


## CASE REPORT

# Calcium sulfate matrix as local antibiotic carrier in the mastoid

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## Abstract

We describe the use of calcium sulfate beads as antibiotic carrier in a patient, who suffered from chronic mastoiditis with consecutive otogenic meningitis due to *Burkholderia cenocepacia*. Our findings suggest a possible role of calcium sulfate matrix as a local antibiotic carrier in the mastoid in complicated mastoiditis cases.

## KEYWORDS

antibiotic carrier, burkholderia cenocepacia, calcium sulfate matrix, mastoid, mastoidectomy, mastoiditis, meningitis

## 1 | INTRODUCTION

Calcium sulfate matrix as a local antibiotic carrier is well established in orthopedic surgery. High local antibiotic concentrations, unachievable via systemic administration, can be achieved over multiple weeks.<sup>1</sup> Known complications after application of calcium sulfate matrix are delayed wound healing with chronic wound drainage, soft tissue inflammation and destruction, as well as elevated serum calcium levels. For the first time, we describe the use of a calcium sulfate matrix as local antibiotic carrier (STIMULAN<sup>®</sup> Rapid Cure, Biocomposites Ltd.) in the mastoid. The presented case is an immunocompromised, 18-year-old female

patient after lung transplantation due to end-stage cystic fibrosis (CF).<sup>2</sup> She suffered from chronic mastoiditis with consecutive otogenic meningitis due to an infection with *Burkholderia cenocepacia*. *B. cenocepacia* is a highly virulent, aerobic, gram-negative bacteria with exceptionally high resistance to common antibiotic agents and considered a relative contraindication for lung transplantation.

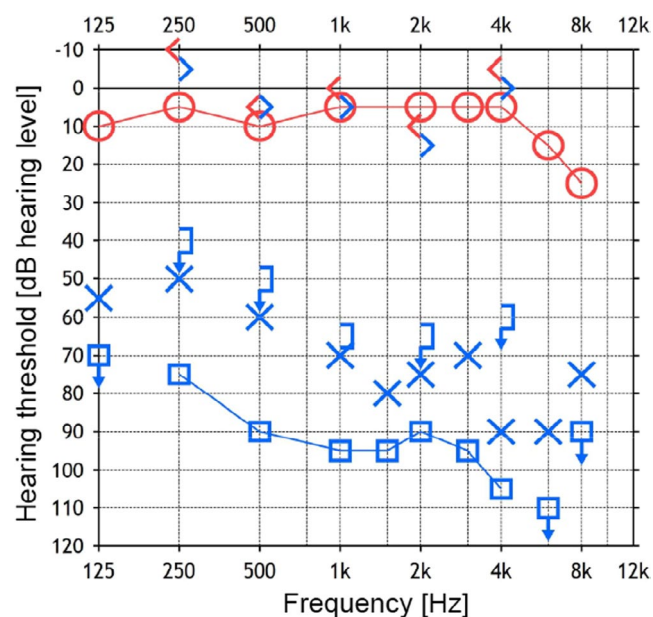
## 2 | CASE HISTORY

The patient gave informed consent to this case report. After bilateral lung transplantation due to end-stage CF

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(compound heterozygote Phe508del/CFTRdele2.3), an 18-year-old female patient developed a progressive lung infection and consecutively through hematogenic spread a chronic mastoiditis with *B. cenocepacia* which could be isolated from the middle ear fluid cultures. Long-term systemic antibiotic treatments with vancomycin, meropenem, cefiderocol, and ceftazidime/avibactam, as well as the placement of a tympanostomy tube (inner diameter 1.5 mm, Tuebingen gold type, Atos Medical, Malmo, Sweden) in the tympanic membrane, were not able to control the disease in the left mastoid post lung transplantation. In the course of the disease, a labyrinthitis with progressive loss of cochleo-vestibular function (Figure 1) and later a positive vertical tilt, intermittent vertical diplopia, and drastically reduced general condition occurred. The computed tomography (CT) scan revealed a completely opacified mastoid as well as middle ear despite the tympanostomy tube in place (Figure 2A-C). On magnetic resonance imaging (MRI), a global leptomeningeal contrast enhancement as well as contrast enhancement in the mastoid, the labyrinth, and the inner auditory canal could be detected. The findings were strongly suggestive for otogenic meningitis (Figure 2D). Due to the deteriorating neurological condition and the exhausted conservative treatment options, a mastoidectomy was recommended despite the highly increased risk of general anesthesia.



**FIGURE 1** Preoperative audiogram showing profound sensorineural hearing loss on the left side and normal hearing thresholds on the right side. Red symbols, right side; blue symbols, left side; circles/crosses, unmasked air conduction threshold; boxes, masked air conduction threshold; diamond brackets, unmasked bone conduction threshold; square brackets, masked bone conduction threshold; downward arrow, no response

During mastoidectomy, a poorly pneumatized mastoid with thickened, inflamed mucosa in the mastoid as well as in the middle ear was detected (Figure 3A,B). There was no dehiscence of the tegmen tympani. After completion of the mastoidectomy, 3 mm beads of a calcium sulfate matrix (10 cc STIMULAN® Rapid Cure, Biocomposites Ltd.) impregnated with 2 g ceftazidime/0.5 g avibactam were placed in the mastoid cavity (Figure 3C,D). The systemic antibiotic treatment with vancomycin, meropenem, cefiderocol, and ceftazidime/avibactam was continued after surgery. Over the following days, the patient showed a complete recovery of the neurological symptoms and general condition, except for the loss of cochleo-vestibular function which persisted. The postauricular incision healed without complications (Figure 4A), and ear microscopy after three weeks showed a tympanic membrane with the tympanostomy tube in place without any signs of infection (Figure 4B). The cone-beam CT scan four weeks after surgery revealed a mostly resolved calcium sulfate matrix in the mastoid cavity and a partly ventilated middle ear (Figure 4C,D). Serum calcium levels were monitored weekly for three months after surgery and remained in the normal range at all times.

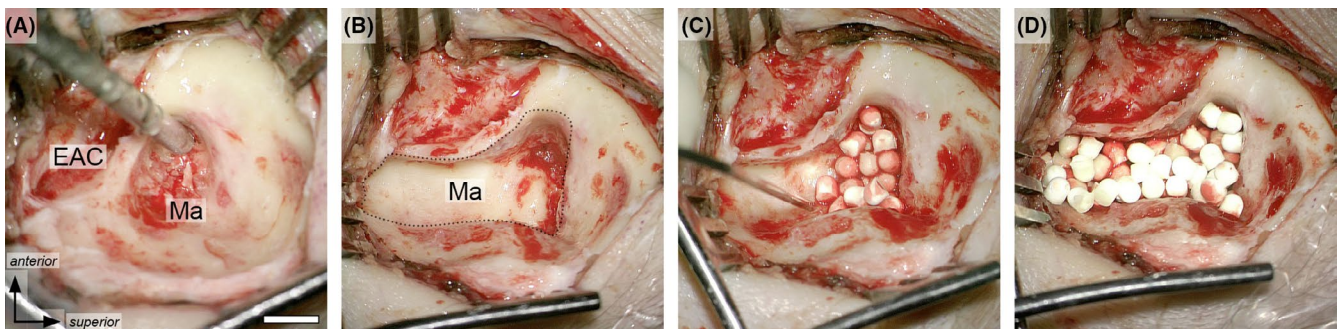
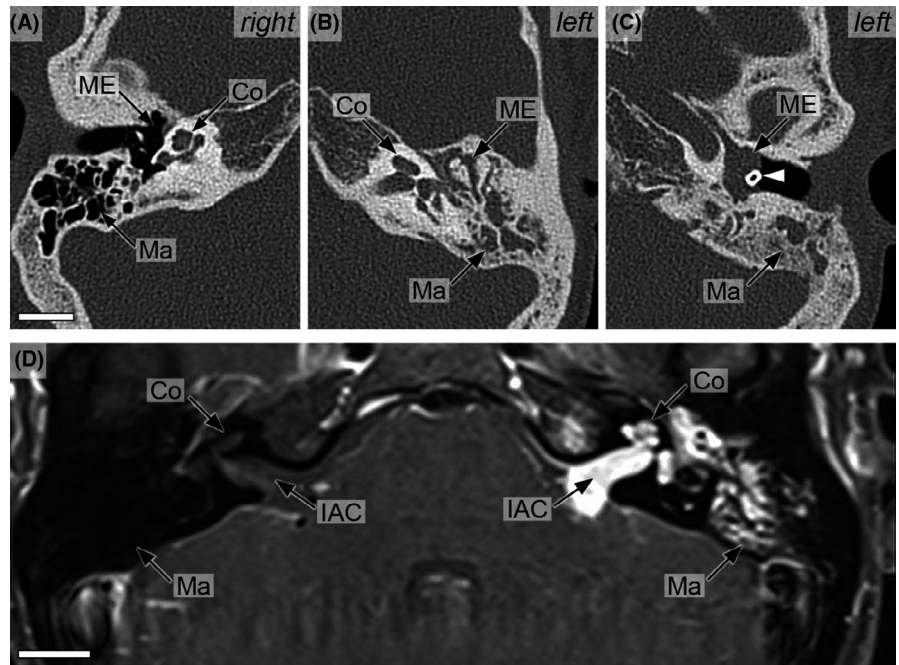
The pulmonary infection with *B. cenocepacia* post lung transplantation was well controlled under the long-term systemic antibiotic treatment at the time of surgery. Currently, 18 months after the lung transplantation and 12 months after the mastoidectomy, the pulmonary situation as well as the situation in the left mastoid are stable and well controlled. No further infect exacerbations occurred.

### 3 | DISCUSSION

This is the first report of a local antibiotic treatment with a calcium sulfate matrix as local antibiotic carrier in the mastoid. In the presented case, the chronic mastoiditis and consecutive complications were progressive despite extensive systemic antibiotic treatment and the placement of a tympanostomy tube. Therefore, the decision for surgical intervention and treatment with a local antibiotic carrier in the mastoid was made. The result suggests that such local antibiotic treatments could play a role in uncontrolled or hard to control (e.g., biofilm) local infections of the mastoid.

The use of calcium sulfate matrix as a local antibiotic carrier is well established in orthopedic surgery as a prophylactic measure and to treat local infections, especially around foreign body material.<sup>3,4</sup> In vitro studies showed that antibiotics are released from calcium sulfate with retained antibacterial efficacy for at least 42 days, efficient even for biofilms and with local

**FIGURE 2** Preoperative imaging of the temporal bones. (A–C) High-resolution CT revealed normal findings on the right side (A) and a completely opacified mastoid (Ma) and middle ear (ME) on the left side with the tympanostomy tube (white arrowhead) (B–C). (D) T1-weighted MRI sequences revealed contrast enhancement in the mastoid, the labyrinth, and the internal auditory canal (IAC) on the left side. Co stands for cochlea. Scale bars: 10 mm



**FIGURE 3** Intraoperative situs (A) After partial mastoidectomy, marked inflammation of the mucosa was found (B) Completed mastoidectomy (black dotted outline) (C–D) Filling the mastoidectomy cavity with calcium sulfate beads impregnated with ceftazidime/avibactam. Abbreviations: EAC stands for external auditory canal, Ma mastoid

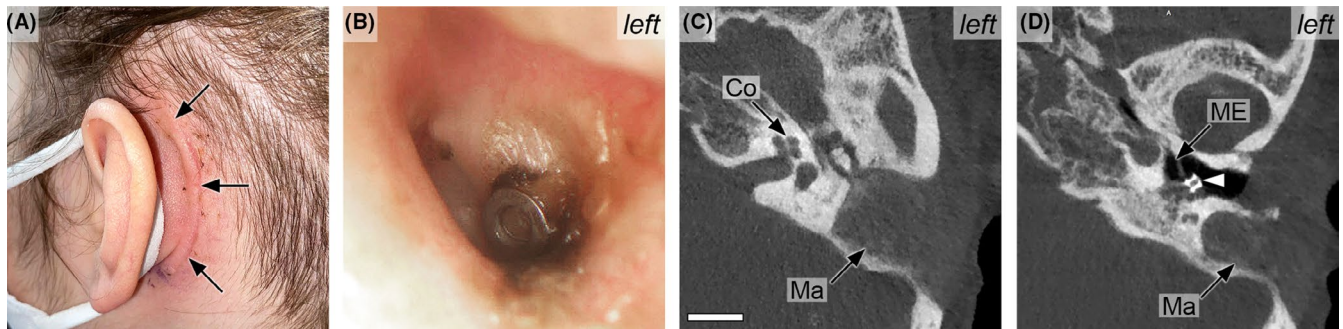
antibiotic concentrations unachievable via systemic administration.<sup>1</sup> Furthermore, the administered antibiotic agent as well as the size of the calcium sulfate carrier can be adapted to each case.

Otogenic meningitis is commonly treated with systemic antibiotics and some sort of surgical intervention, reaching from at least a myringotomy to in some cases a mastoidectomy.<sup>5</sup> As in the presented case, the infection with *B. cenocepacia* could not be controlled despite extensive measures (multi-regiment antibiotic treatment and placement of a tympanostomy tube), we decided to use calcium sulfate as local antibiotic carrier in addition to the surgical drainage of the infected mastoid and continued systemic antibiotic treatment. The intention was to reach a local antibiotic concentration as high as possible. The fast clinical recovery after the intervention suggests a benefit from surgery and/or the local antibiotic agent.

Furthermore, although the additional value of the locally applied antibiotic in the presented case cannot be clearly assessed, no side effects (especially no delayed wound healing or hypercalcemia<sup>6</sup>) due to the application of calcium sulfate beads in the mastoid were recognized and—as expected due to findings in orthopedic patients—the calcium sulfate in the mastoid cavity was partially absorbed at 4 weeks post-surgery.

The proven efficacy of local antibiotic agents in addition to systemic antibiotic treatments and surgical interventions in orthopedic surgery makes them a promising therapeutic option in other fields such as otology. The presented case suggests the safe and effective use of calcium sulfate as an antibiotic carrier in the mastoid, making it an additional therapeutic option for complicated mastoiditis cases as well as infections involving foreign body material (e.g., cochlear implants).





**FIGURE 4** Postoperative findings (A) Healed postauricular incision (black arrows) 2 weeks after surgery (B) Differentiated tympanic membrane with tympanostomy tube in situ at three weeks after surgery (C–D) Postoperative cone-beam CT 4 weeks after surgery. Axial sections show already partially absorbed calcium sulfate beads in the mastoid (Ma) and a partially ventilated middle ear (ME). Co stands for cochlea. Scale bar: 10 mm

## 4 | CONCLUSION

This is the first report of a calcium sulfate matrix as local antibiotic carrier in the mastoid in addition to systemic antibiotic treatment in a complicated case of otogenic meningitis. Due to the high local antibiotic concentrations reached, such local antibiotic treatments could be a useful adjunct in complicated mastoiditis cases or infections after otologic surgeries involving foreign body material (e.g., cochlear implants).

## ACKNOWLEDGMENTS

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## CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

## AUTHOR CONTRIBUTIONS

Adrian Dalbert (AD) was the main author of the manuscript. David Bächinger (DB) collected all clinical data, contributed to writing the manuscript, and prepared the figures. Michael Soyka (MS) and Christof Rösli (CR) contributed to writing the manuscript. Ilhan Inci (II) is the treating thoracic surgeon and contributed to writing the manuscript. Macé M Schuurmans (MS) is the treating pulmonologist and contributed to writing the manuscript. Yvonne Achermann (YA) is the treating infectious disease specialist and contributed to writing the manuscript. Alexander Huber (AH) was the initiator of the manuscript and contributed to preparing figures and writing the manuscript.

## CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

## DATA AVAILABILITY STATEMENT

Data sharing not applicable to this article as no datasets were generated or analysed during the current study.

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