The Journal of International Advanced Otology

J Int Adv Otol 2025; 21: 1–5 • DOI: 10.5152/iao.2025.241721

Original Article

Sinus Vein Thrombosis in Pediatric Patients After Acute Mastoiditis

Aviad Sapir[1], Yotam Eshel[2], Yotam Heilig[1], Hagit Miskin[2], Oren Ziv[1], Sabri El-Saied[1], Daniel M. Kaplan[1]

[1]Department of Otolaryngology-Head and Neck Surgery, Soroka University Medical Center, Ben-Gurion University Faculty of Health Sciences, Beer-Sheva, Israel
[2]Department of Pediatric Hemato-Oncology, Soroka University Medical Center, Ben-Gurion University Faculty of Health Sciences, Beer-Sheva, Israel

ORCID iDs of the authors: A.S. 0000-0002-7446-1788, Y.E. 0000-00093842-9921, Y.H. 0009-0003-9685-582X, O.Z. 0000-0003-3286-9248, D.M.K. 0000-0002-3996-4283.

Cite this article as: Sapir A, Eshel Y, Heilig Y, et al. Sinus vein thrombosis in pediatric patients after acute mastoiditis. *J Int Adv Otol.* 2025, 21(2), 1721, doi: 10.5152/iao.2025.241721.

BACKGROUND: Acute mastoiditis (AM), a complication of acute otitis media, remains a concern despite medical advancements and often leads to severe complications such as cerebral sinus vein thrombosis (CSVT). This study aimed to characterize the clinical, microbiological, and hematological aspects of CSVT secondary to AM in children while assessing the necessity of thrombophilia evaluation in these patients.

METHODS: A retrospective analysis was conducted on pediatric patients with CSVT secondary to AM between January 2015 and December 2022. This study examined clinical data, laboratory and microbiological results, imaging studies, treatment approaches, and patient outcomes.

RESULTS: Seventeen pediatric patients with a mean age of 3 years were included in this study. Most patients were female (76.5%) and of Jewish ethnicity (82.4%). Group A *Streptococcus* is the primary pathogen responsible for this condition. The treatment plan involved the administration of intravenous antibiotics and surgical intervention, including cortical mastoidectomy and ventilation tube insertion. Additionally, anticoagulation therapy with Clexane® was initiated and continued for at least 3 months post event. Follow-up imaging revealed recanalization in most cases within an average of 3 months. Hematologic follow-up revealed no recurrent thrombotic events and low thrombophilia incidence.

CONCLUSION: Cerebral sinus vein thrombosis following AM is a provoked thrombotic event effectively managed with Clexane®. Thrombophilia evaluation may be reserved for patients with a high suspicion of underlying hematological conditions. Follow-up imaging within 3 months post event may be premature.

KEYWORDS: Acute mastoiditis, anticoagulation therapy, cerebral sinus vein thrombosis, thrombophilia

INTRODUCTION

Acute mastoiditis (AM) is an uncommon yet potentially serious infection of the mastoid air cells that typically arises as a complication of untreated or inadequately treated acute otitis media (AOM) in children.[1] While advancements in medical care have reduced the incidence of mastoiditis in children, it continues to be a concern due to the potential for severe complications. One such rare (0.6/100 000 patients annually) but significant complication is cerebral sinus vein thrombosis (CSVT), which can have devastating consequences if not promptly recognized and treated.[2,3]

Cerebral sinus vein thrombosis in the context of AM is a condition that requires heightened clinical awareness, as its presentation can be subtle, with potentially life-threatening complications. The infection extends from the mastoid air cells to the adjacent sigmoid or transverse sinus, leading to venous thrombosis. A thrombosed sinus may increase intracranial pressure, cause cerebral edema, seizures, and form an intracranial abscess. Therefore, early diagnosis and intervention are crucial to prevent further progression and potential neurological sequelae. The diagnosis of CSVT is mainly based on imaging studies such as magnetic resonance venography and computed tomography venography.[4,5]

Corresponding author: Aviad Sapir, e-mail: aviadsap@gmail.com
Received: September 15, 2024 • **Revision Requested:** November 2, 2024 • **Last Revision Received:** November 12, 2024 • **Accepted:** December 18, 2024 • **Publication Date:** March 24, 2025
Available online at www.advancedotology.org

Cerebral sinus vein thrombosis necessitates a comprehensive management approach, including intravenous (IV) administration of antibiotics, surgery, and anticoagulation therapy, to prevent further complications and alleviate neurological sequelae.[6] The traditional approach involved performing a cortical mastoidectomy for AOM. The sinus plate of the sigmoid sinus was then punctured, with a lack of bloody discharge proving CSVT. The sinus was opened, and any clot or abscess was removed.[7] Nowadays, puncturing the sinus is considered unnecessary, and cortical mastoidectomy reaching the sinus plate with the insertion of a ventilation tube is performed. Treatment with anticoagulants, in most cases low molecular weight heparin, such as Clexane® has become the standard of care. The treatment is continued until recanalization of the blood vessel, between 3 and 6 months.[8]

Cerebral sinus vein thrombosis due to AM may be considered as a provoked thrombotic event.[6] Thrombophilia evaluation, including multiple blood and coagulation tests, is costly. Even though current guidelines do not recommend full thrombophilia evaluation for patients with provoked venous thromboembolism,[9] CSVT is a relatively rare complication of mastoiditis; therefore, the recommendation is to complete thrombophilia evaluation,[10] but this evaluation's yield is yet to be determined.[11] In cases of familial or personal history of venous thromboembolism, children must undergo hematologic workups to diagnose/exclude congenital disorders of thrombophilia such as deficiencies of protein C, protein S, and anti-thrombin III; factor V Leiden, Prothrombin 20210A mutation, and antiphospholipid antibodies.[12]

Sparse data exist on this entity, mostly comprising case reports and limited patient series—regarding CSVT in AM cases, drawing definitive conclusions and formulating guidelines remains challenging. The objectives of this study were 2-fold: (1) evaluate clinical and laboratory findings in patients with CSVT in AM and (2) assess whether there is a need to investigate thrombophilia in every patient with CSVT in AM.

METHODS

Medical charts of all children diagnosed with CSVT secondary to AM were reviewed at the Pediatric Division of Soroka University Medical Center (SUMC), a tertiary referral hospital in Southern Israel, from January 2015 to December 2022. The inclusion criteria were children below 15 years of age treated for AM with CSVT, and postoperative follow-up of at least 6 months. Exclusion criteria included children with a history of cochlear implantation and patients with chronic suppurative otitis media with or without cholesteatoma. Patients who did not complete the hematologic follow-up at our institute were also excluded.This study was approved by the Ethics Committee of Soroka University (approval no: 446-18-SOR; date: April 30, 2019) and informed consent was obtained from the patients.

Data were collected regarding patient demographics (ethnicity, sex, and age at diagnosis) and clinical data (fever at admission, length of hospitalization, antibiotic therapy, white blood count (WBC), and coagulation blood test). Bacterial cultures were obtained surgically from the abscess during the procedure.

Post-Hospitalization Management

After discharge, patients were followed up at otolaryngology and pediatric hematology outpatient clinics. Anticoagulants were prescribed for at least 3 months. Familial and personal histories were obtained, along with laboratory blood tests for thrombophilia. We recommend that all patients undergo thrombophilia workups. The laboratory workup included: complete blood count, protein C, protein S, antithrombin II, factors VIII, IX, and XI, activated protein C resistance ratio, Beta-2 glycoprotein, cardiolipin, lupus anticoagulant screening tests for antiphospholipid antibody syndrome, and in some cases factor V Leiden and protein 20210 mutation. Patients were booked for head magnetic resonance imaging 3 months after the event to identify whether recanalization occurred.

Statistical Analysis

Statistical analyses were performed using SPSS version 23.0 (IBM SPSS Corp.; Armonk, NY, USA). Quantitative variables were described as mean ± standard deviation (SD) for normally distributed variables, and medians and interquartile range for other distributions. Frequencies summarize categorical variables from the available data.

RESULTS

About 17 of 25 children with AM and CSVT met the inclusion criteria, with a mean age of 3 years. The demographics of patients are presented in Table 1. Most patients (13 of 17, 76.5%) were female and Jewish (14 of 17, 82.4%). Upon admission, the mean fever was 38.7°C. Laboratory markers of inflammation were elevated, with 16.8 WBC and C-reactive protein (CRP) levels of 9.3 mg/dL. All patients were hospitalized with an average length of stay of 15 days. Patients were treated with IV administration of antibiotics. Ten children (58.8%) were treated with IV Ceftriaxone alone, whereas 6 children (35.3%) received IV Ceftriaxone in combination with metronidazole. One (5.9%) patient was treated with Ceftriaxone and Clindamycin. The antibiotics therapy continued during the hospitalization period (mean time of 15 days), with an additional post-hospitalization course of 10 days.

The pediatric emergency department coagulation laboratory tests were conducted on all children upon admission (Table 2). The average prothrombin time (PT) and activated partial thromboplastin time (aPTT) were 14.1 and 29.3, respectively. Prolonged PT and aPTT times were observed in 7 (41.2%) and 2 (11.7%) cases, respectively. Meanwhile, fibrinogen levels were high in 9 patients (52.9%) and averaged 666 mg/dL.

MAIN POINTS

- Pathogens: Group A *Streptococcus* was the most common pathogen, followed by *Fusobacterium necrophorum*, indicating pathogen prevalence post-pneumococcal vaccine shifts.
- Anticoagulant efficacy: All patients treated with Clexane® had no recurrent thrombotic events, though imaging within 3 months may be premature for assessing recanalization.
- Thrombophilia evaluation: Routine thrombophilia testing may not be necessary in all CSVT cases, as only 1 patient had a relevant familial history and no recurrent events occurred.
- Successful management: Cortical mastoidectomy and antibiotic therapy led to effective recovery with no long-term neurological issues.

Table 1. Demographics

Characteristic	N = 17
Mean age (years)	3.0 ± 2.1
Sex, n/N (%)	
Male	4/17 (23.5%)
Female	13/17 (76.5%)
Ethnicity, n/N (%)	
Jewish	14/17 (82.4%)
Bedouin	3/17 (17.6%)
Hospitalization length (days)	15 ± 6.2
Fever at admission (C°)	38.7 ± 1.4
Antibiotic therapy, n/N (%)	17/17 (100%)
Ceftriaxone, n/N (%)	10/17 (58.8%)
Ceftriaxone + Metronidazole, n/N (%)	6/17 (35.3%)
Ceftriaxone + Clindamycin, n/N (%)	1/17 (5.9%)

Before the surgical intervention, all 17 patients underwent post-contrast head computed tomography (CT) and temporal bone high-resolution CT. Imaging revealed a subperiosteal abscess (SPA) in all children. Five patients had perisinus abscesses. In 1 patient, an epidural abscess was identified. Four children had radiographic thrombosis not solely in the sigmoid but also in the internal jugular vein, transverse sinus, or cavernous sinus.

All patients underwent cortical mastoidectomy reaching the sigmoid sinus bone plate and drainage of the perisinus abscess when present (4 patients). In addition, a ventilation tube was inserted into the tympanic membrane.

The microbiological culture results of all 17 patients are shown in Table 3. In total, 10/17 (58.8%) of cultures were positive. Group A *Streptococcus* was the most common pathogen with 4 cases (40% of positive cultures) followed by *Fusobacterium necrophorum* and non-typeable *Haemophilus influenzae* with 2 cases each. *Streptococcus pneumoniae* and *Streptococcus intermedius* were isolated in 2 single cultures.

Table 2. Blood Tests at Admission

Characteristic	
WBC (cells/mm^3), mean ± SD	16.8 ± 7.4
CRP (mg/dL), mean ± SD	9.3 ± 9.0
PT- (seconds), mean ± SD	14.1 ± 1.8
High PT, n/N (%)	7/17 (41.2%)
Normal PT, n/N (%)	6/17 (35.3%)
aPTT (seconds), mean ± SD	29.3 ± 1.6
High aPTT, n/N (%)	2/17 (11.7)
Normal aPTT, n/N (%)	10/17 (58.8%)
Fibrinogen (mg/dL), mean ± SD	666 ± 232
High fibrinogen, n/N (%)	9/17 (52.9%)
Normal fibrinogen, n/N (%)	3/17 (17.6%)

aPTT, activated partial thromboplastin time; CRP, C-reactive protein; PT, prothrombin time; WBC, white blood count.

Table 3. Microbiology

Characteristic	N = 17
Negative ear culture, n/N (%)	7/17 (41.2%)
Positive ear culture, n/N (%)	10/17 (58.8%)
Positive culture	N = 10
Group A *Streptococcus* n/N positive culture (%)	4/10 (40%)
Streptococcus pneumonia n/N positive culture (%)	1/10 (10%)
Non-typable *Haemophilus influenzae* n/N positive culture (%)	2/10 (20%)
Fusobacterium necrophorum n/N positive culture (%)	2/10 (20%)
Streptococcus intermedius n/N positive culture (%)	1/10 (10%)

Clexane® therapy was initiated during the hospitalization period at a therapeutic dose for at least 3 months following the index event for all patients. Hematologic follow-up was completed in 6 patients, and only one had a familial history of thrombotic events associated with antiphospholipid antibody syndrome. Of the 6 patients who underwent hematological investigation, 1 patient initially had a low level of protein C, which was later normalized in subsequent tests, and protein C deficiency was ruled out. Notably, none of the patients experienced recurrent thrombotic events during follow-up.

About 12 of the 17 patients (70.5%) underwent the recommended magnetic resonance angiography, which was performed on averagely 4 months after surgery. Notably, in 2 instances in which the imaging test was conducted less than 3 months after discharge, thrombus recanalization was found to be incomplete.

None of the patients had long-term neurological sequelae, and all had finished antithrombotic treatment within 1 year. The mean and median follow-up periods were 7 months and 6 months, respectively.

DISCUSSION

In this retrospective case series, we described the clinical, microbiological, and hematological findings of children with CSVT due to AM. The principal findings of the study were as follows: (1) CSVT in the context of AM is not a risk factor for subsequent thrombotic events and (2) dominance of Group A *Sreptococcus* in the pathogenicity.

Our study has several limitations. First, it was a retrospective study. Accordingly, we found that not all patients underwent follow-up imaging, and only 6 patients completed a full thrombophilia workup. Second, the study cohort was relatively small, as the disease is rare. These factors make it difficult to draw unequivocal conclusions.

According to a study conducted at our medical center on patients under 15 years of age, the incidence rate of AM was 10.3/100 000 during the study period (2005-2017). This rate is relatively high when compared to other Western countries.[13] Most cases of AM are limited to the mastoid and do not present or develop further intracranial or extracranial complications, with an estimated rate of 5% of AM cases.[2] Reported AM complication rates vary in the literature and range up to approximately 20% of cases.[14] Management of most cases is conservative, with myringotomy and hospitalization for follow-up and IV administration of antibiotics. Surgery is usually indicated when SPA develops or when there is no response to treatment.[15]

A small group of patients may develop complications, either extracranial or intra-cranial. These cases are defined as complicated AM and require surgical intervention while continuing systemic antibiotic treatment. Complications of SPA and CSVT were observed in 52 (21.8%) and 22 (9.2%) patients, respectively. In a recently published series of 570 children from Israel, there was a significant increase in complicated AM cases with an indication for surgical intervention during the years 2008-2017, with 82 patients undergoing surgery. Of them, 29 (35%) had radiological findings of CSVT, with high rates of *F. necrophorum* in complicated AM cases.[4]

In the current study, the most commonly isolated pathogens were Group A *Streptococcus*, *F. necrophorum,* and non-typeable *H. influenzae*. These findings may be surprising since AM is a complication of AOM, with the leading pathogen being *S. pneumoniae*. Our findings are supported by several studies published after the introduction of pneumococcal conjugate vaccines (PCVs), in which more virulent bacteria were demonstrated in cases of AM complications.[16,17] Yosefof et al[18] emphasized the role of *F. necrophorum* as a dominant pathogen in cases of AM with CSVT. In their series, using cultures and PCR, in a group after the PCV-13 introduction, *F. necrophorum* was isolated in 71% of patients. Moreover, it should be noted that 7/17 cases in our study had negative bacterial cultures, and it cannot be ruled out that the microbiological distribution picture is probably different.

Our data show that performing a follow-up magnetic resonance angiography less than 3 months after the event is probably too early. The timing of recanalization following low molecular weight heparin treatment remains unclear. There is evidence that sinuses may recanalize spontaneously after cortical mastoidectomy and antimicrobial therapy, even without clot evacuation. Neilan et al[19] noted spontaneous recanalization in 52.9% of cases, with slightly higher rates (66.7%) in patients receiving additional anticoagulation. Au et al[20] reported higher rates in non-anticoagulated and anticoagulated patients (75% and 84%, respectively). However, a systematic review contested the benefits of anticoagulation therapy in improving the recanalization rates.[21] The AHA/ASA recommends early follow-up imaging for patients with persistent or worsening symptoms and a 3-6 months follow-up for stable patients.[22] Limitations such as varying degrees of recanalization, timing of follow-up imaging, and the absence of standardized anticoagulation protocols warrant consideration when interpreting these reports.

The lack of recurrent thrombotic events on long-term follow-up and the absence of thrombophilia suggests that thrombophilia evaluation in the case of CSVT due to AM should perhaps be saved for patients with a high level of suspicion for underlying diseases such as family history, atypical severe cases, or recurrent events. However, most of the patients in the study underwent one or more investigations for an underlying hematological disease. Additionally, a previous study from our center[5] aimed to assess the prevalence of thrombophilia in children with otogenic CSVT during a long-term follow-up. Seven patients were recalled after an average of 13 years post CSVT. Among them, 3 (43%) tested positive for at least 1 prothrombotic factor, such as elevated factor IX, reduced protein C and S levels, and elevated anticardiolipin antibodies. Two patients experienced long-term complications, including hearing loss and headaches. Therefore, when the clinician was exposed to an event such as this, professional judgment guided him to apply it clearly, even if partially.

Most patients presented at admission with high fever, elevated CRP and fibrinogen levels, and prolonged PT. These clinical and laboratory markers suggest that high inflammatory status in AM plays a role in the development of CSVT in children. These findings require further investigation and should be compared with patients with AM without CSVT.

CONCLUSION

Cerebral sinus vein thrombosis following AM is a provoked event. Clexane® treatment appears effective in both the short and long term. An imaging test within 3 months may be too early. Further prospective studies are required to define which patients should undergo thrombophilia workup.

Availability of Data and Materials Statement: The data that support the findings of this study are available on request from the corresponding author.

Ethics Committee Approval: This study was approved by the Ethics Committee of Soroka University (approval no: 446-18-SOR; date: April 30, 2019).

Informed Consent: Verbal informed consent was obtained from the patients who agreed to take part in the study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – A.S., D.M.K.; Design – D.M.K.; Supervision – D.M.K.; Resources – Y.E., H.M.; Materials – Y.E., O.Z.; Data Collection and/or Processing – A.S., Y.H.; Analysis and/or Interpretation – A.S., Y.E.; Literature Search – A.S., O.Z.; Writing – A.S., Y.E., S.E.S.; Critical Review – H.M, D.M.K.

Declaration of Interests: The authors have no conflicts of interest to declare.

Funding: The authors declared that this study received no financial support.

REFERENCES

1. Cassano P, Ciprandi G, Passali D. Acute mastoiditis in children. *Acta Biomed*. 2020;91(Suppl 1):54-59. [CrossRef]
2. Favre N, Patel VA, Carr MM. Complications in pediatric acute mastoiditis: HCUP KID analysis. *Otolaryngol Head Neck Surg*. 2021;165(5):722-730. [CrossRef]
3. Ziv O, Sapir A, Leibovitz E, Kordeluk S, Kaplan DM, El-Saied S. Post-operative clinical course in children undergoing mastoidectomy due to complicated acute mastoiditis. *Eur Arch Otorhinolaryngol*. 2022;279(8):3891-3897. [CrossRef]
4. Stern Shavit S, Raveh E, Levi L, Sokolov M, Ulanovski D. Surgical intervention for acute mastoiditis: 10 years' experience in a tertiary Children's Hospital. *Eur Arch Otorhinolaryngol*. 2019;276(11):3051-3056. [CrossRef]
5. Schneider S, Kapelushnik J, Kraus M, El Saied S, Levi I, Kaplan DM. The association between otogenic lateral sinus thrombosis and thrombophilia: a long-term follow-up. *Am J Otolaryngol*. 2018;39(3):299-302. [CrossRef]
6. Kethireddy N, Sama S. Cerebral sinus venous thrombosis in the setting of acute mastoiditis. *Cureus*. 2019;11(2):e4023. [CrossRef]
7. Kaplan DM, Kraus M, Puterman M, Niv A, Leiberman A, Fliss DM. Otogenic lateral sinus thrombosis in children. *Int J Pediatr Otorhinolaryngol*. 1999;49(3):177-183. [CrossRef]
8. Havalı C, İnce H, Gündoğdu EB, et al. The management of elevated intracranial pressure and sinus vein thrombosis associated with mastoiditis: the experience of eighteen patients. *Childs Nerv Syst*. 2022;38(2):421-428. [CrossRef]

9. Goldenberg NA, Abshire T, Blatchford PJ, et al. Multicenter randomized controlled trial on duration of therapy for thrombosis in children and young adults (the Kids-DOTT trial): pilot/feasibility phase findings. *J Thromb Haemost*. 2015;13(9):1597-1605. [CrossRef]
10. Dlamini N, Billinghurst L, Kirkham FJ. Cerebral venous sinus (sinovenous) thrombosis in children. *Neurosurg Clin N Am*. 2010;21(3):511-527. [CrossRef]
11. Young G. How I treat pediatric venous thromboembolism. *Blood*. 2017;130(12):1402-1408. [CrossRef]
12. Monagle P, Cuello CA, Augustine C, et al. American Society of Hematology 2018 guidelines for management of venous thromboembolism: treatment of pediatric venous thromboembolism. *Blood Adv*. 2018;2(22):3292-3316. [CrossRef]
13. Sapir A, Ziv O, Leibovitz E, et al. Impact of the 13-valent Pneumococcal Conjugate Vaccine (PCV13) on acute mastoiditis in children in southern Israel: a 12-year retrospective comparative study (2005-2016). *Int J Pediatr Otorhinolaryngol*. 2021;140:110485. [CrossRef]
14. Luntz M, Brodsky A, Nusem S, et al. Acute mastoiditis—the antibiotic era: a multicenter study. *Int J Pediatr Otorhinolaryngol*. 2001;57(1):1-9. [CrossRef]
15. Loh R, Phua M, Shaw CL. Management of paediatric acute mastoiditis: systematic review. *J Laryngol Otol*. 2018;132(2):96-104. [CrossRef]
16. Cavel O, Tauman R, Simsolo E, et al. Changes in the epidemiology and clinical features of acute mastoiditis following the introduction of the Pneumococcal Conjugate Vaccine. *Int J Pediatr Otorhinolaryngol*. 2018;104:54-57. [CrossRef]
17. Gorphe P, De Barros A, Choussy O, Dehesdin D, Marie JP. Acute mastoiditis in children: 10 years' experience in a French tertiary university referral center. *Eur Arch Otorhinolaryngol*. 2012;269(2):455-460. [CrossRef]
18. Yosefof E, Hilly O, Sokolov M, Raveh E, Yacobovich J, Ulanovski D. Paediatric otogenic sinus venous thrombosis: the role of *Fusobacterium necrophorum*. *Acta Otorhinolaryngol Ital*. 2022;42(4):388-394. [CrossRef]
19. Neilan RE, Isaacson B, Kutz JW Jr, Lee KH, Roland PS. Pediatric otogenic lateral sinus thrombosis recanalization. *Int J Pediatr Otorhinolaryngol*. 2011;75(6):850-853. [CrossRef]
20. Au JK, Adam SI, Michaelides EM. Contemporary management of pediatric lateral sinus thrombosis: a 20-year review. *Am J Otolaryngol*. 2013;34(2):145-150. [CrossRef]
21. Chalmers E, Ganesen V, Liesner R, et al. Guideline on the investigation, management, and prevention of venous thrombosis in children. *Br J Haematol*. 2011;154(2):196-207. [CrossRef]
22. Dmytriw AA, Song JSA, Yu E, Poon CS. Cerebral venous thrombosis: state of the art diagnosis and management. *Neuroradiology*. 2018;60(7):669-685. [CrossRef]