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Research Article

Acute Mastoiditis in Children: Can We Predict Intracranial Complications?

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Abstract

Background: Controversy exists regarding the use of routine cranial imaging to detect unapparent intracranial complications among children with acute mastoiditis (AM).

Objectives: We aim to study the proportion of intracranial complications among children with AM, and to determine whether such complications might be anticipated.

Methods: Children ≤ 18 years hospitalized with AM, 2005-2012, were included. Clinical and laboratory parameters of patients with and without intracranial complications, diagnosed by cranial computed tomography, were retrospectively compared.

Results: Overall, 203 children were included, of whom 8 (3.9%) had intracranial complications. *Streptococcus pneumoniae* (26%) and *Streptococcus pyogenes* (16%) were the most common pathogens. There was no statistical difference between those with and without intracranial complications regarding age, temperature on presentation, white blood cell count, and c-reactive protein levels. Two of the eight children with intracranial complications (25%) exhibited neurological signs.

Conclusions: AM may be complicated by noteworthy intracranial complications. Most children with these complications did not exhibit ominous clinical or laboratory findings. Cranial imaging might be necessary to detect intracranial complications.

Keywords: Acute mastoiditis, Intracranial complications, Sinus vein thrombosis, S. pneumonia, ranial imaging

Introduction

Acute mastoiditis (AM) is a suppurative infection of the mastoid air cells and is the most common infectious complication of acute otitis media (AOM) [1,2]. The incidence and the microbiology underlying AM are thought to be influenced by the introduction of pneumococcal vaccine as well as the watchful waiting approach with antibiotics for AOM. Despite a decrease in the rate of *Streptococcus pneumoniae (S. pneumoniae)* cultured from middle ear effusion following the widespread use of pneumococcal vaccine, there have been dynamic changes in the incidence of AM in several

countries, with an initial decline followed by a recent increase [3, 4]. Moreover, recent studies now demonstrate that *Group A Streptococcus* is emerging as a significant pathogen in AM [5].

The interplay between withholding antibiotics for AOM and resultant AM is controversial, with studies showing both increases and stable incidence rates in countries where conservative management guidelines for AOM were employed [6,7]. In Israel, the watchful waiting approach for the management of AOM began in 2004, and the pneumococcal conjugated vaccine was introduced into the nation's immunization policy in 2004.

It is well established that AM is primarily a clinical diagnosis, consisting of postauricular swelling, erythema, tenderness, and protrusion of the auricle [7,8]. However, AM can lead to both severe intracranial (e.g., intracranial abscess formation, venous sinus thrombosis) and extracranial (e.g., subperiosteal abscess, osteomyelitis of the temporal bone) complications, with a reported proportion ranging from 6.8% to 55% [1, 9-11]. While some of the extracranial complications of patients with AM are overt, most patients with intracranial consequences do not exhibit neurological signs, and complications can be detected only through cranial imaging (computed tomography [CT] or magnetic resonance imaging [MRI]). Given the risk of these intracranial thrombotic and infectious complications, some centers advocate the incorporation of cranial CT in the evaluation of children with AM [11], while others advocate close follow-up with the decision to obtain cranial imaging only for those patients with suspected complications [2,12-14].

To the best of our knowledge, there is only scant literature examining clinical or laboratory predictors of intracranial complications in patients with AM. Go et al. found persistent otalgia or otorrhea while on oral antibiotics with associated neurologic symptoms to be ominous signs suggestive of an intracranial complication [9].

The aim of the current study is to evaluate the proportion of intracranial complications among children presenting with AM, and to determine whether these complications might be anticipated early in the patient's hospital course.

Methods

Subjects were children ≤ 18 years of age who were hospitalized with AM between 2005 and 2012 at either of two medical centers in Northern Israel (n=203). The clinical diagnosis of AM was based on post-auricular swelling, erythema, tenderness, and protrusion of the auricle. Children with sub-acute or chronic mastoiditis (duration of symptoms > 4 weeks), immunodeficiency disorders, or previous ear/auricular surgeries were excluded from the study.

At Bnai Zion Medical Center, hereafter designated Center 1, cranial CTs without and with contrast were preformed routinely on admission in most of the children. In contrast, at HaEmek Medical Center, hereafter designated Center 2, cranial CTs were obtained only in select cases – i.e., for those patients with a complicated course or suspected to have an intracranial complication. Demographic, clinical, laboratory, and imaging data of patients with and without intracranial complications were retrospectively recorded. The study was approved by the Institutional Review Board.

Statistics

Data were presented as mean ± standard deviation (range) or n (%). Continuous data were compared using the Student t-test or the Mann-Whitney test for non-normally distributed data. A chi-square or Fisher's exact test, where appropriate, was used to compare categorical data. Logistic regression was used to predict complications among patients who had a CT scan. Statistical significance was considered as $p<0.05$.

Results

During the study period, 203 children aged 18 years or under were diagnosed with AM: 87 children in Center 1 and 116 children in Center 2. The baseline characteristics, clinical, laboratory, and imaging data for children presenting with AM at Centers 1 and 2 are presented in Table 1. Cranial CT showed that eight (3.9%) of the 203 children diagnosed with AM had intracranial complications, six (8%) at Center 1 and two (2%) at Center 2.

Microbiology of Acute Mastoiditis

Culture specimens from tympanic membrane paracentesis, ear discharge, and abscess aspirate were available for 183 children (90.1%). Bacterial pathogens were recovered in 123 (67%) of the patients sampled. *S. pneumonia* comprised 49 (26%), *Group A Streptococcus* 30 (16%), and *Pseudomonas aeruginosa* 17 (9%) of the isolated pathogens (Table 2). Sixty (33%) of the samples were without growth.

Intracranial Complications

The most common intracranial complication was sigmoid sinus thrombosis (n=6). Other intracranial complications included transverse sinus thrombosis (n=1), lateral sinus thrombosis (n=1), temporal lobe abscess (n=1), and perisigmoid sinus empyema (n=1). Two children had two concomitant intracranial complications (sigmoid sinus thrombosis and perisigmoid sinus empyema; sigmoid sinus thrombosis and temporal lobe abscess). Two (25%) of the eight children with an intracranial complication, one at each medical center, exhibited neurological sign/s. The first patient presented with febrile seizures and abducens nerve palsy and developed gait instability during

Table 1. Clinical, laboratory, and imaging data of children presenting with acute mastoiditis at Centers 1 and 2 between 2005 and 2012

	Center 1 (n=87)	Center 2 (n=116)	Total (n=203)	p-value
Age (years)	2.1± 2 (0-16)	2.7±2.5 (0.2-12)	2.4±2.3 (0-16)	0.28
Gender Male Female	 51 (59%) 36 (41%)	 56 (48%) 60 (52%)	 107 (52.7%) 96 (47.3%)	0.14
Temperature on admission (ºC)	37.8±1.1 (35.8-41.0)	37.8±1.0 (36.0-41.0)	37.8±1.0 (35.8-41.0)	0.93
Otorrhea	26 (30%)	23 (20%)	49 (24.6%)	0.14
WBC[1] (*10^3 ml)	19.6±6.0 (5.4-33.7)	17.8±6.0 (7.6-33.3)	18.6±6.1 (5.4-33.7)	0.04
CRP[2] (mg/L)	101.0±78.6 (4.4-414.2)	129.5±79 (13.1-268.0)	106.5±79.1 (4.4-414.2)	0.1
Cranial CT[3]	72 (83%)	10 (9%)	82 (40.4%)	<0.001
Intracranial complications	6 (7%)	2 (2%)	8 (3.9%)	<0.08

Abbreviations: [1] WBC: white blood cells; [2] CRP: C-reactive protein; [3] CT: computed tomography.

1. Continuous data are presented as mean ± 2 standard deviations (range); categorical data are presented as number (%).

Table 2. Culture findings of children presenting with acute mastoiditis (n=183)

Culture finding	Number (%)
Streptococcus pneumoniae	49 (26)
Group A *Streptococcus*	30 (16)
Pseudomonas aeruginosa	17 (9)
Haemophilus influenzae	6 (3)
Candida species	4 (2)
Staphylococcus aureus	3 (1)
Moraxella catarrhalis	1 (1)
Proteus mirabilis	1 (1)
Enterococcus spp	1 (1)
Fusobacterium necrophorum	1 (1)
Haemophilus parainfluenzae	1 (1)
Enterobacter spp	1 (1)
≥ 2 pathogens	8 (4)
Negative culture	60 (33)

hospitalization (cranial CT finding of lateral sinus thrombosis); the second patient developed gait instability and became lethargic three days after admission (cranial CT findings of sigmoid sinus thrombosis and perisigmoid sinus empyema).

Predictors of Intracranial Complications

Table 3 depicts the demographic, clinical, and laboratory data of children with AM, with and without intracranial complications. There was no significant difference between those with and without intracranial complications with regard to mean age, temperature on presentation, white blood cell count, C-reactive protein level, and the presence of otorrhea.

Microbiology of Intracranial Complications

Pathogens isolated from children with intracranial complications were as follows: penicillin non-susceptible (MIC 0.125) *S. pneumonia* (n=1), *Haemophilus Influenzae non-type B* (n=1), *Group A Streptococcus* (n=1), *Fusobacterium necrophorum* (n=1), *Escherichia coli* (n=1), and *Streptococcus constellatus* (n=1).

Table 3. Clinical and laboratory data of children with acute mastoiditis with and without intracranial complications at Centers 1 and 2 between 2005 and 2012.

	Intracranial complications (n=8)	No intracranial complications (n=74)	p-value
Age (years)	3.4±3.6 (2.7, 0.0-11.6)	2.1±1.7 (1.7, 0.2-7.7)	0.23
Gender Male Female	 4 (50%) 4 (50%)	 45 (61%) 86 (39%)	 0.71
Temperature on admission (ºC)	37.4±0.8 (36.2-38.3)	37.9±1.1 (35.8-40.0)	0.25
Otorrhea	1 (12%)	26 (36%)	0.68
WBC[1] (*10^3 ml)	20.7±5.8 (20.1, 12.7-32.1)	19.4±6.1 (18.9, 7.6-33.7)	0.26
CRP[2] (mg/L)	128.3±77.8 (131.6, 17.5-226)	103.4±78.3 (87.8, 4.4-414.2)	0.43

Abbreviations: [1] WBC: white blood cells; [2] CRP: C-reactive protein.
Continuous data are presented as mean ± 2 standard deviations (range); categorical data are presented as number (%).

Discussion

In the current study, 3.9% of children diagnosed with AM had intracranial complications, and only two of the eight patients with these sequelae displayed ominous neurological signs. We also found that while *S. pneumonia* was the most common isolate in these patients, Group A *Streptococcus* grew on 16% of the cultures and was the second most common identified pathogen.

The interplay between the widespread use of pneumococcal vaccine and the adaption of a watchful waiting policy for managing AOM has tremendous ramifications on the incidence and microbiology of AM. Indeed, our results reaffirm other recent studies that have noted a change in the pathogens causing AM, with a decrease in the rate of *S. pneumoniae* following the widespread use of a conjugated pneumococcal vaccine and the emergence of Group A Streptococcus as an important virulent cause of AM [3, 5]. With regard to changes in incidence, as early as 2001 Van Zuijlen et al. showed that in the Netherlands, withholding antibiotics or, at best, delaying antibiotic administration resulted in an increase in AM [6]. In the U.S., the introduction of heptavalent pneumococcal conjugate vaccine led to an initial decline in AM levels, but was followed by a subsequent increase in incidence levels to the pre- pneumococcal conjugate vaccine level of 12/100,000 among children younger than 2 years of age [4].

Not surprisingly, in the current study, the detection of intracranial complications was higher in the medical center in which brain imaging was routinely employed, reaching a high of 8%. This rate is slightly higher than previous studies reporting 3.2-6.8% of patients with AM having intracranial complications [9,15,16]. Notably, these studies preceded the era of widespread conjugated vaccine administration and the watchful waiting approach to AOM, whereas the years spanned by our study followed the establishment of Israel's policy of withholding antibiotics for AOM. As expected, *S. pneumoniae* was the predominant pathogen in all of the studies [9,15,16]. Moreover, most of the children with acute mastoiditis [15,16], as well as those with acute mastoiditis with resultant intracranial complications [9], received antibiotics prior to their hospital admission.

In a recent study of MRI as a means of diagnosing AM, 3 out of 23 children with mastoiditis (13%) had intracranial complications, demonstrating the great potential of MRI for assessing mastoiditis complications. In the aforementioned study, the clinical course of the children with intracranial complications was not described, and so we are unaware whether or not there might have been any means of identifying these children [17]. Stahelin-Massik reported that 38% of patients with acute, subacute, and chronic mastoiditis having intracranial complications did not demonstrate clinical evidence suggestive of intracranial complications (sinus vein thrombosis and epidural abscesses) [11]. In our study, most children (75%) with AM and intracranial complications showed no ominous signs or symptoms suggestive of an intracranial process.

As most children with intracranial complications did not exhibit neurological signs or symptoms, we explored whether these complications might be predicted early in the hospital course. We found no clinical or laboratory finding that could be used to predict intracranial complications in patients with AM. To the best of our knowledge, scant literature has target-

ed this clinical question. Go et al. found that persistent otalgia or otorrhea while on oral antibiotics with associated neurologic symptoms are ominous signs suggestive of intracranial complications (sigmoid sinus thrombosis, epidural abscess, and meningitis) related to AM [9]. Oestreicher-Kedem et al. reported that among children with AM during 1999-2001, white blood cell count differentiated between those with and without severe complications; however, that study did not distinguish between intracranial and extracranial complications [10]. Bilavsky et al. found that high fever, elevated C-reactive protein, and absolute neutrophil count at presentation distinguished children with complicated AM between 2003-2007, but here too, intracranial and extracranial complications were not separately assessed [1].

The difference between the clinician's ability to predict intracranial and extracranial complications associated with AM in comparison to isolated intracranial complications may stem from the different pathogeneses involved. Most intracranial complications are thrombotic, and may therefore not result in the elevation of inflammatory markers to the degree that is encountered in extracranial complications, which are predominantly infectious.

The present study has several potential limitations. First, as it involved only two medical centers, the modest number of children with intracranial complications limited the statistical power to detect potential predictors. Second, it is a retrospective study, in which long-term neurological outcomes of children with intracranial complications and those who did not undergo cranial CT were not assessed. These limitations suggest the importance of a large prospective study with long-term follow-up of children with AM who did and did not undergo cranial imaging to further elucidate the role of this imaging for all children presenting with AM.

Conclusions

AM may be complicated by severe intracranial complications, and the implications of such sequelae are not negligible. Most of the children with AM having intracranial complications in the current study did *not* exhibit neurological signs. Demographic, clinical, and laboratory data did not aid in the prediction of intracranial complications among children presenting with AM. Thus, our findings emphasize the valuable role of cranial imaging of children with AM in order to detect potentially severe intracranial complications. Prospective studies should continue to explore whether routine cranial imaging is warranted in all children presenting with AM.

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