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ORIGINAL ARTICLE

Acute mastoiditis in the pneumococcal vaccine era

Ana I. Navazo-Eguía,[a,*] David Conejo-Moreno,[b] Gregorio De-La-Mata-Franco,[b] Alicia Clemente-García[a]

[a] *Servicio de Otorrinolaringología, Complejo Hospitalario de Burgos, Burgos, Spain*
[b] *Servicio de Pediatría, Complejo Hospitalario de Burgos, Burgos, Spain*

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KEYWORDS
Acute mastoiditis;
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Abstract
Introduction and objectives: Acute mastoiditis is the most common complication of acute otitis media. Recent studies have noticed an increase in cases. The goal of this study was to review acute mastoiditis cases diagnosed in children younger than 14 years old.
Material and methods: A retrospective study of all patients under 14 years old admitted with a diagnosis of mastoiditis between 1996 and 2008 was performed. Epidemiological, laboratory and clinical variables were analysed.
Results: Sixty-one charts were reviewed. The mean age was 28 months; 55.7% of the patients were male. Most cases were in the autumn and winter; 79% occurred from 2002 to 2008. Most cases (82%) had antecedents of an upper airway catarrhal process and 60.7% had a clinical diagnosis of acute otitis media. Prior antibacterial agent therapy had been administered in 55.7% of the cases. Culture of middle ear effusions was performed in 48 patients, revealing *Streptococcus pneumonia* in 39.7%, *Haemophilus influenzae* in 2%, *Staphylococcus aureus* in 12.5% and *Pseudomonas aeruginosa* in 8.3%. Cultures were sterile in 18 patients (37.5%). Of the pneumococcal isolates, 26.2% were resistant to penicillin or third generation cephalosporins. Most cases (93.4%) responded well to antibacterial therapy alone or with myringotomy. There were complications in 7 patients (11.5%). Mastoid surgery was performed in 4 patients.
Conclusions: Acute mastoiditis shows a rising incidence in recent years. The most commonly isolated form is the pneumococcus, the high rates of antibiotic resistance in our study being notable. Treatments with antibiotics alone or in combination with myringotomy are effective in less severe forms.

PALABRAS CLAVE
Mastoiditis aguda;
Vacuna antineumocócica;
Mastoidectomía

Mastoiditis aguda en la época de la vacuna antineumocócica

Resumen
Introducción y objetivos: La mastoiditis aguda (MA) es la complicación más frecuente de la otitis media aguda. Estudios recientes muestran un incremento de su incidencia en los últimos años.

*Corresponding author.
E-mail address: navazoeguia@telefonica.net (A.I. Navazo-Eguía).

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El objetivo de este estudio fue revisar los casos diagnosticados en nuestro hospital en menores de 14 años.

Material y métodos: Estudio retrospectivo de pacientes menores de 14 años ingresados por MA entre 1996 y 2008. Se analizaron diversas variables epidemiológicas, analíticas y clínicas.

Resultados: Se revisaron 61 casos, 55,7% varones. La edad media fue de 28 meses. El 79% de los casos se presentaron después del año 2002, la mayoría en los meses de otoño e invierno, y con el antecedente de proceso catarral de vías altas. El 60,7% refería diagnóstico clínico previo de otitis media aguda, tratada en el 55,7% con antibiótico. Se realizó cultivo en 48 pacientes, aislándose en ellos: *Streptococcus pneumoniae* en el 39,7%, *Haemophilus influenzae* en el 2%, *Staphylococcus aureus* en el 12,5%, y *Pseudomonas aeruginosa* en el 8,3%. El cultivo fue estéril en 18 pacientes (37,5%). De los neumococos aislados, el 26,2% presentaron resistencia a penicilina o cefalosporinas. La mayoría (93,4%) de los pacientes fueron tratados con antibióticos solos o asociados a miringotomía, realizándose mastoidectomía en 4 casos. En 7 casos de mastoiditis se presentaron complicaciones (11,5%).

Conclusiones: La MA muestra una incidencia en aumento en los últimos años. El germen más frecuentemente aislado es el neumococo, destacando las altas tasas de resistencias antibióticas en nuestro estudio. Los tratamientos con antibióticos solos o asociados con miringotomía son efectivos en las formas menos severas.

Introduction

Acute mastoiditis (AM) is the most common complication of acute otitis media (AOM).[1] In the pre-antibiotic era, AOM was associated with AM in almost 50% of patients. Of these, 20% suffered subperiosteal abscesses and 2.3% developed intracranial complications; the majority of them required surgical interventions.

The introduction of antibiotics significantly reduced the incidence of AM, making it into more of a medical than a surgical condition. In 1946, House referred to a 50% decrease in the number of cases being admitted for AM, and an 80% decrease in the number of mastoidectomies.[2]

At present, in developed countries, the annual incidence of AM in children under 14 is between 1.2 and 4.2 per 100,000. In recent years, many studies have shown an increase in the number of cases.[3-15] For some authors, the reason appears to be an increase in pneumococcal resistance to penicillin and other antibiotics.[5,8,9] Other studies[6,13] attribute it to a tendency not to treat uncomplicated otitis media, and to the fact that young children are more exposed to it in nurseries, leading to a higher number of cases of upper respiratory tract infections and acute otitis media.

Patients and method

We conducted a retrospective study of patients under 14 admitted to our hospital between 1996 and 2008 with a diagnosis of acute mastoiditis. External otitis with retroauricular involvement, trauma and acute otitis media with retroauricular adenitis (with or without evidence of acute mastoiditis) were considered as exclusion criteria.

The diagnosis was clinical, established from the medical history and physical examination of the patients. These presented at least one physical sign compatible with mastoiditis, such as swelling and/or retroauricular erythema or auricle displacement, plus clinical and otoscopic signs of AOM at the time of hospital admission or during the two weeks prior to it. A mastoid subperiosteal abscess was diagnosed in cases of fluctuant swelling.

When performed, the radiographies of the mastoid air cells were requested by the paediatrician in the emergency unit, mainly during the early years of the study and before the current consensus was reached with the otolaryngology unit. An axial computed tomography (CT) scan was performed when spread of infection to neighbouring structures was suspected, or when the patient presented unsatisfactory progress despite adequate treatment. In the case of suspected spread of infection to the central nervous system, a magnetic resonance imaging (MRI) was performed.

The cultures in our study came from samples obtained after spontaneous ruptures or were obtained by myringotomy, puncture or drainage of the mastoid abscess.

The variables analysed were gender, age, seasonal incidence, year of onset, personal history of maternal breastfeeding, vaccination, nursery attendance, previous AOM cases, duration of symptoms prior to admission, presence or absence and type of prior antibiotic treatment, medical symptoms, examination, leukocyte count, C-reactive protein (CRP), bacterial culture, treatment on admission, duration of hospital stay, imaging studies, complications and surgical treatment.

For qualitative variables, we used a descriptive analysis, through the distribution of frequencies, expressed in percentages. For quantitative variables, we used a measure of central tendency expressed as mean and standard deviation. The Chi-square test was used for the comparison of means between qualitative variables, and Student's t-test or analysis of variance (as appropriate) was used to compare the means for paired samples after checking the application conditions. The corresponding nonparametric tests were used when these conditions were not met. A value of $P<.05$ was considered as statistically significant. A logistic regression analysis was performed to assess the role of supposedly relevant variables.

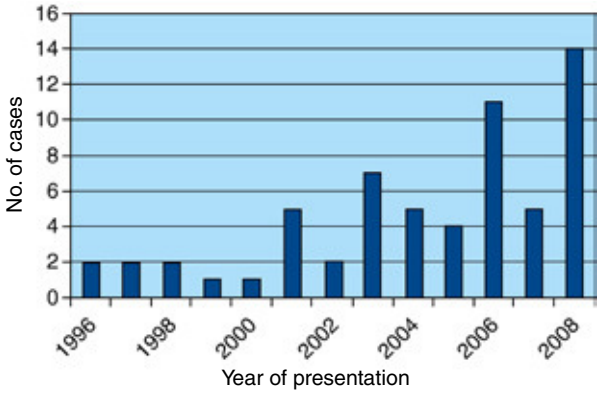

Figure Incidence of acute mastoiditis.

All analyses were conducted with version 14 of the SPSS statistical analysis software package (SPSS Inc., Chicago, IL, USA).

Results

A total of 61 cases were studied. The mean age of our patients was 27.7 months (±28.3), and 55.7% were male. Most cases (75.7%) occurred in the autumn and winter months. A total of 78.8% cases occurred after 2002, which is the year when heptavalent pneumococcal conjugate vaccine was introduced, and 23% took place in the last year of the study (Figure).

Up to 24.6% of cases presented a history of otitis during the first year of life. A further 88.5% of patients had been breastfed for at least three months and 78.7% had attended a nursery on a regular basis. Since the introduction of the heptavalent pneumococcal conjugate vaccine in 2002, 75% of the cases had been vaccinated.

The most frequent causes of mastoiditis were acute infection of upper respiratory tract in 82% of cases and AOM in 60.7% of children. Up to 55.7% had received antibiotics prior to admission: amoxicillin-clavulanate in 22.6% of cases, amoxicillin in 11.3%, cefuroxime in 11.5%, cefixime in 3.3% and macrolides in 3.3% The mean duration of symptoms before hospitalisation was 4.33 days (±5.11). The most frequent symptoms were fever (93.4%), otalgia (85.2%), suppuration (29.5%), rejection of doses (45.9%), vomiting (26.2%) and torticollis (1.6%).

On examination, the left ear was more commonly affected (58%), presenting suppuration (32.8%), retroauricular swelling (85.2%), retroauricular erythema (91.8%), auricular detachment (90.2 %) and retroauricular abscess (6.6%).

A simple mastoid radiography (requested by the paediatrician in the emergency unit) was performed in 34.4% of cases. In 52.5% of cases, CT scans were performed, showing coalescence and osteitis in 84.4%, cholesteatoma in 3.1% and mastoid abscess in 12.5% The MRI was performed in 4.9% of cases and showed no intracranial complications in any of them.

The most significant analytical data were mean leukocytosis of 14,940 (±5,489) and mean CRP of 121 (±100).

Table 1 Epidemiological variables

	1996-2001	2002-2008	*P*
Males	61.5%	54.2%	.440
Maternal breastfeeding	92.3%	87.5%	.534
Nursery attendance	84.6%	77.1%	.436
Prior antibiotic treatment	46.2%	58.3%	.318
Complications	0%	14.6%	.169
Age, months	30.85	26.94	.663
C-reactive protein on admission	73.46	134.33	.053

Cultures of middle ear exudates were performed in 78.7% of patients. The samples analysed were obtained from spontaneous discharge, myringotomy or drainage of the mastoid abscess. The bacteria isolated from the cultures were: *Streptococcus pneumoniae* in 39.7%, *Haemophilus influenzae* in 2%, *Staphylococcus aureus* in 12.5%, and *Pseudomonas aeruginosa* in 8.3%; they were negative in 37.5% of cases. Up to 26.2% of the pneumococcal isolates were resistant to penicillin or third-generation cephalosporins.

All patients received intravenous antibiotic therapy at the hospital, with a mean treatment duration of 9.8 (±4) days. The most commonly used antimicrobial was cefotaxime (34%), followed by amoxicillin-clavulanate (3%). Initial combined therapy with cefotaxime and cloxacillin was used in 32% of cases and with cefotaxime and vancomycin in 24% After the microbiological analysis, the antibiotic was not changed in 62.3% of cases, one of the two drugs was removed in 27.9%, and the treatment was modified due to antibiotic resistance in 9.8% of cases. No corticosteroid treatment was used. The mean hospital stay was 9.8 (±4) days.

Myringotomy with tympanostomy tube placement was performed in 42.7% of cases. Up to 81% of cases were treated with topical antibiotics. Mastoidectomy was performed in 4 cases (6.6%) due to one, or several, of the following reasons: cholesteatoma with facial paralysis, subperiosteal abscess and lack of response to treatment.

CRP on admission (*P* .001) was significantly related with the need for mastoidectomy, but not with other variables analysed (gender, age, microorganism isolated, antibiotic resistance, history of vaccination, previous treatments).

Complications occurred in 11.5% of patients: labyrinthitis (1 case), facial paralysis (1 case), hemiparesis (1 case) and subperiosteal abscess (4 cases). CRP on admission was associated significantly (*P* .014) with the presence of complications, with no relation to other variables analysed (age, gender, microorganism isolated, antibiotic resistance, history of vaccination, treatment received).

We analysed the differences in epidemiological and clinical variables between the cases presented before and after the introduction of pneumococcal conjugate vaccine in 2002. No statistically significant differences were found (Table 1).

Discussion

By contiguity, AOM is generally accompanied by a transient acute mastoiditis that affects the mucosa to varying

degrees and is spontaneously reversible after treating the otitis. This phenomenon is known as mastoidism and presents no clinical signs of mastoiditis, which is why it is more commonly referred to as tympanomastoiditis rather than AOM.

The first stage of AM is associated with hyperaemia of the middle ear mucosa. In the second stage, an exudate develops in the middle ear, the mastoid process fills with inflammatory exudate and this leads to periostitis without bone destruction. Erythema, oedema and retroauricular swelling also appear. In the third stage, the middle ear exudate becomes purulent and may cause tympanic membrane perforation. The inflamed mucosa subsequently blocks the *aditus ad antrum* and pus accumulates. As the inflammatory process progresses, cytokines activate osteoclasts, causing decalcification and bone resorption, and leading to coalescent mastoiditis.

Complications may develop at any stage: in the early stages as a result of thrombophlebitis of the venules that drain the middle ear, and in the coalescence stage due to erosion of the inner or outer table of the mastoid process.[16]

This review analysed 61 cases of acute mastoiditis diagnosed at our hospital between 1996 and 2008. This represents an average of 4.7 cases per year. However, as can be seen in Figure, it should be noted that 50% of these cases were diagnosed in the past 3 years. We can therefore conclude that the incidence of acute mastoiditis in our population has recently increased significantly. These results are consistent with some international and national studies indicating a growing incidence of AM cases in children in recent years.[3-15]

Recent publications have documented an increase in the incidence of AM in children under 2 years.[3,4] Some suggest that this disease now mainly affects children of this age,[7] possibly due to early nursery attendance, where children are exposed to the risk of recurrent AOM. In our review, the mean age of onset was 27.7 months (±28.1); 75.8% (46 cases) were younger than 2 years and 78.7% of them attended nurseries.

It has not been proven that inappropriate, delayed or lack of antibiotic treatment for AOM is associated with a significant increase in the number of cases of mastoiditis or related complications.[13] In our study, over half the cases (55.7%) had previously received antibiotic treatment and, of these, 26.2% had been treated with amoxicillin-clavulanate. No statistically significant differences were found between the cases that occurred before and after the introduction of the pneumococcal conjugate vaccine.

A culture of the ear effusion was performed in 78.7% of patients, in 70% of them following a myringotomy. The national consensus document (2007) on the treatment of AOM[17] recommends waiting for 48 hours before carrying out a myringotomy if progress is unsatisfactory despite antibiotic treatment. Other authors[1,10,14] argue in favour of early myringotomy for all patients with acute mastoiditis to obtain an early positive culture. Due to the increase in the number of AM cases in our hospital in recent years, we have endorsed the latter approach. This justifies the high number of myringotomies carried out in our study and the number of cultures obtained.

The existence of sterile cultures in 37.5% of our samples may be related to previous antibiotic therapy. Pneumococcus is the bacterium that most commonly causes AM in the majority of series, a fact reflected in our series (39.7% of cultures performed). We have not found any significant differences between the bacteria isolated before and after the introduction of the pneumococcal vaccine (Table 2).

Table 2 Culture from ear exudate

	1996-2001	2002-2008	Total
Negative	50%	34.2%	37.5%
Streptococcus pneumoniae	30%	42.1%	39.7%
Haemophilus influenzae	0%	2.6%	2%
Pseudomonas	10%	7.9%	8.3%
Staphylococcus aureus	10%	13.1%	12.5%

In our study, 26.2% of pneumococcal isolates presented resistance to penicillin or cephalosporins. In 2007, Roddy et al[18] reported a significant increase in pneumococcal resistance in the U.S. over the last decade. Thorne et al[8] later reported an increase in cases of subperiosteal abscesses. In our country, several authors[9,10] have reported an increase in the virulence of AOM-associated bacteria and in the incidence of suppurative complications.

Before 2002, the pneumococcus most commonly associated with AM was serogroup 19, mainly serotype 19F. The heptavalent pneumococcal conjugate vaccine (PCV7) was introduced in our country in 2002. It covers the 7 serotypes that cause invasive infection in children (serotypes 4, 6B, 9V, 14, 18C, 23F, and 19F). Subsequent studies have shown a decrease in the rate of invasive pneumococcal disease.[19,20]

However, we observed a replacement of vaccine serotypes with serotypes not included in the vaccine colonising the nasopharynx, in particular serotype 19A (associated with AOM). Several studies have also shown multiple antibiotic resistance of serotype 19A, with an increase of subperiosteal abscesses.[8,21,22] In our series, 14 cases occurred during 2008; serotype 19A was found in 2 cases of pneumococcal isolates (31.6%), without antibiotic resistance.

H. influenza is the second most common pathogen causing AOM in children. However, it is rarely isolated in mastoiditis, a fact that has been attributed to this bacterium being less aggressive than pneumococcus.[23] In our series, it was found in just 1.6% of the cultures performed.

The information obtained from the cultures is vitally important in deciding on antibiotic treatment in situations of increased incidence of resistant bacteria cases. A myringotomy with aspiration and subsequent culture provides diagnostic and therapeutic benefits, which is why many authors recommend it in all patients with suppurative complications of AOM,[9,10,24] especially in children under 2.[25]

Diagnosis is mainly clinical: it should be suspected based on the medical history and clinical examination of the patient. Simple radiographs have not proven useful for reaching a diagnosis.[7,26] There is controversy regarding the routine performance of a CT scan and some authors advocate its use in all cases.[27,28]

In contrast, there are those who argue that most patients can be managed safely without the need for a CT scan. These

Table 3 Type of antibiotic

	1996-2001	2002-2008	Total
Erythromycin	0%	2.1%(1)	1.6%(1)
Amoxicillin-clavulanate	0%	4.2%(2)	3.3%(2)
Cefotaxime	53.8%(7)	31.3%(15)	36.1%(22)
Cefotaxime-cloxacillin	38.5%(5)	29.2%(14)	31.1%(19)
Cefotaxime-vancomycin	0%	31.3%(15)	24.6%(15)
Cefuroxime	7.7%(1)	2.1%(1)	3.3%(2)
Total	13 cases	48 cases	61 cases

authors believe that CT scans should be reserved for cases with uncertain diagnosis, possible complications, suspected cholesteatomas, unsatisfactory progress with medical treatment and as preparation for a mastoidectomy.[29] In our series, CT scans were performed in 52.5%of cases for one, or more, of the aforementioned reasons.

In the pre-antibiotic era, AM was treated with cortical mastoidectomy. Currently, authors who advocate this treatment claim that an immediate drainage of the mastoid abscess theoretically reduces antibiotic use and hospital stay, and could prevent intracranial extension of the infection.[30]

The role of surgical treatment is questioned by other authors, who defend a more conservative attitude and advocate treatment with myringotomy, along with a culture and intravenous antibiotics. The following are considered as indicators of the need for radical mastoidectomy: slow progression of AM despite medical treatment, the presence of cholesteatoma, the presence of external or abscessed mastoiditis in children weighing over 15 kg, and intracranial complications.[17,31-33]

Due to the increase in cases of AM, myringotomy is considered as a treatment option during the episode and not only when no improvement is observed after antibiotic treatment.[9,10,24] Early myringotomy and insertion of a transtympanic drainage tube during hospitalisation will not only offer the advantage of obtaining an early culture, but also the drainage and ventilation of the middle ear and mastoid air cells from the antrum. The moment when the transtympanic drain can be inserted will depend on the course of the disease and on the availability of hospital resources (scheduled or emergency surgery). Middle ear cultures become more valuable when initial antibiotic treatment fails.[14]

Mastoidectomy was performed in 6.6%of our cases, for the following reasons: cholesteatoma with facial paralysis, subperiosteal abscess (2 cases) and lack of response to treatment (1 case). The remaining cases were treated with intravenous antibiotics (Table 3) alone or associated with myringotomy, with or without a transtympanic drainage tube.

Some authors have found a significant association between the numerical value of analytical data (such as the presence of a leukocytosis with neutrophilia, an elevated erythrocyte sedimentation rate or CRP elevation) and progression towards complications and need for surgery.[27,34] According to some authors, knowing about these potential predictive factors would help us to be prepared for the development of mastoiditis complications and thus improve its treatment.[10,35,36]

In our study, CRP upon hospital admission was significantly associated with the presence of complications and the need for a mastoidectomy, but the low number of complications recorded in our work has prevented the predictive analysis of this variable.

Conclusions

From our review study, we can conclude that:

- The incidence of acute mastoiditis has increased in recent years, affecting mainly children under 2 years of age.
- Pneumococcus is the most common causative agent. Cases of pneumococcus resistant to penicillin and third-generation cephalosporins have increased significantly in recent years.
- Treatment with antibiotics alone or in combination with myringotomy and ventilation tubes is effective in less severe forms. Mastoidectomy is indicated in cases of exterior mastoid abscess, intracranial complications, cholesteatoma and purulent otorrhea and/or granulation tissue for more than two weeks.
- C-reactive protein values are associated with the possibility of complications and the need for a mastoidectomy.

Conflict of interest

The authors declare no conflict of interest.

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