

Success in changing from intravenous to oral antibiotics in pediatric intracranial infections: report of three cases

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Abstract

Introduction: Acute bacterial rhinosinusitis is a common infection in children. Intracranial complications like subdural empyema or brain abscess are rare, albeit with significant morbidity and neurological sequelae. **Case report:** We present three clinical cases of intracranial suppurative complications secondary to sinus infection in which the transition to oral antibiotic therapy took place between day 14 and day 21 of intravenous treatment. In all, both neurosurgery and otorhinolaryngology surgery with empyema and sinus drainage were performed, the bacterial etiology was identified and clinical cure was achieved with no relapses. **Discussion:** Although the early transition to oral antimicrobials has been adopted in some countries, effectiveness and safety remain uncertain. The optimal timing for the transition to oral antibiotic therapy is not well established, but an early switch to oral treatment has been suggested to be equally effective and safe.

Keywords: Intracranial infections. Oral therapy. Levofloxacin. Chloramphenicol. Linezolid.

Sucesso na transição de terapêutica endovenosa para terapêutica oral em infeções intracranianas em idade pediátrica: relato de três casos

Resumo

Introdução: A sinusite aguda bacteriana é uma infeção frequente em idade pediátrica. As complicações intracranianas, como o empiema subdural ou o abscesso cerebral, são raras, mas apresentam significativa morbilidade com sequelas neurológicas graves. **Relato do caso:** Apresentamos três casos clínicos de complicações supurativas intracranianas secundárias a sinusite aguda bacteriana nos quais a transição para a antibioticoterapia oral foi realizada entre o 14º e o 21º dia de antibioticoterapia endovenosa. Em todos os casos, foi realizada drenagem dos seios perinasais e do empiema, o agente etiológico foi identificado e a resolução clínica foi alcançada sem recidivas. **Discussão:** Embora a transição precoce para antibioticoterapia oral tenha sido adotada em alguns países, a sua eficácia e segurança permanecem incertas. O momento ideal para esta transição não se encontra bem estabelecido, todavia tem sido sugerido que a transição precoce para a terapêutica oral seja igualmente eficaz e segura.

Palavras-chave: Infeções intracranianas. Terapêutica oral. Levofloxacina. Cloranfenicol. Linezolid.

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Keypoints

What is known

- Subdural empyema and brain abscess are rare complications of acute bacterial rhinosinusitis.
- The effectiveness and timing of the switch to oral antibiotics has been extensively debated, but no recommendations are offered.

What is added

- We present three clinical cases of intracranial suppurative infections in which early transition to oral antibiotic therapy was made.
- In all three cases described, the outcome was favorable with no recurrence of the infectious process.

Introduction

Acute bacterial rhinosinusitis (ABRS) is a common infection in children¹. It is estimated that eight percent of viral upper respiratory infections may be complicated with secondary ABRS². In children, sinusitis usually has a benign evolution with orbital complications being the most common, while intracranial complications, like subdural empyema, brain abscess, meningitis and cerebritis, occur less frequently, with an estimated incidence of 4–5.3/1,000,000^{3,4}.

Suppurative intracranial complications are often caused by *streptococci* but may also stem from *staphylococci* or be polymicrobial⁵. Besides the advances in cranial imaging, antibiotic therapy selection and surgery, they remain a significant source of neurological morbidity³ and the mortality rate is still as high as 3.7–24%⁴.

The total length of antibiotic treatment for intracranial suppurative infections ranges from four to eight weeks⁴. No recommendation is offered for early transition to oral antimicrobials because of a lack of data. The effectiveness and timing of the switch to oral antibiotics has been extensively debated⁶. This case series studies show successfully-treated patients who transitioned to oral treatment as early as one to two weeks after starting intravenous therapy^{7,8}.

Case description

We present three clinical cases of empyema and brain abscess secondary to sinus infection in which the switch to oral antibiotic therapy was performed successfully (Table 1).

Case 1

A 13-year-old female patient, with a history of asthma, was admitted to the pediatric emergency department with a one-week history of fever, rhinorrhea and headache. Brain Magnetic Resonance Imaging (MRI) showed pansinusopathy complicated by a right paramedian frontopolar empyema. The patient was subjected to a bilateral antrostomy and full frontoetmoidectomy with frontal

sinus drainage followed by a right frontal craniotomy with subdural convexity, parafalcial empyema drainage and cranialization of the frontal sinus. She was started on empiric antibiotic therapy with ceftriaxone, vancomycin (two days) and metronidazole (nine days) initially, then moved to a single regimen with intravenous flucloxacillin (12 days) after identifying methicillin-sensitive *Staphylococcus aureus* from the pus culture. A switch to oral antibiotic linezolid took place on day 14 and a total of four weeks of antibiotic therapy was completed. The patient fully recovered and the control CT scan (Fig. 1) did not show any recurrence of the infection at the 12 week follow-up visit.

Case 2

An 11-year-old female patient, with a history of allergic rhinitis and a recent hospital admission from pansinusitis complicated with postseptal cellulitis. She was readmitted one month later, with a nine-day clinical history of fever, headache and vomiting. The examination showed a decrease in left-sided muscle strength of 4/5 and marked left-sided facial palsy. The initial CT scan revealed pansinusopathy with right-sided extra-axial frontopolar collections. The patient underwent a bilateral antrostomy and frontal sinusotomy followed by a right frontal craniotomy and drainage of the empyema. Empirical antibiotic treatment with ceftriaxone, vancomycin and metronidazole was started. The latter two were discontinued after identifying *Streptococcus intermedius* from the pus culture. On day 10 after surgery, she presented with a progressively worsening headache. A brain MRI was performed, which showed recurrence of the empyema and a worsening mass effect. She was then taken back to the operative room to enlarge the craniotomy and re-drain the empyema; the antibiotic therapy was upscaled to meropenem and vancomycin. Due to the resurgence of fever, eighteen days later, another brain MRI (Fig. 2) was performed, revealing a left frontobasal intraparenchymal abscess. Intravenous chloramphenicol was added. Three weeks after initial treatment, she was transitioned to oral chloramphenicol. Due to slight pancytopenia and increased lactates,

Table 1. Summary of the three clinical cases

	Case 1	Case 2	Case 3
Age	13	11	14
Duration symptoms (days)	7	9	14
Symptoms	Fever; Headache; Rhinorrhea	Fever; Headache Vomiting; Slight left-sided hemiparesis	Fever; Headache; Vomiting
Imaging	MRI: pansinusopathy; right paramedian frontopolar epidural empyema	CT-scan: pansinusopathy; right frontopolar empyema. MRI day 10 and day 18: Subdural empyema and left frontobasal abscess	MRI: pansinusopathy; left frontal epidural empyema
Microbiology (pus)	<i>S. aureus</i>	<i>S. intermedius</i>	<i>S. constellatus</i>
ENT surgery	Antrostomy; full frontoethmoidectomy; frontal sinus drainage	Antrostomy; frontal sinusotomy; frontal sinus drainage	Antrostomy; bilateral anteroposterior ethmoidectomy
Neurosurgery	Empyema drainage and cranialization of the frontal sinus	Empyema drainage (two step surgery)	Empyema drainage
Empiric antibiotics	Ceftriaxone, vancomycin and metronidazole		
Oral antibiotics	Linezolid	Chloramphenicol/Levofloxacin	Levofloxacin
Transition to oral	Day 14	Day 21	Day 21
Total treatment	Four weeks	Nine weeks	Four weeks
Follow-up	Full recovery; no evidence of active infection on control CT scan at 12 weeks	At eight weeks: full recovery; control MRI with no evidence of active infection	Full recovery; no evidence of active infection on control CT scan at four weeks

chloramphenicol was discontinued and oral levofloxacin was initiated until she had completed nine weeks post-operative antibiotic therapy. There was a rapid recovery of pancytopenia and neurological deficits. Two months after being discharged from the hospital, the patient was asymptomatic and the MRI did not show any recurrence of the infectious process.

Case 3

A 14-year-old female patient, with no relevant medical history, was admitted to the pediatric emergency department with a 14 day history of fever, headache and vomiting. The MRI showed pansinusopathy complicated by left frontal intracranial empyema. Empirical antibiotic therapy was initiated with ceftriaxone, vancomycin and metronidazole. Upon admission, the patient was submitted to antrostomy and bilateral anteroposterior ethmoidectomy. Due to a worsening headache, a CT scan was performed on the fifth day of hospitalization, which showed bilateral anterior frontal subdural

empyema. The patient underwent a frontal craniotomy and empyema drainage. *Streptococcus constellatus* was identified from the pus culture and antibiotic therapy was changed to cefotaxime and clindamycin. In the third week of treatment, she was transitioned to oral antibiotics with chloramphenicol. The patient developed an erythematous maculopapular rash which could not be definitively attributed to any of the antibiotics. The antibiotic therapy was switched to levofloxacin. She completed a total of four weeks of antibiotic therapy. Three months later, she remained asymptomatic, with no evidence of recurrence of the infectious process in the brain CT scan.

Discussion

In our short series, we used three different oral antibiotics in the transition strategy, as early as two weeks after surgery, with clinical cure and no relapses.

Chloramphenicol is a broad-spectrum antibiotic effective against gram-positive, gram-negative and anaerobic

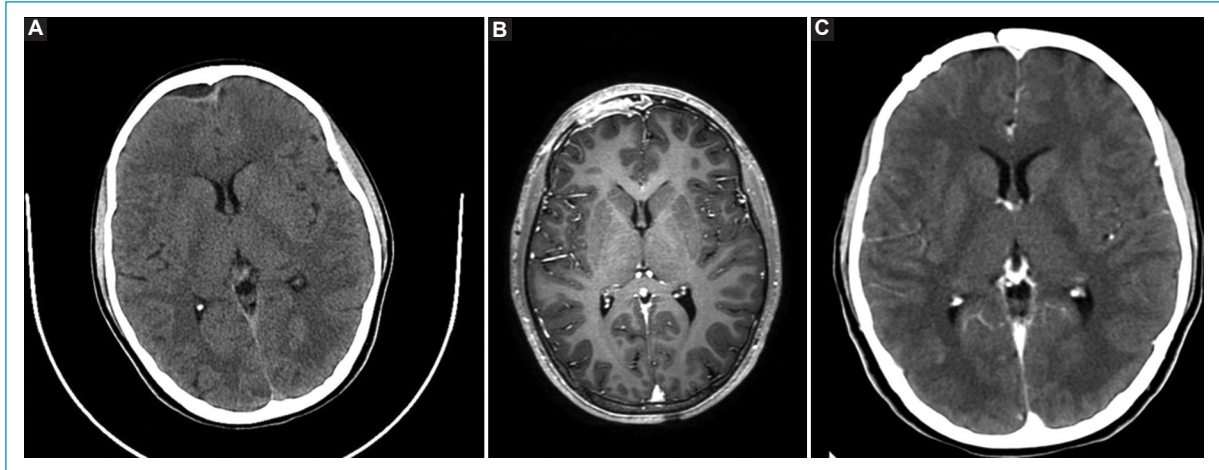


Figure 1. Epidural empyema in a 13-year-old girl (case 1). **(A)** axial CT scan showing a right-sided extra-axial frontal infectious collection; **(B)** axial T1 MRI with gadolinium on day 24 of antibiotic therapy (day 10 of linezolid) and **(C)** axial CT scan with contrast, eight weeks after completing the antibiotic therapy regimen with prior empyema surgical drainage.

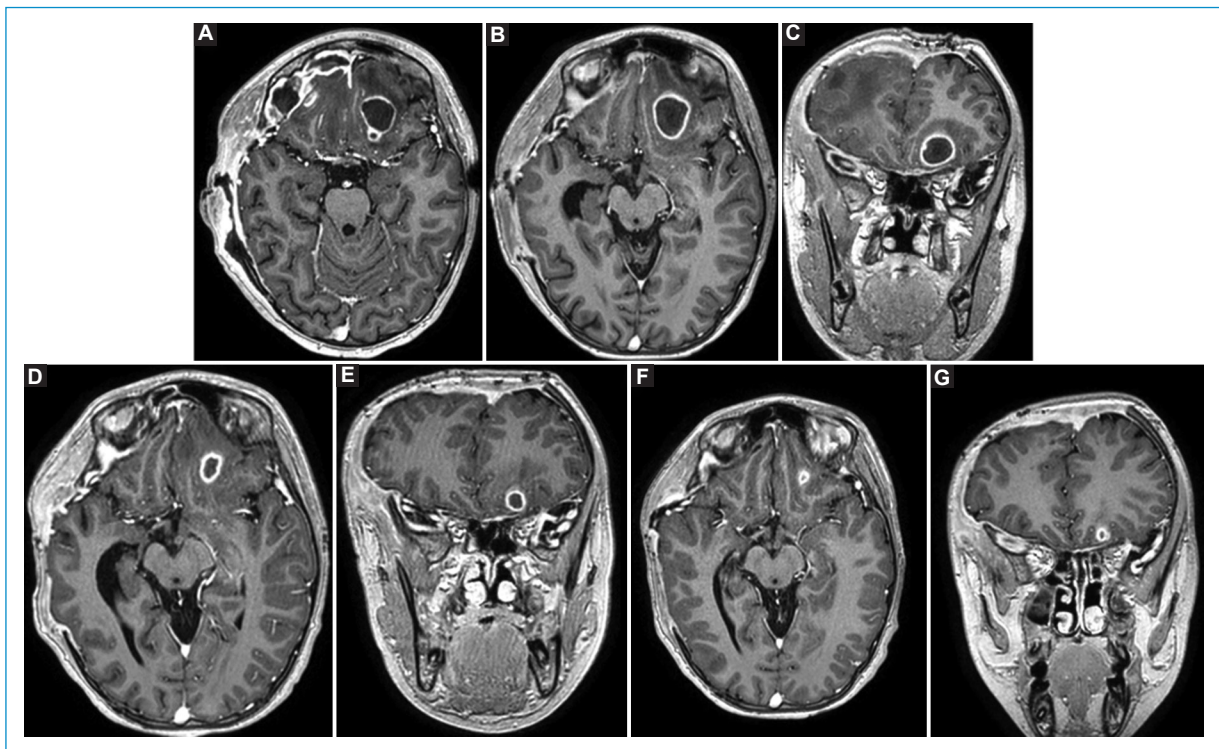


Figure 2. Subdural empyema complicated by intraparenchymal abscess in an 11-year-old girl (case 2). **(A)** axial T1 MRI with gadolinium; **(B, C)** axial and coronal T1 MRI on the ninth day of chloramphenicol (total of two days of oral therapy); **(D, E)** axial and coronal T1 MRI on day 12 of levofloxacin (total of 14 days of oral therapy); **(F, G)** axial and coronal T1 MRI, two weeks after completing the antibiotic regimen, showing regression of the intraparenchymal abscess.

bacteria with a good diffusion capacity in the central nervous system (CNS)⁷. Higher doses and longer treatments (over 14 days) are risk factors for hematological toxicity that is usually reversible, as observed in case 2⁹.

Levofloxacin has proved to be effective and well tolerated as an oral regimen⁷. Its high oral absorption and lipophilic characteristics promote CNS penetration, bolstering efficacy in treating CNS infections,

Table 2. Summary of literature review for switching from intravenous to oral antibiotics for pediatric intracranial infections

Review	Summary
Bodilsen et al. / <i>Clinical Microbiology and Infection</i> 30 (2024) 66e89	No recommendation. For early transition to oral antimicrobials in patients with a brain abscess, there is insufficient evidence at the time of writing to provide a recommendation.
Dodson D et al. / <i>Oral Antibiotics for Intracranial Infections</i> , OFID (2022)	Levofloxacin-based oral regimens were effective. Criteria for transitioning patients to oral antibiotics for intracranial infections should be established.
Lauda-Maillen et al. / <i>Eur J Clin Microbiol Infect Dis</i> (2020)	Switch to oral antibiotic therapy during the first 14 days of brain abscess treatment for patients with a favorable clinical evolution may reduce the hospital stay and the risk of parenteral catheter-related adverse events.

including those that are deep-seated or intraparenchymal^{10,11}.

Systemic absorption of linezolid approaches 100% following oral administration. Linezolid binds poorly to serum proteins, penetrating well into most body compartments, and is used in treating gram-positive bacterial CNS infections¹². Oral therapy allows for a quicker hospital discharge and eliminates the risks of a central venous catheter.

Extended intravenous treatment has been considered essential for managing patients with a brain abscess and intracranial infections. However, in recent years, some experts recommended early transition to an appropriate oral regimen after one or two weeks of intravenous treatment in patients with a good clinical response^{6,7}. Gilchrist et al. conducted a retrospective, observational study of 42 children with intracranial empyema admitted to a pediatric neurosurgical center. The median total antibiotic duration was 47 days and in 16 cases, after a course of intravenous therapy, antibiotics were switched to an oral agent. They selected children for the switch to oral agents where there was adequate source control, down-trending or normalized inflammatory markers and no clinical features suggestive of disease recurrence. The oral agent was most commonly amoxicillin/clavulanic acid with a transition at a median of 33 days¹³. As in the cases we described above, the outcome was favorable with no recurrence of the infectious process. Bodilsen et al. summarized the current evidence for early

transition to oral antimicrobials in children and adults with a brain abscess. Although there is insufficient evidence to provide a recommendation, in a 2023 narrative review, the authors concluded that early transition to oral antimicrobials in patients with an uncomplicated brain abscess may be beneficial due to the convenience of the treatment and potential decreased risks associated with prolonged hospitalization and intravenous lines⁶.

Although the early transition to oral antimicrobials has been adopted in some countries, effectiveness and safety remain uncertain^{6,7,14}. The optimal timing for a transition to oral antibiotic therapy is not well established (Table 2), but an early switch to oral treatment has been suggested to be equally effective and safe and should be considered in patients with controlled infection, after effective surgical drainage and with confirmed tolerability to suitable oral antibiotics.

Author contributions

R. Sousa: Conceptualization, literature search, draft writing and preparation, approval of the final version. M. Andrade, J. Jonet: Conceptualization, literature search, approval of the final version. S. Lemos, F. Prata, V. Oliveira, M.M. Santos, J.G. Marques: Review and editing, approval of the final version.

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Conflicts of interest

None.

Ethical considerations

Protection of humans and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

Confidentiality, informed consent, and ethical approval. The authors have followed their institution's confidentiality protocols, obtained informed consent from patients, and received approval from the Ethics Committee. The SAGER guidelines were followed according to the nature of the study.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

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