International Journal of Pediatric Otorhinolaryngology 92 (2017) 32–37

Contents lists available at ScienceDirect

International Journal of Pediatric Otorhinolaryngology

journal homepage: http://www.ijporlonline.com/

Review article

Acute mastoiditis in children: Middle ear cultures may help in reducing use of broad spectrum antibiotics

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ARTICLE INFO

Article history:
Received 3 August 2016
Received in revised form
6 November 2016
Accepted 7 November 2016
Available online 10 November 2016

Keywords:
Acute mastoiditis
Children
Acute otitis media
Complications

ABSTRACT

Background: Acute mastoiditis (AM) is a suppurative infection of the mastoid air cells, representing the most frequent complication of acute otitis media. AM remains an important entity in children due to its potential complications and sequelae. We aim to describe the cases of AM admitted at our department, identify risk factors potentially associated with complications and analyse the changes in clinical approach of AM over time.

Methods: Case review of clinical files of children admitted with acute mastoiditis from June 1996 to May 2013 at a Lisbon metropolitan area hospital. Data was divided into two groups (prior and after May 2005) in order to evaluate changes in AM approach over the years.

Results: 135 AM episodes were included. The median age was 3.8 years and 42% children were less than 24 months of age. Symptoms at presentation included fever (69%), ear pain (56%) and otorrhea (40%). Complications occurred in 22% patients and were more common in children under 24 months (33% vs 15%, $p \leq 0.01$).

Leukocyte count was significantly higher in children with complications (16.7 vs 14.5 $\times$ 10^9/μL, $p \leq 0.05$) as was C-Reactive Protein value (13 vs 6.3 mg/dL, $p \leq 0.001$). There was a significant association between the development of complications and C-Reactive Protein value at admission (OR 1.892; IC95%: 1.018 −2.493, $p \leq 0.01$). The optimal cut-off value was 7.21 mg/dL.

Over time there was a significant increase in middle ear cultures obtained by tympanocentesis during surgery (2% vs 16%, $p \leq 0,01$) and also a decrease in the use of broad spectrum antibiotherapy as initial treatment (52% vs 25%,$p \leq 0,001$).

Conclusions: Children under 24 months, with high leukocyte count or with high C-Reactive Protein value should be monitored closely since complications tend to be more frequent. A CRP value of 7.21 mg/dL at admission seems to be a good cut-off to monitor children for potential complications.

Throughout the period analysed more cultures were performed allowing identification of the pathogens and implementation of appropriate antibiotic therapy.

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http://dx.doi.org/10.1016/j.ijporl.2016.11.002
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1. Introduction

Acute mastoiditis is a suppurative infection of mastoid air cells with symptoms lasting less than one month. It is the main complication of acute otitis media (AOM) affecting 1 in 400 cases (0,24%) [1].

The middle ear is connected to the mastoid by the *aditus ad antrum*. Therefore, most episodes of AOM are associated with inflammation of the mastoid mucosa [2,3].

When the inflammatory process persists, obstruction of the *aditus ad antrum* occurs and purulent material accumulates within the mastoid cavities evolving to acute mastoiditis [2,4,5]. If infection extends to the periosteum underlying the mastoid process, periosteitis may develop. As the pressure increases, destruction of the bone matrix occurs causing acute mastoiditis with osteitis [4]. Once cortical destruction develops, the infection may progress to adjacent structures.

Signs and symptoms may include fever, ear pain, post-auricular tenderness and pinna protrusion [2,6]. The most commonly involved pathogen is *Streptococcus pneumoniae* although *Haemophilus influenzae, Streptococcus pyogenes, Staphylococcus aureus* and *Pseudomonas aeruginosa* may also be involved [4,6,7].

Acute mastoiditis is more common in boys and has a peak incidence between the second and third years of life, similar to that of AOM. This peak is associated not only with the physiological immaturity of the immune system but also with the small size of the *aditus ad antrum* in this age group, favoring its obstruction during the inflammatory process of otitis [4,6]. The proximity of the mastoid to the facial nerve, jugular vein, internal carotid artery, sigmoid sinus, meninges and brain is crucial to the development of complications [2,4].

Acute mastoiditis has once been a major cause of hospitalization in children, decreasing dramatically since the introduction of antibiotics [2]. Authors disagree on whether its incidence is increasing in the last years [2,7–14]. Since acute mastoiditis remains an important entity in pediatrics, knowledge of its pathophysiology in each institution remains of extreme importance.

In this report, we aim to describe the cases of acute mastoiditis admitted at our department of pediatrics and identify risk factors potentially associated with complications. We also intend to analyse the changes in the clinical approach of acute mastoiditis over the years at our department regarding diagnostic exams, treatment, complications and follow-up.

2. Material and methods

Case review of clinical files of children admitted to the department of pediatrics with acute mastoiditis in the period from June 1996 to May 2013 (seventeen years).

Acute Otitis Media was defined based on the American Academy of Pediatrics (AAP) guidelines as the presence of moderate to severe bulging of tympanic membrane, new onset of otorrhea not due to otitis externa or as the presence of mild bulging of the tympanic membrane associated with a less than 48 h onset of ear pain or intense erythema of the tympanic membrane [15].

Inclusion criteria were the coexistence of AOM and one or more clinical signs suggestive of acute mastoiditis: peri-auricular inflammation signs such as erythema, blush or edema, loss of retro-auricular crease or displacement of the pinna. All children were evaluated by an otolaryngology expert at admission.

Cases of acute mastoiditis diagnosed by image exams without clinical symptoms were excluded.

The children's medical history was reviewed focusing on the previous episodes of AOM. Recurrent AOM was defined according to AAP guidelines as either three AOM episodes in six months period or four or more episodes in one year [15]. Personal background of otorhinolaryngologic disease was defined as the presence of one or more of the following: recurrent AOM, adenoidal hypertrophy, sinusitis or previous episode of acute mastoiditis.

Complications of acute mastoiditis were divided into intracranial (meningitis, venous thrombosis and cerebral abscess) and extracranial (facial paralysis, subperiosteal abscess, abscess of Bezold and labyrinthitis). It was considered a risk factor for complicated acute mastoiditis if the child was under twenty-four months, had a background of otorhinolaryngologic disease, had an episode of AOM treated with antibiotics in the three months prior to admission and also if the child was under antibiotic therapy for AOM. Leukocytosis was defined as total leukocyte count equal to or greater than two standard deviations for age and sex.

Broad spectrum antibiotics were defined as the ones effective against a wide range of infectious microorganisms including both gram positive and gram negative bacteria such as ceftriaxone and cefuroxime.

Changes in clinical practice regarding the approach of acute mastoiditis were analysed based on the previously published report by Salgueiro B et al. [7]. This was a retrospective case series undertaken at the same department of pediatrics that included all acute mastoiditis admissions from June 1996 through May 2005. A clinical protocol was implemented after data analysis in 2005. The protocol defined the diagnostic criteria for acute mastoiditis, as well as a structured approach for the child with suspect AM concerning the need for diagnostic exams and the empirical antibiotic therapy instituted.

In this report we considered two distinct time periods: before and after the protocol implementation. Patients were divided into two distinct groups: group A (admission from June 1996 through May 2005) and group B (admission from June 2005 through May 2013).

Statistical analysis was performed using SPSS® 21.0 (SPSS, INC., Chicago, USA). For numerical variables with normal distribution, the mean and standard deviation were calculated. The median, minimum and maximum values were calculated for non-normal distribution variables. The comparative analysis was performed using a *chi*-square test for categorical variables. For continuous variables with normal distribution the student t-test was performed and for continuous variables with non-normal distribution the Mann-Whitney test.

3. Results

3.1. Epidemiology

In the period analysed there were 135 acute mastoiditis episodes that met the inclusion criteria. Most patients were boys (60%) and caucasian (90%). The median age was 3.8 years (range 4.7 months–16.3 years). 57 children (42%) were less than 24 months of age and 17% less than 12 months. Only 16% were more than ten years old.

The highest number of admissions (15%) was in 2006. Most cases occurred during summer (31%), particularly in August (15%). The year distribution is represented in Fig. 1. History of previous otorhinolaryngologic disease was documented in 53 children (39%): recurrent AOM (36%), adenoidal hypertrophy (10%), previous episode of acute mastoiditis (10%) and sinusitis (3%).

3.2. Clinical findings and diagnostic exams

All children had AOM at admission. Signs and symptoms at presentation included fever (69%), ear pain (56%) as well as otorrhea (40%). Two patients presented with peripheral facial paralysis. One child was in septic shock at admission. The median length of time between the beginning of symptoms and hospital admission was three days (range 1–14 days).

Analysis with complete blood count and C-Reactive Protein (CRP) were performed in every patient. The majority (72%) had leukocytosis, with a mean value of $15.1 \pm 5.4 \times 10^9/\mu L$. Mean CRP value was 5.4 mg/dL (range 0.2–43 mg/dL).

In 45 children (33%) cultures were obtained from either the ear canal (31), middle ear (13) or abscess drainage (one). In 26 cultures (58%) bacterial growth was documented. Of the cultures obtained from ear canal swab, 18 (58%) isolated *Pseudomonas aeruginosa* (one of which also isolated *Staphylococcus aureus),* four *Streptococcus pneumoniae* and in one grew an unidentifiable gram-negative bacilli. Cultures from the middle ear were obtained by tympanocentesis during surgery with *Streptococcus pneumoniae* being isolated in two (15%). *Streptococcus pyogenes* was isolated in the culture of purulent material obtained during a retro-auricular abscess drainage. Cultures contamination rate was 11%.

Computed Tomography Scan (CT-Scan) was performed in 89% children, mainly (87%) either at admission or during the first day of hospitalization. In two children (1.5%) Magnetic Resonance Image (MRI) was also performed due to suspicion of intracranial complications after CT-Scan.

3.3. Antibiotic therapy and surgery

In the three months prior to admission, 71 children (53%) had been under antibiotics, 91% to treat acute otitis media. At admission 45 children (33%) were under antibiotherapy for AOM. There was no information available about the duration of treatment prior to admission.

All children started empiric intravenous antibiotic therapy. 131 (90%) were started on monotherapy with either amoxicillin/clavulanic acid (47%), ceftriaxone (36%) or cefuroxime (6%). The remaining 14 patients were treated with combined antibiotherapy due to concomitant external otitis (5%) or presence of complications.

During hospitalization antibiotic therapy was adjusted in 18 (13%) patients: in nine switched to broad spectrum antibiotics (six cases with complications detected on CT-Scan and three cases without clinical improvement after 72 h of therapy); in two children adjusted to a narrower spectrum antibiotic after CT-Scan images showed no evidence of complications that were initially suspected. In seven children therapeutic adjustment was made after culture results.

31 (23%) children underwent surgery, mostly (65%) in the first two days after admission. 29 children underwent myringotomy with insertion of ventilation tubes, six children underwent drainage of post-auricular abscess and six children underwent mastoidectomy. All patients submitted to mastoidectomy had osteitis and two of them also had post-auricular abscesses that were drained during the surgical procedure.

3.4. Complications

Complications occurred in 30 children (22%). Fig. 1 documents the evolution of complications throughout the years. CT-Scan was performed in all of them. 19% of complications were extracranial: post-auricular abscess (10%), post-auricular phlegmon (6%), Bezold abscess (2%), facial paralysis (2%) and occipital osteomyelitis with

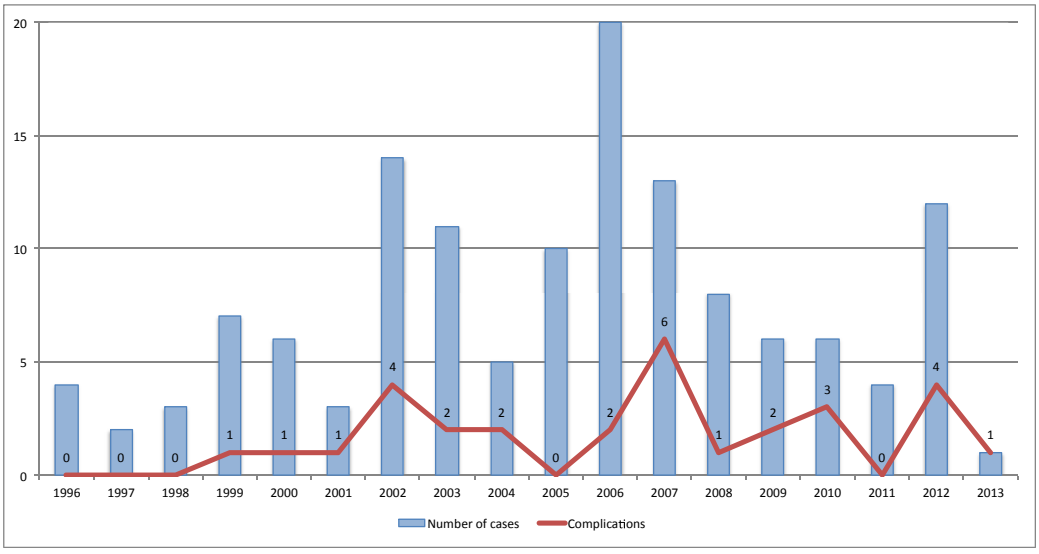

Fig. 1. Year distribution of acute mastoiditis admissions and complications (either intracranial or extracranial) over the years (in 1996 only seven months were analysed and in 2013 only five months).

atlanto-occipital septic arthritis (0.7%). Intracranial complications occurred in three children (2%): one had a subperiosteal abscess, one had internal jugular vein thrombosis and one eight-month boy had lateral sinus thrombosis, cerebritis and a temporal lobe cerebral abscess. The latter presented in septic shock and died eighteen days after admission. The mortality rate was 0,7%.

Children under twenty-four months had significantly more complications than older patients (33% vs 15%, p = 0.006). As far as laboratory findings are concerned: leukocyte count was significantly higher in children with complications (16.7 ± 6.1 × 10^9/μL vs 14.5 ± 5.1 × 10^9/μL, p = 0.046) as was CRP value (13 ± 10.9 mg/dL vs 6.3 ± 6 mg/dL, p = 0.001). Table 1 illustrates the comparison between children with and without complications.

A logistic regression model performed with variables associated with complications revealed a significant association with CRP value (OR 1.892; IC95%: 1.018–2.493, p = 0.01) -Table 2. The accuracy obtained from the Receiver Operating Characteristic (ROC) curve for CRP value was 0.703 (IC95% 0.585–0.821). The optimal cut-off point for C-Reactive Protein was 7.21 mg/dL (sensitivity 66%; specificity 73%).

3.5. Follow-up

Eight children (6%) had more than one episode of acute mastoiditis and one child had two relapses. In five cases (63%) the second episode occurred less than a year after the first one.

Most children (88%) had follow-up appointments by an otorhinolaryngology expert after discharge and fifty-eight (43%) also by a pediatric infectious disease expert. Information about the length of follow-up was not available.

3.6. Management of acute mastoiditis over the years

We compare two different time periods, before and after the implementation of an acute mastoiditis protocol in our department. In the period from June 1996 through May 2005 (group A) there were 58 admissions comparing to 77 from June 2005 through May 2013 (group B).

In the former years (group B) an increased in diagnostic exams was registered: ear exudate cultures (21% vs 43%, p = 0.007) due to the increase in middle ear cultures obtained by tympanocentesis during surgery (2% vs 16%, p = 0.005). There was also a significant increase in CT-Scans (76% vs 99%, p = 0.001).

Regarding empiric antibiotic therapy at admission, in group B significantly more children were started on amoxicillin/clavulanic acid (31% vs 57%, p = 0.003) whereas in group A a significant higher number of children was medicated either with ceftriaxone (52% vs 25%, p = 0.001) or cefuroxime (10% vs 1%, p = 0.02). Group B tend to have more complications (19% vs 25%, p = 0.43) and more children were submitted to surgery (17% vs 28%, p = 0.19) albeit not a significant number. Hospitalization length was significantly higher in group B (7.8 ± 4.1 vs 10.4 ± 8 days, p = 0.01).

There were more children with follow-up consultations in the latest years, both by an otorhinolaryngology expert (79% vs 97%, p = 0.001) and infectious diseases expert (12% vs 67%, p = 0.001). Table 3 illustrates the differences between the two groups.

4. Discussion

There is no consensus on the variation of acute mastoiditis incidence in the last years [9,11–14,16]. Most reports are not population based and more importantly, antibiotic prescription politics for children diagnosed with AOM differ in several countries, which may contribute to data differences. In our analysis the distribution was irregular over time, although there was a peak in 2006 and a higher percentage of cases occurred after 2005- Fig. 1.

Of the total, 42% children were under 24 months and this group had significantly more complications that older children (p = 0.006), similar to what's described by other data [1,5,12,17,18]. This reflects the anatomic and immunologic particular features of this age group which predisposes them not only to the disease but also to its complications [4,6].

Leukocyte count was significantly higher in children with complications (16.7 × 10^9/μL vs 14.5 × 10^9/μL, p = 0.046) as was C Reactive Protein value (13 mg/dL vs 6.3 mg/dL, p = 0.001), as also reported previously [4]. A CRP value higher than 7.21 mg/dL at admission was associated with 1.9 times more risk of complications. The accuracy of the logistic regression was 0.703 which is a fair value specially when we are concerning possible distinct medical approaches upon a laboratory cut-off value. When evaluating children at admission, the pediatrician becomes aware that more than two-thirds (66% sensitivity) of children with a CRP value higher that 7.21 mg/dL will have complications and hence require a different vigilance than if this value is lower than 7.21 mg/dL when the vast majority (73% specificity) will not have a complicated mastoiditis episode. Although more studies are needed to confirm this data, establishing a cut-off value is of utmost importance since it identifies at admission children with higher potential for complications and allows a tighter surveillance.

Ear exudate cultures were performed in only 33% of cases, a very modest number when compared to other reports [13,18,19]. Although 33 children underwent surgery, only 39% middle-ear

Table 1
Analysis of acute mastoiditis complications.

		Complications Yes (n = 30)	No (n = 105)	P
Age ≤ 24 months	Yes	19	38	**
	No	11	67	
Previous otolaryngology diseases	Yes	9	44	+
(recurrent AOM, adenoidal hypertrophy, sinusitis and/or previous episodes of AM)	No	21	61	
Antibiotics for AOM < 3months prior to admission	Yes	17	54	+
	No	13	51	
Antibiotics at admission	Yes	16	52	+
	No	14	53	
Leukocyte count	Mean (×10^9μL)	16.7 ± 6.1	14.5 ± 5.1	*
C-Reactive Protein (CPR)	Mean (mg/dL)	13 ± 10.9	6,3 ± 6	**
Surgery	Yes	17	14	**
	No	12	92	
Recurrences	Yes	1	8	+
	No	29	96	

Legend: AOM: acute otitis media; AM: acute mastoiditis; +p > 0,05; *0,05 ≤ p ≤ 0,01; **0,01 ≤ p ≤ 0,001.

Table 2
Analysis of potential risk factors for developing complications (logistic regression).

	IC 95%			
	OR	Lower	Upper	p value
Age ≤ 24 months	0,472	0156	1431	0,185
Previous otolaryngology diseases*	1059	0,365	3074	0,916
Antibiotics for AOM <3months prior to admission	0,547	0034	8676	0,669
Antibiotics at admission	1209	0,083	21,167	0,840
Leukocyte count	1041	0,948	1143	0,403
C-Reactive Protein (CPR)	1892	1018	2493	0,010*

Legend: AOM: acute otitis media; * defined as recurrent AOM, adenoidal hypertrophy, sinusitis and/or previous episodes of acute mastoiditis.

Table 3
Clinical management of acute mastoiditis over time.

	Group A (n = 58)	Group B (n = 77)	p
Ear cultures	21%	43%	**
Ear canal	19%	26%	+
Middle Ear	2%	16%	**
Abscess drainage	–	1.3%	+
CT-Scan	76%	99%	**
Inicial antibiotherapy			
Monotherapy	93%	83%	+
Amoxicilin/clavulanic acid	31%	57%	**
Ceftriaxone	52%	25%	**
Cefuroxime	10%	1.3%	*
Combined antibiotherapy	7%	17%	+
Surgery	17%	28%	+
Complications	19%	25%	+
Hospitalization length (mean/days)	7.8 ± 4,1	10.4 ± 8	*
Recurrences	5%	9%	+
Follow-up consults			
Otolaryngology	79%	97%	**
Infectious Diseases	12%	67%	**

Legend: Group A: admissions from June 1996 through May 2005; Group B: admissions from June 2005 through May 2013. + p > 0,05; * 0,05 ≤ p ≤ 0,01; ** 0,01 ≤ p ≤ 0,001.

cultures were obtained. All *Pseudomonas aeruginosa* isolates were collected from the ear canal, one of which also isolated *Staphylococcus aureus*. These pathogens are part of the ear canal saprophyte flora and therefore considered contamination, or simultaneous infection, of the ear canal by some authors [12]. Some reports considered that even when isolated, *Pseudomonas aeruginosa* and *Staphylococcus aureus* are not the main causative agents of acute mastoiditis and so antibiotic treatment should not be modified unless the clinical course is complicated [12,19]. In our study, only two (15%) cultures collected from the middle ear during surgery were positive, both for *Streptococcus pneumoniae*. If we consider *Pseudomonas aeruginosa* as a local flora agent, *Streptococcus pneumoniae* was the most common pathogen, as also documented in other series [1,2,13,17].

Most authors agree that the diagnosis of acute mastoiditis is clinical. It is still controversial when CT-Scans should be performed. It is consensual that image exams should be performed in case of a prolonged or complicated course of disease or when clinical signs suggest complications [2,12]. Some reports state that in most pediatric patients there is no evidence supporting that CT-Scan alters patient outcome [4,14,20]. However, other authors suggest that clinical examination is not able to identify all cases of complications and therefore additional exams should be performed whenever the patient is treated conservatively [21]. In our department, CT-Scan was widely used, especially in the last years (after May 2005 all but one child was submitted to this exam)- Table 3. To our knowledge, CT-Scan was important to characterize the extent of the disease and to exclude complications, allowing the institution of appropriate therapy right at admission, since 87% of exams were performed in the first 48 h of hospitalization. It is possible that by performing CT-Scans almost as a routine may have led in some cases to treatment of image findings instead of treating children based only on clinical signs. Nonetheless this approach allows early detection of complications before they are clinically evident.

Evaluating the approach to acute mastoiditis in our department over the years, some conclusions can be drawn. In latter years, significantly more ear effusion cultures were performed (p = 0.007), especially more middle ear cultures. This reveals the growing concern in identifying the pathogen responsible for the disease. Thus an appropriate directed antibiotherapy can be implemented therefore avoiding broad-spectrum antibiotics and potential future resistances.

A major limitation of this study is its retrospective design. As a prolonged period of time was analysed, it was difficult to collect data from the initial study period. However we believe that including all acute mastoiditis admissions of our department is an asset and allows the evaluation of the disease management over the years.

5. Conclusion

The possibility of severe complications and consequent future sequelae determine that acute mastoiditis remains an important entity in pediatrics. Children under 24 months of age presenting with important leukocytosis or high C-Reactive Protein value at admission should be monitored closely since complications tend to be more frequent.

In our department there has been an effort over to years to identify the pathogens responsible for the disease as well as changing antibiotic politics to avoid potential resistances.

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