF IV, Yu VL (2004) The changing face of malignant (necrotizing) external otitis: clinical, radiological, and anatomic correlations. *Lancet Infect Dis* 4:34–39
- Granstroem G, Hanner P, Edebo L, Fornander J (1990) Malignant external otitis caused by *Pseudoallescheria boydii*. Treatment with hyperbaric oxygenation. In: *Proceedings from the XVIth EUBS-meeting, Amsterdam*, pp 41–49
- Hall PJ, Farrow JB (1993) *Aspergillus* mastoiditis. *Otolaryngol Head Neck Surg* 108:167–170
- Hanna E, Hughes G, Eliachar I, Wanamaker J, Tomford W (1993) Fungal osteomyelitis of the temporal bone: a review of reported cases. *Ear Nose Throat J* 72:537–541
- Happel KI, Nelson S (2005) Alcohol, immunosuppression, and the lung. *Proc Am Thorac Soc* 2(5):428–432
- Harley WB, Dummer JS, Anderson TL, Goodman S (1995) Malignant external otitis due to *Aspergillus flavus* with fulminant dissemination to the lungs. *Clin Infect Dis* 20:1052–1054
- Hern JD, Almeyda J, Thomas DM, Main J, Patel KS (1996) Malignant otitis externa in HIV and AIDS. *J Laryngol Otol* 110:770–775
- Kountakis SE, Kemper JV Jr, Chang J, DiMaio DJM, Stiernberg CM (1997) Osteomyelitis of base of the skull secondary to *Aspergillus*. *Am J Otolaryngol* 18:19–22
- Kuruvilla G, Job A, Mathew J, Ayyappan AP, Jacob M (2006) Septate fungal invasion in masked mastoiditis: a diagnostic dilemma. *J Laryngol Otol* 7:1–3
- Malone DG, O’Boynick PL, Ziegler DK, Batnitzky S, Hubble JP, Holladay FP (1992) Osteomyelitis of the skull base. *Neurosurgery* 30:426–431
- Meltzer PE, Kelemen G (1959) Pyocyanous osteomyelitis of the temporal bone, mandible and zygoma. *Laryngoscope* 69:1300–1316
- Menachof MR, Jackler RJ (1990) Otogenic skull base osteomyelitis caused by invasive fungal infection. *Otolaryngol Head Neck Surg* 102:285–289
- Munoz A, Martinez-Chamorro E (1998) Necrotizing external otitis caused by *Aspergillus fumigatus*: computed tomography and high resolution magnetic resonance imaging in an AIDS patient. *J Laryngol Otol* 112:98–102
- Ohki M, Ito K, Ishimoto S (2001) Fungal mastoiditis in an immunocompetent adult. *Eur Arch Otorhinolaryngol* 258:106–108
- Patel SK, McPartlin DW, Philpoti JM, Abramovich MS (1999) A case of malignant otitis externa following mastoidectomy. *J Laryngol Otol* 113:1095–1097
- Petrak RM, Pottage JC Jr, Levin S (1985) Invasive external otitis caused by *Aspergillus fumigatus* in an immunocompromised host (Letter). *J Infect Dis* 151:196
- Phillips P, Bryce G, Shepherd J, Mintz D (1990) Invasive external otitis caused by *Aspergillus*. *Rev Infect Dis* 12:277–281
- Reiss P, Hadderingh R, Schot LJ, Danner SA (1991) Invasive external otitis caused by *Aspergillus fumigatus* in two patients with AIDS. *AIDS* 5:605–606

33. Ress BD, Luntz M, Telischi FF, Balkany TJ, Whiteman ML (1997) Necrotizing external otitis in patients with AIDS. *Laryngoscope* 107:456–460
34. Rowlands RG, Lekakis GK, Hinton AE (2002) Masked pseudomonas skull base osteomyelitis presenting with a bilateral Xth cranial nerve palsy. *J Laryngol Otol* 116:556–558
35. Shelton JC, Antonelli PJ, Hackett R (2002) Skull base fungal osteomyelitis in an immunocompetent host. *Otolaryngol Head Neck Surg* 126:76–78
36. Shupak A, Greenberg E, Hardoff R, Gordon C, Melamed Y, Meyer WS (1989) Hyperbaric oxygenation for necrotizing (malignant) otitis externa. *Arch Otolaryngol Head Neck Surg* 115:1470–1475
37. Slack CL, Watson DW, Abzug MJ, Shaw C, Chan KH (1999) Fungal mastoiditis in immunocompromised children. *Arch Otolaryngol Head Neck Surg* 125:73–75
38. Sreepada GS, Kwartler JA (2003) Skull base osteomyelitis secondary to malignant otitis externa. *Curr Opin Otolaryngol Head Neck Surg* 11:316–323
39. Stanley RJ, McCaffrey TV, Weiland LH (1988) Fungal mastoiditis in the immunocompromised host. *Arch Otolaryngol Head Neck Surg* 114:198–199
40. Strauss M, Fine E (1991) Aspergillus otomastoiditis in acquired immunodeficiency syndrome. *Am J Otol* 12:49–53
41. Subburaman N, Chaurasia MK (1999) Skull base osteomyelitis interpreted as malignancy. *J Laryngol Otol* 1113:775–778
42. Yao M, Messner AH (2001) Fungal malignant otitis externa due to *Scedosporium apiospermum*. *Ann Otol Rhinol Laryngol* 110:377–380
43. Yates PD, Upile T, Axon PR, de Carpentier J (1997) Aspergillus mastoiditis in a patient with acquired immunodeficiency syndrome. *J Laryngol Otol* 111:560–561