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# Chronic otitis media following infection by non-O1/non-O139 *Vibrio cholerae*: A case report and review of the literature

European Journal of  
Microbiology and  
Immunology

10 (2020) 3, 186–191

DOI:

[10.1556/1886.2020.00013](https://doi.org/10.1556/1886.2020.00013)

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Received: June 17, 2020 • Accepted: July 08, 2020

Published online: August 13, 2020

## CASE STUDY



## ABSTRACT

We report a case of a chronic mesotympanic otitis media with a smelly purulent secretion from both ears and recurrent otalgia over the last five years in a six-year-old girl after swimming in the German Baltic Sea. Besides *Staphylococcus aureus* a non-O1/non-O139 *Vibrio cholerae* strain could be isolated from patient samples. An antibiotic therapy with ciprofloxacin and ceftriaxone was administered followed by atticotomy combined with tympanoplasty. We conclude that *V. cholerae* should not be overlooked as a differential diagnosis to otitis infections, especially when patients present with extra-intestinal infections after contact with brackish- or saltwater aquatic environments.

## KEYWORDS

*Vibrio cholerae*, otitis media, *Staphylococcus aureus*, otalgia, chronic otitis media

## BACKGROUND

Otitis media is defined as an infectious inflammatory condition of the middle ear, particularly affecting children. Two types of otitis media are typically differentiated [1, 2]. Acute otitis media constitutes a painful inflammation of the middle ear mucous membranes, usually caused by viral or bacterial infection, displaying a rapid onset, often accompanied with otalgia, fever, hearing loss and even a tympanic perforation with otorrhoea [3, 4]. Chronic mesotympanic otitis media is characterized by a persistent central tympanic membrane defect. Despite antibiotic therapy, chronic mesotympanic otitis media may be the result of an acute otitis media [4]. Other factors leading to a chronic mesotympanic otitis media are a tubal occlusion, a mechanical, thermal or chemical injury, a blast trauma or of iatrogenic origin (e.g. drainage of the middle ear by a tympanic tube) [5]. Patients with craniofacial malformations are at increased risk of developing a chronic mesotympanic otitis media. Chronic mesotympanic otitis media is one of the most common chronic infectious diseases worldwide [6] and hearing loss constitutes one of the most common sequelae of chronic mesotympanic otitis media. Life threatening intracranial complications such as brain abscesses and meningitis have also been described [7].

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Microbiological analyses are helpful in order to distinguish chronic mesotympanic otitis media from an acute otitis media. Bacterial species causing acute otitis media include *Streptococcus pneumoniae*, *Staphylococcus aureus*, *Haemophilus influenzae* and *Moraxella catarrhalis* [8]. In case of chronic mesotympanic otitis media, both, aerobic and obligate anaerobic bacteria might be considered as causative infectious agents: *Pseudomonas aeruginosa* and *S. aureus* are the most common aerobic microbial species, followed by *Proteus vulgaris* and *Klebsiella pneumoniae* [1, 9] whereas anaerobic pathogens including *Bacteroides* spp., *Clostridium* spp., *Peptococcus* spp., *Peptostreptococcus* spp., *Prevotella melaninogenica* and *Fusobacterium* spp. are rather rarely isolated from patients suffering from chronic mesotympanic otitis media, however [1, 2]. An exacerbation of chronic otitis media may be observed in the course of upper respiratory tract infections or following water penetration through the tympanic membrane into the middle ear during bathing or swimming [1].

*Vibrio cholerae* are rarely isolated from human patient samples in Germany and if so, usually after having acquired the bacteria abroad in high prevalence countries [10]. *V. cholerae* consist of more than 200 serogroups. To date best characterized are the cholera toxin producing O1 and O139 serogroups, representing the strains causing epidemic cholera with subsequent diarrhoeal illness [11, 12]. However, infections following a second group of non-O1/non-O139 serogroups are characterized by self-limiting milder gastrointestinal illnesses that are less frequently associated with extra-intestinal infectious manifestations including ear infections, but also wound infections, skin and soft tissue infections, cholangitis, peritonitis, meningitis, and septicaemia [10, 13–17]. Commonly *Vibrio* bacteria are found as natural inhabitants of brackish- or saltwater aquatic environments in association with chitinous organisms, aquatic plants,

phytoplankton and protozoa [15, 18, 19]. The pathogen transmission primarily takes place via non- or insufficient filtered drinking water and contaminated food. Given that high water temperatures facilitate infections with *Vibrio* spp., peak prevalences of illnesses are documented in the late summer [20, 21]. For the first time we here report a case of chronic otitis media upon infection with non-O1/non-O139 *V. cholerae* in a six-year-old girl who had acquired the *Vibrio* strain most probably after swimming in the German Baltic Sea.

## CASE PRESENTATION

In January 2019, a six-year-old girl presented to a tertiary medical centre with clinical signs of a chronic mesotympanic otitis media that was accompanied with smelly purulent secretion from both ears lasting for five years. Due to the recurrent otalgia the patient had undergone an adenectomy and drainage of the middle ear on both sides at the age of one year. In addition, at the age of two, the girl had undergone a prolonged recovery after a mastoiditis treated by a left-side mastoidectomy. Since the otalgia could neither be sufficiently treated by oral nor by intravenous treatment with antibiotics such as penicillin and cefuroxim, the patient had to undergo a mastoidectomy on the right side in 2016. Anamnestic inquiry revealed no travel outside of Germany in the past six years, however, the mother reported frequent travels to the German Baltic sea, last in September 2018. Upon microscopic examination, a granulated central defect could be detected in the two lower tympanic quadrants of the right ear (Fig. 1), whereas in the left ear a kidney-shaped perforation was observed. Furthermore, both ears showed a purulent secretion. The Weber test revealed a lateralized result to the left ear and the Rinne's test was weakly negative.

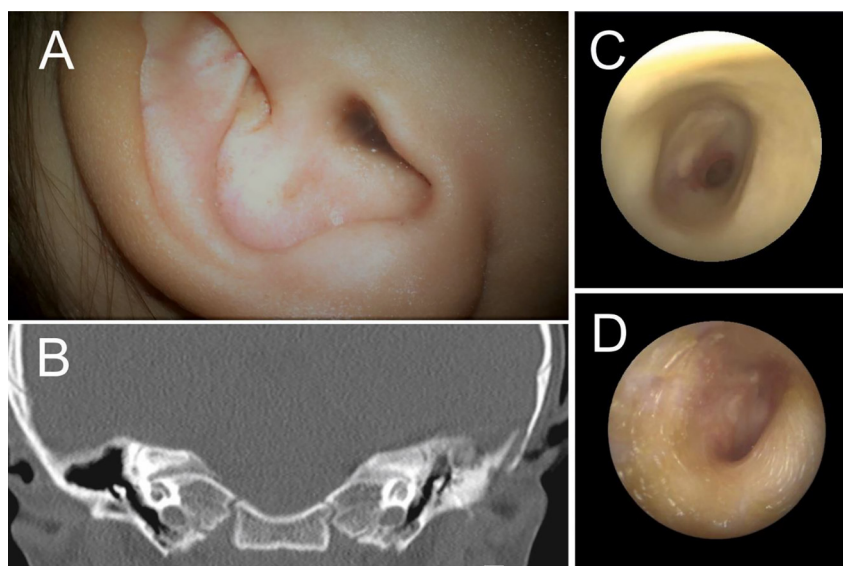


Fig. 1. (A) Right ear before antimicrobial and surgical treatment (B) CT showed a radical cavity on the right side (C) Otoscopic examination of the right ear after antimicrobial treatment (D) Otoscopic examination of the right ear three months after surgical treatment

A spontaneous nystagmus was not observed, however. The data obtained in the audiogram matched to a conductive hearing loss (Fig. 2). There was no pain on palpation of the mastoid process.

As therapy, a bilateral tympanoplasty, starting on the right side, was considered. The pre-interventional computed tomography (CT) showed a bilateral mastoid cavity with motion artifacts and a cutis enlargement in the right ear canal. There was no evidence of inflammatory mastoid involvement (Fig. 1). Additionally, an otic swab from the exudate was taken and subjected to microbiological analyses. *S. aureus* was isolated from both ears, accompanied by common skin bacterial commensals. Remarkably, *V. cholera* non-O1/non-O139 was additionally isolated in substantial amount from the right ear. Therefore, an inpatient treatment with ciprofloxacin ear drops and intravenous ceftriaxone (2 g once a day) was initiated prior to surgery. Five days later, both isolated pathogens were longer be isolated from a second microbiological swab analysis, and the atticotomy combined with tympanoplasty type III Partial Ossicular Replacement Prosthesis (PORP) could be carried out (Fig. 1). Intraoperatively, a compacted mucosa of the mastoid and tympanum appeared on the right side. The tuba auditiva was intact. The surgical treatment of the left ear followed within the same year.

## DISCUSSION AND CONCLUSIONS

*V. cholerae* constitutes a natural inhabitant of brackish or saltwater aquatic environments [19]. In addition to the best characterized O1 and O139 serogroups responsible for the epidemic cholera, also the non-O1 and non-O139 serogroups with less epidemic potential can be found. These non-O1/non-O139 strains are known to cause milder gastrointestinal infections and other rather non-specific infections in humans [11, 12, 15, 17]. Over the last years the numbers of infections with non-O1 and non-O139 *V. cholera* strains have been increasing [22]. Most of the case reports describe relatively mild gastrointestinal illness, ear and wound infections, whereas also cases of bacteraemia have been reported, however [13, 16, 20].

In the Western population, and particularly in Germany, *V. cholerae* infections are rarely documented. Most non-O1 and non-O139 *V. cholerae* infections diagnosed in Germany result from travelling to foreign countries [20]. In Germany there is no standard screening for *V. cholerae* infections. In case of chronic mesotympanic otitis media *P. aeruginosa* and *S. aureus* are the most common aerobic microbial species [1]. Life-threatening infections with the non-O1 and non-O139 serogroups are commonly reported in immunosuppressed patients, but very rarely in immunocompetent individuals without comorbidities [23]. The here presented patient was suffering from a chronic ear infection. Given potential associations with host and environmental factors (contaminated water supply), it is likely that the chronic ear infection may have facilitated the *V. cholerae* infection.

Since *V. cholerae* ear infections can only hardly, if at all, be differentiated from ear infections caused by other pathogens by clinical aspects, a microbiological analysis including isolation and species identification is crucial. The antimicrobial therapy of *V. cholerae* ear infections should comprise cephalosporins, fluoroquinolones or tetracyclines, if necessary in combination [10]. Whereas non-O1/non-O139 strains are sensitive to most antibiotic agents [24, 25], antimicrobial resistance of *V. cholerae* isolates has only been reported to aminoglycosides, ampicillin and carbapenems to date [26–28].

In the German coastal regions [29] and lakes but also in other European countries, pathogenic non-O1 and non-O139 *V. cholerae* isolates have been described (Table 1) [10, 29]. Due to the reported climate change we might experience an increased water temperature in the coastal regions, seas and lakes of central Europe. In consequence, the abundance of *V. cholerae* in these areas may rise [22] and more patients with *V. cholerae* infections present to the health services, particularly in hot summer periods. An association of *Vibrio* infections and increasing water temperature in the Baltic Sea has already been described [21, 22, 30]. High water temperatures (optimal temperature between 20 and 45 °C [31]) alone are not sufficient enough for an optimal propagation of this pathogen, given that salinity and distinct pH-levels (optimal growth conditions at pH between 6.5 and 9.0 [31]) comprise important prerequisites. The lowest salinity levels

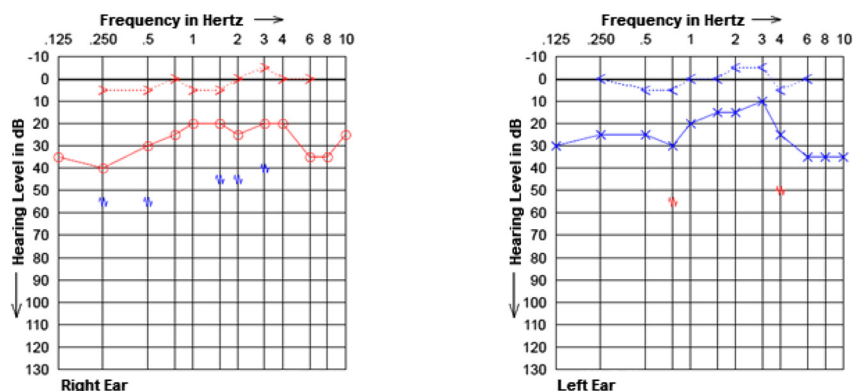


Fig. 2. Mean right and left ear pure-tone thresholds showing a conductive deafness on both sides.

Table 1. Case reports from the literature of otitis caused by *Vibrio cholerae* non-O1/O139 strains. Modified after [15]

Reference	Case reported	Age/gender (m = male, f = female)	Place	Environmental
[33]	Prolonged middle-ear inflammation	10/m	Sweden	Bathing in the Baltic archipelago
[34]	Middle ear infection	-/-	United States	Exposure to salt water
[35]	Chronic external otitis	12/f	Belgium	Unknown
[36]	Middle ear infection	-/-	Romania	Unknown
[37]	Otitis Media	20/f	Belgium	Swimming in a swimming pool
	External otitis one year after eardrum transplant	15/m		Unknown
[38]	Otitis media	-/-	Germany	Unknown
[39]	Chronic recurrent Otitis media	8/f	Austria	Unknown
	Otitis externa	14/m		Swimming in Lake Neusiedl (year 2000)
	Otitis media	49/m		Unknown
	Otitis externa	22/m		After vacation (unknown location)
	Otitis media	9/m		Swimming in Lake Neusiedl (year 2004)
	Otitis media	9/f		Swimming in Lake Neusiedl (year 2005)
[40]	Otitis externa	64/f	Mauritius	Bathing in the Pacific Ocean
[41]	Ear infection	-/-	United Kingdom	Unknown
[20]	Otitis	-/-	Germany/Austria	Exposure to Coastal regions, Lakes
[42]	Otitis externa	21/f	Austria	Swimming in Lake Neusiedl (year 2015)
[22]	Ear-infection with ear secretion	-/-	Sweden and Finland	Exposure to Coastal regions
[15]	Otitis media	27/m	Israel	Water skiing accident on the Murray River in Australia (year 2011)
[43]	Acute otitis externa	35/m	Spain	Exposure to Mediterranean bathing site
[44]	Otitis media	11/m	France	Swimming in Lake Apremont
The current study	Chronic otitis media	5/f	Germany	Bathing in the German Baltic sea

can be found in rivers and lakes (0.15–0.25%) as well as in the Baltic sea coast (0.8%), whereas the many regions of the Atlantic and the Mediterranean Sea comprise areas with too high levels of salinity (3.5%) [32].

Most reported patients with non-O1 and non-O139 *V. cholerae* ear infections presented with otitis externa or acute otitis media, whereas only two cases with a prolonged middle-ear inflammation have been reported to date (Table 1). Notably, i.) most reported non-O1 and non-O139 *V. cholerae* associated cases were detected in Europe, ii.) almost all patients of different age and gender were not suffering from immunosuppressive comorbidities, and iii.) infections were linked to contaminated water (Table 1). In the present case, the patient presented a mesotympanic otitis media, preexisting for several years. The cases described in the literature often showed an acute event followed by an acute infection without specific previous medical history. The bilateral tympanic perforation described here is most likely the result of a tympanic drainage in infancy leading to a superinfection by *V. cholerae*. The ear is particularly

susceptible to penetrating water. There are favourable conditions for the multiplication of pathogens, especially in combination with *S. aureus*.

An untreated otitis media may be associated with complications culminating in a permanent damage of the ear. Other known complications are hearing loss, vertigo, facial paralysis, subperiosteal abscess and labyrinthitis [45, 46]. In addition to the intra-cranial complications also extra-cranial complications have been described [47, 48]. Fortunately, the young female patient in the current report did not display such complications.

In conclusion, physicians working in coastal and also high-latitude regions must be aware of non-O1 and non-O139 *V. cholerae* associated morbidities, especially when patients present with extra-intestinal infections after contact with brackish- or saltwater aquatic environments. Improved diagnostic evidence and clinical awareness of these emerging pathogens is therefore needed [22]. It may be advisable that clinicians alert at-risk patients. *V. cholerae* should not be overlooked as a differential diagnosis to otitis infections.



## CONSENT

Written informed consent was obtained from the parents for publication of this case report. A copy of the written informed consent is available for review by the Editor-in-Chief of this journal.

*Funding sources:* None.

*Authors' contributions:* SVB analysed and interpreted the patient data and was a major contributor in writing the manuscript. PW performed the microbiological examination and draughted the manuscript. MMH provided constructive advice to the study and the manuscript. All the authors were in agreement on the final version of the manuscript.

*Competing interests:* Markus M. Heimesaat is a member of the editorial board. The authors declare that they have no competing interests.

## ACKNOWLEDGEMENTS

We thank the Robert Koch-Institute (ZBS 2, Speziallabor für hochpathogene mikrobielle Erreger) for typing the *Vibrio cholerae* strain.

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