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Microbiology in complicated head and neck infections

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Abstract. *Microbiology in complicated head and neck infections. Objective*: To identify the pathogens associated with complicated ear, throat and sinus infections and to link the relevant susceptibility patterns to the empirical therapy currently advised in the Dutch guidelines.
Study design: Retrospective, descriptive study of consecutive cases.
Setting: Tertiary referral centre.
Patients: All consecutive patients with a complicated ear, nose and throat infection who underwent surgery at a tertiary referral centre during a six-year period. The term 'complicated' was used to define infections that had spread outside the primary region of infection (middle ear cavity, pharyngeal mucosa, or paranasal sinus) and which therefore, under our policy, required surgical intervention.
Main outcome measure: Microbiological culture and susceptibility pattern
Results: A total of 96 patients were included in this study. The predominant causative organisms for the infections were *Streptococcus pneumonia,* beta hemolytic streptococci and *Streptococcus milleri* for ear, throat, and sinus infections, respectively. These were all susceptible to the recommended empirical therapy. Cultures from 6 patients yielded coagulase-negative staphylococci resistant to frequently used antibiotics.
The mortality rate in our series was 13% for ear infections. This was caused by complicated infections in young children and patients with cholesteatoma. Ten per cent of the ear infections in adults yielded *Pseudomonas aeruginosa* and 25% yielded anaerobes.
Conclusions: Ear infections in young children and in patients with cholesteatoma should be treated aggressively. Our results suggest that patients with intracranial complications stemming from ear infections should preferably be treated with a combination therapy including antibiotics targeting gram negatives and anaerobes.
The role of coagulase-negative staphylococci, especially in neck abscesses, may be more important than has been thought until now.

Introduction

Complications in ear, throat or sinus infections may manifest extracranially and/or intracranially. The intracranial spread of infection in particular may result in significant increases in morbidity and mortality. The diagnosis and management of intracranial complications are challenging and require close collaboration between specialists in otorhinolaryngology, neurosurgery and infectious diseases. Surgical drainage and systemic antibiotic treatment are required as soon as possible, preferably by means of a culture-directed intravenous antibiotic treatment with good cerebrospinal fluid penetration. Often, however, treatment starts before the results of the culture and antibiogram are known. The selection of antimicrobial agents for empirical therapy should be based on the susceptibility pattern of the commensal flora of the upper respiratory tract present in the community, and by considering the effect of previous antimicrobial therapy or prophylaxis that may select resistant strains.[1-3]

Table 1 presents the current antibiotic recommendations for our selected patient groups, as stipulated in the National Electronic Antibiotic Guide 'SWAB-id' of the Dutch Working Party on Antibiotic Policy. However, these recommendations were not yet available during the inclusion period of our study. So in this study we retrospectively identified the pathogens associated with complicated ear, throat and sinus infections and linked their susceptibility pattern to the empirical therapy currently recommended.

Material and methods

Over a period of six years, the first author registered all consecutive

Table 1

Type of infection and therapy advised according to the National Electronic Antibiotic Guide 'SWAB-id' of the Dutch Working Party on Antibiotic Policy

Infection	Causative micro-organism	First-choice antibiotic recommendation
Ear		
Mastoiditis	Unkown	Amoxicillin/clavulanic acid
Meningitis	Unknown	Ceftriaxon
	Streptococcus pneumoniae	Penicillin
	Staphylococcus aureus	Flucloxacillin
Brain abscess	Unkown	Ceftazidim + penicillin + metronidazole
	Pseudomonas aeruginosa	Ceftazidim + ciprofloxacin
	Staphylococcus aureus	Flucloxacillin
	Streptococcus milleri	Penicillin
Throat		
Pharyngeal abscess	Unknown	Amoxicillin/clavulanic acid
Sinus		
Sinusitis		Amoxicillin

patients presenting with complicated infections who subsequently underwent surgery at the Otorhinolaryngological clinic of the UMC Utrecht (Netherlands).

Data were collected retrospectively from in-patient records and post-discharge letters. The laboratory information system was reviewed for pathogens and susceptibility patterns.

Infections were defined as 'complicated' when the infection had spread outside the primary region (middle ear cavity, pharyngeal mucosa, or paranasal sinus), making surgical intervention necessary under the terms of our policy. Peritonsillar abscesses were not included.

Results

Complicated ear infections

Patient characteristics

The group consisted of 38 patients (24m/14f). The mean age was 27, 47% of the patients were younger than 10 years and 21% were older than 60 years.

Risk factors

A known risk factor was identified in 14 patients (36%): previous otological infections (5), cholesteatoma (3), prior radiotherapy because of a maxillacarcinoma and a meningioma (2), Down syndrome (2), M. Wegener (1), and alcohol abuse (1).

Clinical entity

The complicated ear infections of the 38 patients consisted of: mastoiditis (16), meningitis (10), septic sigmoid sinus thrombosis (6), subdural empyema (4), epidural empyema (3), meningoencephalitis (3), and intracranial abscess (3). Some patients had more than one complication. There were no facial palsies in our group.

Type of surgery

The following surgical interventions were performed: mastoidectomy/atticoantrotomy (28); a radicalisation of the temporal bone (8); neurosurgical interventions (6); retroauricular puncture of the abscess and a middle ear ventilation tube (1) and a middle ear ventilation tube (1) (these last two interventions were in two children aged 2 and 0 years).

Empirical therapy

Most patients (94%) initially received amoxicillin/clavulanic acid, ceftriaxon, metronidazole, clindamycin or a combination including at least one of these.

Mortality and morbidity

Five patients died of complicated ear infections. Three of these were children aged 0-4 suffering from a complicated, acute otitis media (2 meningitis / 1 sigmoid sinus thrombosis). The other two were a male patient aged 25 years and a 72-year-old female with cholesteatoma (subdural empyema / intracranial abscess). One patient developed critical illness neuropathy and one patient became deaf.

Complicated throat infections

Patient characteristics

This group consisted of 37 patients (25m/12f). The mean

age was 36 years, with children younger than 10 in only 6 cases (16%), and elderly patients above 60 years in 4 cases (11%).

Risk factors

A dentogenic focus or recent (less than 10 days before onset of symptoms) visit to their dentist (4); a recent trauma (2); alcohol abuse (2); tumour resection, neck dissection and radiotherapy in the past (1) a squamous cell carcinoma of the lung (1).

Clinical entity

The group of neck abscesses consisted of: I) parapharyngeal abscess (20), retropharyngeal abscess (6), and II) sub-mandibular (7) or sublingual (1). In 3 patients, the site of infection was elsewhere: one patient had a fasciitis necroticans, one perivertebral spread and one lymphadenitis with abscess formation. Mediastinal spread was found in two patients.

Type of surgery

To treat these complications, neck drainage was performed 22 times, a transoral approach or puncture on eight occasions. A primary, combined neck and transoral approach was planned in two patients. Two other patients suffered a spontaneous rupture of the abscess into the mouth or pharynx during intubation prior to surgery. Three patients underwent other types of drainage for their specific disease. Thoracic surgery was performed in the two patients with mediastinal involvement.

Empirical therapy

Most patients (89%) initially received amoxicillin/clavulanic acid, ceftriaxon, metronidazole, clindamycin or a combination with at least one of these.

Mortality and morbidity

One patient died of a fasciitis necroticans. Six patients needed a tracheostoma.

Complicated sinus infections

Patient characteristics

This group consisted of 21 patients (14m/7f). In this group the mean age was 26, with 5 patients younger than 10 (24%), and only 1 patient aged above 60 years (5%).

Risk factors

Cystic fibrosis (1), a history of severe trauma capitis (1)

Clinical entity

Subdural empyema (6), orbital cellulitis (5), subperiostal abscess (4), epidural empyema (4), meningitis (1), intracranial abscess (1), orbital flegmone/ abscess (2). Several patients suffered more than one complication.

Type of surgery

Surgery consisted of an external approach (primary) on a total of 10 occasions. Particularly in the case of frontal sinus complications, a nasal endoscopy was performed upon completion of the surgery. On six occasions, the approach was endonasal. On five different occasions, a combined approach was indicated from the beginning.

On seven occasions, neurosurgical intervention had been planned to take place during the same session. This included two immediate cranialisations. After the initial endonasal drainage, one cranialisation was postponed until the patient (a 75-year-old lady with an epidural empyema) had recovered sufficiently to undergo further surgery. A 15-year-old girl with a complicated course of subdural empyema underwent multiple surgery.

Empirical therapy

Most patients (90%) initially received amoxicillin/clavulanic acid, ceftriaxon, metronidazole, clindamycin or a combination including at least one of these.

Mortality and morbidity

None of the patients suffering a complication of sinusitis died. However, serious neurological morbidity was seen in the young girl with subdural empyema.

No further specifications will be given since the duration of illness prior to admission, prior use of antibiotics, and the duration of hospitalisation varied greatly depending upon the clinical entity. (Nevertheless, we would like to add that no striking findings were noticed relating to these factors).

Cultures and antibiogram

Cultures of the abscesses, cavities, pus, blood, and liquor – or at least one of these – were obtained from all patients during surgery and/or upon admission or hospitalisation. Positive cultures were obtained from 77 patients. Negative cultures were associated with antibiotic use prior to microbiological sampling in 18 of the 19 patients (12 ear, 1 neck, and 6 sinus).

Table 2 shows the relative occurrence of the different species. Pure cultures were found in 18 cultures from otogenic infection, 21 neck cultures, and 11 sinus-related cultures; multiple organisms were identified in 9 cultures from otogenic infections, 15 neck-infection-related cultures, and 4 sinus-related cultures. The mixed cultures were mostly from adult

Table 2
Isolated pathogens (number of strains) of complicated infections originating from ear, neck and sinuses

	Ear		**Neck**		**Sinus**	
Number of patients Mixed cultures **Total/** monocultures	**a 20** 8	**c 18** 1	**a 31** 13	**c 6** 2	**a 16** 4	**c 5**
Gram positives						
S. pneumoniae **12**/10	**6**	**5**			**1**	
Staph. aureus **12**/4	**6**		**3**	**1**	**2**	
CNS **16**/1	**4**		**11**		**1**	
S. pyogenes **21**/15	**4**		**13**	**3**		**1**
Beta streptoc. Gr. C/F/G **5**/4			**5**			
S. milleri **11**/7	**1**		**3**		**7**	
Viridans streptococci **9**/1	**1**		**7**	**1**		
Coryne bacterium **1**	**1**					
Eikenella corodens **1**			**1**			
Lactococcus lactis **1**					**1**	
Gram negatives						
P. aeruginosa **4**/2	**2**				**2**	
Burkholderia Picketti **1**		**1**				
E.coli **2**	**1**		**1**			
P. mirabilis **3**/1	**2**		**1**			
Gram neg. rod, **2**			**2**			
H. influenzae **2**/2		**1**				**1**
Moraxella catharalis **1**			**1**			
Anaerobes						
Bacteroides species, Pepto-streptococci, *Fusobacterium necrophorum*, Anaerobe Gram positive rod **17**/2	**6**	**1**	**8**		**1**	**1**
Propioni bacterium **6**/3			**5**		**1**	
Others						
Actinomyces turensis **1**			**1**			
Actinomyces meyeri **1**			**1**			
M tuberculosis **1**			**1**			

a = adult, c = child (under 10 years of age); CNS = coagulase negative staphylococci.

patients. In the complicated ear infections the most common bacteria found were *Streptococcus pneumoniae* and *Staphylococcus aureus*. *Pseudomonas aeruginosa* was present in two out of three cases with cholesteatoma. In the neck abscesses, these were mainly beta hemolytic streptococci and coagulase negative staphylococci (CNS). The most prevalent species in the sinus-related cultures was *Streptococcus milleri*. More than one culture was obtained from some patients. These 'double' results are also shown in Table 2 and therefore some bacteria (5 CNS, 2 *viridans streptococci*, 2 *S. pneumonia*, 2 beta hemolytic streptococci Gr. A) are listed more than once. (This "double count" was a feature in five patients with neck abscesses and three patients with complicated ear infections. This is a consequence of the small differences that were sometimes found in the antibiograms).

On a total of 37 occasions, resistance (r) to one of the antibiotics was found in the antibiogram, as stated in the laboratory reports. This was a feature in only thirteen patients. Resistance was found on eight occasions in a patient with a subdural empyema caused by a cholesteatoma. Her report listed the following pathogens: *Proteus mirabilis*,

Table 3

Percentage of susceptibility for the most frequent species and the empirical therapy

	Percentage, n							
	Peni	**Amoxi**	**Augm**	**Ctx**	**Erythro**	**Clinda**	**Cipro**	**Ceftaz**
Gram +								
S pneumoniae	100%, 13	100%, 1		100%, 1	91%,11	100%, 4	100%, 1	
Staph. aureus	100%, 1	100%, 3			100%, 3	100%, 13	100%, 2	
CNS	100%, 2	100%, 1			53%, 15	60%, 15	100%, 9	
S pyogenes	93%, 14				100%, 15	86%, 7		
S. milleri	100%, 11				83%, 6	100%, 11	100%, 1	
S. viridans	100%, 10				83%, 6	100%,8		
Gram -								
P. aeruginosa							100%, 2	100%, 3
P. mirabilis		67%, 3	100%, 3	100%, 3				100%, 1

Peni = penicillin, amoxi = amoxicillin, augm = amoxicillin/clavulanic acid, ctx = ceftriaxon, erythro = erythromycin, clinda = clindamycin, cipro = ciprofloxacin, and ceftaz = ceftazidim; CNS = coagulase negative staphylococci.

Pseudomonas aeruginosa and CNS. This patient died as a consequence of the infection, which had probably progressed due to the fact that the *Proteus mirabilis* was resistant to the first three antibiotics given before the results of the antibiogram were known. Another patient probably had the same CNS as a pathogen in the blood culture, a neck abscess pus culture, and a pleural puncture culture. If we were to exclude this strain of CNS (two out of the three times) on the grounds that this constitutes a "double count", this would result in a total of 13 patients with 16 different strains, six of which involved CNS, and 32 resistant counts. Still, most bacteria were sensitive to the antibiotics tested by the antibiogram (see Table 3).

Discussion

The results from reports in the literature vary widely regarding the pathogens of ear, throat and sinus infections due to various problems such as sampling methods, transport and isolation media, isolation methods, specimen selection, sample size, and prescription of antibiotics before culture, or the presence of organisms difficult to culture. The variation could be attributable to a lack of specialised techniques for obtaining anaerobic cultures.[4-7] These factors may have affected our report as well.

In this study, data were collected and analysed retrospectively and not according to a protocol determined in advance. Furthermore, our patients were mostly referred to our tertiary centre and so our group probably consisted of cases at the severe end of the infection spectrum, with a possible selection bias as a result. Many patients received antibiotics prior to admission to our hospital and this may also have affected the results. A final drawback of this study is that our data are not suitable for general use in other regions, since susceptibility patterns may vary throughout the world.

The mean age of our patients with complicated ear infections was 26.9 years, which is comparable to the mean age in the literature.[8] However, this age distribution differs from the group of patients suffering from neck abscesses and sinusitis. We found a larger number of young children suffering from complicated ear infections than we did in the other two groups. These young children had the highest mortality rate in our study population. In this group, complications occurred without any apparent previous infections or otological history. Sixty-four patients in our group were male and the approximately 2:1 gender ratio was consistent in all three categories. Some studies concur with our male predominance, others do not.[8,9]

Meningitis was mentioned as the most frequent intracranial complication in another study and the development of more than one intracranial complication is not rare either.[9] Our overall mortality rate of 5 out of 38 cases (13%) is comparable to the literature, which states rates of 7% to 18%.[9] In our series, the adult mortality was related to cholesteatoma in both cases.

One recent study showed anaerobes and *Staphylococcus aureus* to be the most frequently identified species in patients with intracranial complications as a result of a middle ear infection. However, the three cultures obtained from the intracranial abscesses in that study showed *Klebsiella* twice and CNS once. Other authors who focused on inner ear and facial nerve complications found *Streptococcus pneumoniae*, beta-hemolytic streptococci, *Staphylococcus aureus* and CNS in a majority of cases. In those studies, bacteria were resistant to the tested antibiotics in 28% to 43% of all cases.[5,8]

Like others before us, we conclude that early ear surgery is necessary when there are intracranial complications to reduce mortality further.[6,8] We advocate aggressive therapy and intervention, especially for young children and patients with cholesteatoma.

The microbiology of deep neck infections changes with time: the pattern can be polymicrobial and so contemporary reports from different countries may reveal different common pathogens.[3,10,11] This factor could also be influenced by the local antibiotic policy. This makes it difficult to compare results from individual studies.

The site of deep neck infections is most often the lateral pharyngeal space, followed by the submandibular space. In 31% of patients, the infection involved more than one deep space. Some studies found an odontogenic source to be the most common origin. This may be related to the different admission departments.[7,11] Other studies mention a high percentage of associated systemic disease as well. Our data largely concur with the data presented until now in the literature.

The microbiology of acute sinusitis is well established according to some authors, the major pathogens being aerobic and facultative aerobic bacteria: *Streptococcus pneumoniae*, *Haemophilus influenzae* and *Moraxella cattharalis*.[12] The most common organisms isolated in another study were *Streptococcus viridans*, and *Staphylococcus aureus*.[3] In chronic sinusitis the predominant isolates are *Haemophilus influenzae, Staphylococcus aureus* and anaerobic bacteria.[4,12] In our group *Streptococcus milleri* predominated. *Haemophilus influenzae* and *Moraxella cattharalis* were not isolated. *Streptococcus milleri* was a common pathogen in sinus-related complications in another report as well.[1]

Some reports find that intracranial complications of sinusitis in children are caused exclusively by acute sinusitis. By contrast, in adults, chronic sinusitis is more often the cause.[1] Adolescents are affected more frequently than younger children, presumably due to the more complete pneumatisation of the paranasal sinus.[2]

Epidural abscess is probably the most common intracranial complication. Epidural abscesses form more slowly with a less progressive presentation than subdural empyema. So when evaluating patients presenting with forehead swelling and sinusitis, the clinician should consider the possibility of a concurrent intracranial infection, even in the absence of neurological findings.[1]

Other authors have observed significant rates of concurrent orbital complications with intracranial complications. It has been suggested that these complications may have prompted patients to seek medical care sooner, leading to an earlier diagnosis of the intracranial complications than might otherwise have been the case. Earlier diagnosis, in turn, may contribute to improved outcome.[1,13] This may also have been the reason for our low morbidity and mortality rate in the group with sinus-related infections.

Antibiotic use, overuse and misuse contribute to the growing problem of antibiotic resistance. Significant increases in resistance rates for several basic antibiotics were recently identified. One study showed a 93% resistance of *Staphylococcus aureus* to penicillin G, 29% to azithromycin, and 14% to clindamycin. Twenty-five per cent of *Streptococcus pneumoniae* strains presented intermediate resistance and 25% presented resistance to penicillin, and 75% of strains were also resistant to clarithromycin, azithromycin, and clindamycin.[5] Staphylococci had a poor susceptibility rate to penicillin in 27% of odontogenic cases.[11] Moreover, there has been an increase in the incidence of MRSA infections.[10] Low incidences of resistance, on the other hand, may be attributed to the stringent use of antibiotics.[6] The percentage of resistant bacteria that we registered is not high. This may be due to the relatively low antibiotic prescription rate in the Netherlands.[14]

A high proportion of anaerobes were found in diabetic patients and in patients with odontogenic abscesses. Some authors state that patients with intracranial complications following chronis

suppurative otitis media should receive empirical broad-spectrum intravenous antibiotics with adequate anaerobic cover, for example with metronidazole.[3,5] Our results show a relatively large number of anaerobes in complicated ear infections in adults as well. We therefore also advise adequate anaerobic coverage for complicated ear infections. In the case of cholesteatoma, *Pseudomonas aeruginosa* might be present and it should therefore be covered as well. (In our group, all *Pseudomonas aeruginosa* were still sensitive to ciprofloxacin, gentamicin, tobramycin and ceftazidim.) This advice would imply a change in the current empirical therapy.

Furthermore, in our series, CNS accounted for an overwhelming proportion of resistance. There is considerable ongoing debate in the literature about the true pathogenicity of CNS.[4] Other authors before us have also noted the drug resistance and the high proportion of these bacteria found in cultures.[6] The CNS were often found in mixed cultures and the patients from whom we obtained these bacteria had often received antibiotics prior to the culture. (This was true of the vast majority of our patients). Moreover, these CNS were resistant to erythromycin, clindamycin, ciprofloxacin as well as other frequently used antibiotics. No resistance to vancomycin was noted in our group.

Conclusion

Complicated ear infections in particular still result in a high mortality rate. Our results suggest that young children and patients with cholesteatoma should be treated aggressively since they are most vulnerable and at risk. Antibiotic treatment in this group should cover both anaerobes and pseudomonas adequately.

In the Netherlands, the percentage of strains resistant to antibiotics remains rather low compared with other countries. CNS were the pathogens with the highest number of resistant strains and they may therefore play a more important role, especially in deep space neck infections, than suggested until now.

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