Successful management of a cerebral abscess secondary to chronic cholesteatoma caused by *Prevotella melaninogenica* and *Peptococcus anaerobius* – A case report and literature review

Carlo Guli a, Luigi Basile a, Francesca Graziano a,⁎, Paola Di Carlo b, Domenico Gerardo Iacopino a, Antonio Cascio b, Rosario Maugeri a

a Department of Experimental Biomedicine and Clinical Neurosciences, School of Medicine, Neurosurgical Clinic, University of Palermo, Italy
b Department of Sciences for Health Promotion and Mother & Child Care, Section of Infectious Diseases, University of Palermo, Italy

**Abstract**

Cerebral abscess following cholesteatomatous otomastoiditis is a life-threatening complication and poses diagnostic and therapeutic challenges. We report a case of life-threatening cerebritis and cerebral abscess due to a collection of pus from an aerobic super infections occurring months after the apparent resolution of an otogenic brain abscess in a 67-year-old immunocompetent Italian female. Two gram-positive anaerobic pathogens were isolated during secondary neurosurgical procedures and antibiotic treatment was adopted to resolve the complications. Another objective of this study was to review the literature on gram-positive anaerobic pathogens and brain abscess complications in patients with fistula, and to highlight the importance of short imaging in monitoring treatment during long-term antibiotic therapy for otogenic brain abscess to avoid abscess recurrence. Isolating the strain and monitoring response to treatment with magnetic resonance imaging may improve the prognosis. The study also highlights the need for a close cooperation between infectious disease consultants and neurosurgeons.

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left-sided hearing loss. WBC count was $26 \times 10^9$/L (79% neutrophils, 17% lymphocytes and 4% monocytes) and serum C-reactive protein level (CRP) was 45 mg/dl (normal range 0.08–1.5 mg/dl) and there was no diagnosis of HIV. Five months before admission, the patient had undergone a petrosectomy, followed by transtemporal drainage of an otogenic brain abscess. The surgical procedure was performed in another hospital in Eastern Sicily, Italy. Her post-operative course was normal. Signs and symptoms of infection resolved but severe left-sided hearing loss persisted.

When the patient came to our attention, brain CT and Gd-enhanced MRI images showed a parenchymal alteration in the left temporal lobe at the inferior and middle temporal gyrus with intense Gd-enhancement and brain swelling (Fig. 1). These findings appeared to be compatible with cerebritis and abscess. Following an evaluation of clinical and radiological findings and multidisciplinary consultation, the patient underwent a neurosurgical-otolaryngology procedure, with extension of the previous left subtotal petrosectomy, evacuation of the abscess with subsequent reconstruction of the floor of the temporal fossa, and intradural irrigation with antibiotic solutions. Once completed, fibrin sealant (Vivostat®) was sprayed on the operative field, in order to prevent CSF leakage [11–15]. During the surgical procedure, a yellowish-green, foul-smelling material was aspirated, believed to be consistent with pyogenic brain abscess. Samples were taken for microscopic examination and culture to identify the strain. The results turned out to be difficult to interpret, remaining negative until day six. The patient was started on an empirical antimicrobial regimen of ceftriaxone [intravenous (iv) 2 g every 12 h], vancomycin (500 mg every 6 h), and metronidazole (500 mg every 6 h) to pending further microbiological results. The patient’s clinical condition improved over the post-operative period. On day 5, a CT scan of the brain showed a significant reduction in the area of post-contrast enhancement, indicating that the intraparenchymal infectious alteration had reduced.

However, after one week of treatment the patient became comatose, with onset of partial seizures in the buccal rhyme and right arm, and hyperyrexia. CT and Gd-enhanced MRI documented the presence of enhanced tissue in the left tympanic cavum and in the left temporal region, suggesting meningoencephalitis in the left parietal-occipital-temporal and thalamic region. On hospital day 9, *Prevotella melaninogenica* and *Peptostreptococcus anaerobius* were yielded in the bacterial culture of intraoperative biopsy samples. Conventional methods for identifying anaerobic species rely on microbiological culture coupled with biochemical tests for phenotypic species-level
identification. Routine laboratory procedures including colony morphology and biochemical tests were carried out to identify strains in clinical isolates [16]. Special potency anaerobic antimicrobial susceptibility disk patterns (vancomycin, kanamycin, colistin), catalase, spot inoculum, Rapid ANA II system (Remel, Lexena, KS, USA) or Vitek2 (bioMérieux, St. Louis, MO, USA) were used. Susceptibility of the strains to antibiotics was determined using CLSI breakpoint recommendations for anaerobes [17,18]. A new combined antibiotic treatment clistatin/imipenem (1 g every 8 h iv) plus clindamycin (600 mg every 6 h iv) in addition to metronidazole was started pending antibiotic results. We observed a rapid improvement of the patient’s clinical condition, with fever and seizures disappearing just 48 h after the new therapy was started. The antibiotic data were available after 3 days of starting the second antibiotic therapy regimen, and showed that the Prevotella isolate was susceptible to clindamycin 0.015, imipenem, and meropenem MICs of <0.05 μg/ml; the strain was resistant to penicillin G MICs of ≥1 μg/ml, ciprofloxacin and it was a β-lactamase producer. It showed a MIC to metronidazole of 2 μg/ml. Peptostreptococcus anaerobius was resistant to amoxicillin and amoxicillin-clavulanic acid, 3 and 6 μg/ml, respectively and susceptible to clindamycin 0.25 μg/ml, metronidazole 0.05 μg/ml, imipenem 0.06 μg/ml and meropenem 0.25 μg/ml. The last combined antibiotic regimen was switched to metronidazole plus imipenem clistatin for 4 weeks. The patient recovered completely after 1 month and was transferred to other hospital for motor rehabilitation.

3. Discussion

The first-line treatment of otogenic brain abscess includes immediate decompression of the abscess, prompt eradication of the primary otogenic nidus, and active prevention of abscess recurrence. Otogenic brain abscesses with intracranial complications are often located adjacent to the temporal lobe and cerebellum, with the middle segment of the temporal lobe and lateral lobe of the cerebellum most highly affected. In our patient’s case, we used the transtemporal approach to drain the otogenic brain abscess; recently, other approaches to otogenic intracranial abscess have been proposed [19–21]. Cranial and facial bone osteomyelitis is usually caused by oral flora that, like in our case, spread from a contiguous soft-tissue source or from a sinus, ear or dental infection. In our case, the strains of pathogens isolated suggested that although the patient did not have any documentation following the operation that showed minimum bone patency, the authors believe that a fistula was responsible for the subsequent cerebral infection complication caused by pathogens which are normally found in the oral cavity. We observed two challenging anaerobic bacteria in our patient’s case: Prevotella melaninogena and Peptococcus spp. These microbes are notoriously difficult to identify microbiologically, and in the last few years some strains resistant to routinely-used antibiotics have been prevalent in their antibiotic sensitivity pattern. Prevotella melaninogena, previously known by other names including Fusiformis nigrescens, Bacteroides nigricans and Bacteroides melaninogenicus, is so-called because producing colonies that become darker and darker the longer they are incubated (some strains require up to three weeks); the brown, or less commonly black pigment is due to a haematin derivative and not to melanin as was originally thought; moreover, the type of blood used in the preparation of the media culture inactivated the brown, or black pigment. Peptostreptococcus spp. is sensitive to a variety of antibiotics: it is always sensitive to clindamycin and metronidazole which are the drug of choice, sensitivity to penicillin, chloramphenicol, erythromycin and tetracycline varies. Recently Macrolide resistance in Peptostreptococcus spp. was reported [24]. A percentage of P. anaerobius showed resistance to amoxicillin-clavulanic acid and rare isolates to clindamycin [17–19]. Treatment of anaerobic infections is complicated by their slow growth in culture, their polymicrobial nature and their growing resistance to antimicrobials. Antimicrobial therapy is often the only type of therapy required, but in some infections it is an important adjunct to drainage and surgery. Because anaerobes are generally isolated mixed with aerobes, the chosen antimicrobial regimen should provide adequate coverage of both. Antimicrobials with adequate intracranial penetration advocated for these infections are: metronidazole, penicillin, meropenem and chloramphenicol [24–25]. The antimicrobials that are most effective against anaerobes are: metronidazole, carbapenems (imipenem, meropenem, doripenem, ertapenem), chloramphenicol, combinations of a penicillin and beta-lactamase inhibitor (ampicillin or ticarcillin plus clavulanate, amoxicillin plus sulbactam, piperacillin plus tazobactam), tigecycline, cefoxitin and clindamycin [25]. In our case, we initially combined clindamycin and metronidazole although the use of multiple drugs active against anaerobes is not necessary and puts the patient at risk for additional drug toxicities. Data and guidelines do not support the use of two anti-anaerobic drugs in clinical practice, with two exceptions - Clostridium difficile infection and necrotizing fasciitis [26]. In our case report, the decision to use both clindamycin and metronidazole for 8 days was due to susceptibility data and severity of post-operative complications. Moreover, in our case we noted an excellent carbapenem synergy, in particular imipenem clistatin plus metronidazole, although imipenem is more neurotoxic than other such as meropenem.

4. Conclusion

Metronidazole’s excellent bactericidal activity makes it an important component of most antimicrobial regimens for brain abscess, with a lower incidence of neurotoxicity. Finally, early diagnosis by imaging studies is extremely important to guide surgical drainage and prevent permanent neurological sequelae. Recent studies describe advances in diagnosis and techniques, and a trend for draining brain abscesses via minimally invasive surgery is emerging. Probably, in the near future, diagnosis confirmation and treatment monitoring with magnetic resonance spectroscopy would allow a greater number of patients to be managed with medical treatment alone.

References


