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ORIGINAL PAPER

Mastoiditis in children: a prospective, observational study comparing clinical presentation, microbiology, computed tomography, surgical findings and histology

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Abstract The aim of this study was to obtain comprehensive data on clinical presentation, microbiology, computed tomography, surgical findings and histology in acute, sub-acute and chronic mastoiditis. We performed a prospective, observational study in children under 16 years of age presenting to our institution during the 2-year period beginning in April 2000. The children were examined and their condition treated in accordance with a standardized protocol elaborated by the paediatric, otolaryngology (ORL) and radiology departments. Thirty-eight patients were hospitalized (22 with acute mastoiditis, seven with sub-acute mastoiditis, nine with chronic mastoiditis). There were 30 complications present in 21 patients (55%). *Streptococcus pyogenes* was the most common pathogen (7/24 cases), followed by *Streptococcus pneumoniae* (4/24 cases). Mastoid surgery was performed in 29 patients. Histology of mastoid tissue revealed predominantly acute inflammation in two cases, mixed acute/chronic inflammation in 19 cases and predominantly chronic inflammation in seven cases. Radiologic data were evaluated retrospectively. Spiral, volume-based high-resolution (HR) computed tomography (CT) of the temporal bone had a sensitivity of 100%, specificity of 38%, positive predictive value (PPV) of 50% and negative predictive value (NPV) of 100% in detecting coalescence of mastoid trabeculae. Cranial CT with contrast had a sensitivity of 80%, specificity of 94%, PPV of 80% and NPV of 94% in identifying intra-cranial extension. Conclusion: histological evidence suggests that sub-acute/chronic infection underlies not only sub-acute and chronic mastoiditis, but most cases of acute mastoiditis as well. HR-CT of the temporal bone is effective in ruling out coalescence. Cranial CT is valuable in identifying intra-cranial extension. Cranial and HR-CT are recommended in the examination of children with mastoiditis.

Keywords Mastoiditis · Children · Acute otitis media · Temporal bone computer tomography · Temporal bone histology

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Abbreviations

ORL	otolaryngology
CT	computed tomography
HR	spiral, volume-based, high resolution
AOM	acute otitis media
PPV	positive predictive value
NPV	negative predictive value

Introduction

In the past 10 years many centres throughout Europe and the United States of America have reported an increased incidence of mastoiditis [2, 8, 11, 17, 23, 26]. In 1999 we

noted an increased occurrence of mastoiditis at our hospital. Anticipating a continued resurgence of mastoiditis in our region, we designed a prospective, observational study of mastoiditis in children presenting to our institution, a cantonal, tertiary, referral children's hospital in Switzerland serving a total population of 500,000.

To date, studies of mastoiditis have been predominantly retrospective and have emphasized clinical and microbiological aspects of the most common form, acute mastoiditis. We included children with not only acute mastoiditis, but sub-acute and chronic mastoiditis as well. The purpose of the study was to compare data on clinical presentation, microbiology, computed tomography, surgery and histology in children with mastoiditis. The children were examined and treated in accordance with a standardized protocol elaborated by the paediatric, otolaryngology and radiology departments.

Methods

During the 2-year period beginning April 2000, patients under the age of 16 years admitted to our hospital who met the inclusion criteria as shown in the Appendix were prospectively accrued. The inclusion criteria were designed to include all patients with acute, sub-acute, and chronic mastoiditis. Acute mastoiditis was defined as acute otitis media (AOM) and the presence of at least one of the clinically characteristic, local signs of mastoiditis (retro-auricular erythema, swelling, tenderness, protrusion of the auricle) [3, 27]. Sub-acute mastoiditis was defined as history of recurrent AOM or otitis media with effusion, and the presence of non-specific signs (e.g. failure to thrive, fever, irritability) or a complication of mastoiditis (e.g. sinus vein thrombosis, cranial nerve palsy, increased intracranial pressure), and opacity of the mastoid seen on temporal bone computed tomography (CT) [3, 10, 27]. Chronic mastoiditis was defined as chronic, painless, suppurative, otitis media of at least 6 weeks' duration, characterized by failure to resolve after a 10-day trial of per os antibiotic therapy and associated with mastoid opacity on temporal bone CT [3, 7, 27]. Patients with previous mastoiditis or cholesteatoma were excluded from the study. Cranial and/or high-resolution computed tomography (HR-CT) of the temporal bone were performed to assess coalescence of mastoid trabeculae/compacta and intracranial extension [1, 3, 7, 10, 27]. CT was not necessary to confirm the diagnosis of acute mastoiditis [27]. CT was required to confirm the diagnosis of sub-acute [3, 10] and chronic mastoiditis [3, 7]. Mastoid opacity alone on CT, without the above-mentioned historical or clinical evidence, was not diagnostic of mastoiditis [27]. Lack of mastoid opacity on CT ruled out mastoiditis.

Radiographic examination consisted of cranial CT performed in the axial plane at 4 mm intervals, both with and without contrast and/or spiral, volume-based, high-resolution, axial CT of the temporal bone. Coalescence was defined as loss of the honeycomb-like trabecular septae and/or erosion of the lateral or intra-cranial cortical bone visualized on HR-CT of the temporal bone. Initially, coalescence was assessed qualitatively. Upon reviewing the data of the first 24 patients, we decided to analyse the radiological data according to the scoring system described by Antonelli et al. [1]. The data of all 35 patients were subsequently evaluated retrospectively, in accordance with this method, by one radiologist unaware of the patients' clinical outcomes (O.R.). The presence of coalescent mastoiditis of the trabeculae, lateral compacta and sigmoid sinus compacta was thus assessed at three levels (caudal, equiplanar and rostral to the cochlea) and graded numerically: 1, definitely normal; 2, probably normal; 3, uncertain; 4, probably abnormal; 5, definitely abnormal. We considered HR-CT scans with a grade of 4 or 5 at any level of any bone type to demonstrate radiographic evidence of coalescence. Upon review of the first 24 patients, analysis showed that cranial CT was superior for the evaluation of intra-cranial extension, whereas HR-CT of the temporal bone was superior for detection of coalescence. For the final analysis cranial CT was evaluated exclusively for its value in detecting intracranial extension, and HR-CT of the temporal bone was evaluated exclusively for its value in detecting coalescence.

Histological specimens from patients who had undergone mastoid surgery were assessed by one pathologist unaware of the patients' clinical outcomes (M.M.). Specimens were assessed in two categories: acute inflammation (characterized by fibrin matrix, infiltration with granulocytes, and bone necrosis) and chronic inflammation (consisting of scarring/granulation tissue and presence of lymphocytes, plasma cells and histiocytes) [5]. Each category was graded from 0 to 2, according to the density and composition of the respective inflammatory infiltrate: 0=none, 1=moderate, and 2=dense. Patients with a grade of 1 or 2 in a category and with a grade of 0 in the other category were considered to have pure-type inflammation (e.g. acute *or* chronic). Patients with a grade of 1 or 2 in both categories were considered to have mixed-type inflammation (e.g. acute *and* chronic).

Standardized management of mastoiditis was based on existing practices at our institution, which were in conformity with current practices reported in the literature [7, 12, 27]. When otorrhoea was present, secretions were obtained for bacterial culture prior to initiation of intravenous antibiotic treatment. Specimens were also obtained for culture at mastoid surgery or myringotomy. Antibiotic treatment consisted of intravenous administration of high-dose amoxicillin-clavulanic acid (150 mg/kg per day) for both acute and sub-acute mastoiditis. In cases of chronic mastoiditis, ceftazidime (200 mg/kg per day) was added.

Between one and several doses of antibiotics were given before surgery, depending on the indication and timing of the operation. Antibiotic coverage was modified according to clinical course and bacterial sensitivity patterns.

Indications for mastoid surgery were determined prospectively: severe general condition at presentation (e.g. lethargic or septic appearance), the presence of a complication, failure to improve after intravenous treatment with antibiotics for 48 h (acute mastoiditis), or failure to improve after 5–7 days of intravenous administration of antibiotics (sub-acute and chronic mastoiditis). Myringotomy was performed when an intact, bulging, tympanic membrane was present.

Data were collected during the patient's hospital stay by means of a questionnaire, which was filled out by the house officer. The questionnaire consisted of the protocol case inclusion criteria, radiological findings on CT indicative of mastoiditis and its complications, and a listing of clinical complications of mastoiditis, as shown in the Appendix. In addition, the questionnaire assessed data concerning history of the present illness and previous otolaryngology (ORL) involvement, physical examination of the ear and mastoid, laboratory studies (white blood count, C-reactive protein, cultures) and hospital course (choice of antibiotics, indication for and type of surgical management).

The initial protocol was delineated, presented and distributed to all admitting senior and junior residents of the paediatric and ORL departments and to the participating radiologist. Upon admission of a patient with suspected mastoiditis on clinical grounds (in accordance with the case inclusion criteria above), both paediatric and ORL departments were jointly responsible for patient treatment. CT examinations were carried out within 48 h. Intravenous antibiotic therapy was instituted immediately, as delineated earlier in the Methods section. Evaluation of radiography and the necessity for surgery was discussed in team with the paediatric, ORL and radiology senior house officers. In the case of mastoid surgery, the indication (as enumerated above) was noted by the ORL operator. During the hospital stay, study data were collected by the paediatric house officer. Patient assignment to acute type, sub-acute type or chronic type mastoiditis was made by the principal author according to the study data obtained and the imaging results, as defined at the beginning of the Methods section.

Statistical analysis was performed with the two-tailed Fisher's exact test.

Results

There were 38 patients with mastoiditis hospitalized in our institution during the 2-year period beginning in April 2000. Only the initial 38 episodes are included in the following analyses. Two patients were not entered into the study because of known pre-existing cholesteatoma. One patient with acute otitis media perforata and CT examination did not fulfill the case definition on the basis of lack of additional clinical criteria.

For the study period we calculated an average incidence for all types of mastoiditis of 21 per 100,000 per year in children under 16 years of age in our canton. The incidences in the 2-year periods 1996–1998 and 1998–2000 were 1.1 per year and 2.2 per year, respectively. The incidence for the 2-year period 2002–2004 following our study was 7.7 per year.

The ages of the patients ranged from 7 months to 14 years, with a median of 4.9 years (acute 4.5 years, sub-acute 4.1 years, chronic 6.4 years). Ten patients (26%) were under 2 years of age. Nine patients were of non-central-European origin (four from Turkey, two from Kosovo-Albania, one from Serbia, one from Vietnam, one from Colombia). Twenty-two patients had acute mastoiditis, seven had sub-acute mastoiditis, and nine had chronic mastoiditis. Intra-operatively confirmed mastoid coalescence was found significantly more often in patients with acute mastoiditis (10/15 surgically treated patients, Fisher's exact test, $P=0.025$) than in those with sub-acute mastoiditis (2/7 surgical patients) or chronic mastoiditis (1/7 surgical patients).

There was no history of a previous episode of AOM in 45% (10/22) of patients with acute mastoiditis in comparison with 14% (1/7) of patients with sub-acute mastoiditis. Oral treatment with antibiotics had been prescribed during the 2 weeks prior to hospitalization in 47% of all patients (18/38: ten acute, four sub-acute and four chronic). Type of antibiotic taken was divided as follows: 11 patients were taking an amino-penicillin, two a macrolide, three a cephalosporin, three multiple antibiotics (one patient quinolone then cephalosporin, one patient amino-penicillin then macrolide, and one patient cephalosporin then amino-penicillin). Two patients with acute mastoiditis and two patients with sub-acute mastoiditis had been diagnosed with AOM by a doctor in the previous 2 weeks, but antibiotic treatment had been intentionally withheld.

Table 1 depicts complications of mastoiditis, which were present in 55% (21/38) of the patients. Eight patients suffered from more than one complication. In 38% (8/21) of patients complications were clinically silent and were only detected by CT (five sinus vein thromboses, three epidural abscesses). The median age of patients with complications was 4.3 years, compared to 4.9 for the whole sample.

Bacterial pathogens were recovered in 24 of 33 patients sampled. Five patients were not sampled because there was no tympanic membrane perforation and neither myringotomy nor mastoidectomy was performed. The most frequent

Table 1 Mastoiditis complications in 21 patients (n = total number of patients with complications/total number of patients in that category of mastoiditis)

Complication	Acute mastoiditis (n=13/22)	Sub-acute mastoiditis (n=5/7)	Chronic mastoiditis (n=3/9)	Total
Sinus vein thrombosis	3	1	1	5
Pseudotumor cerebri				
with recovery	1	2		3
with optic nerve atrophy		1		1
Facial nerve palsy	1			1
Abducens nerve palsy	1			1
Vertigo	1			1
Hearing loss (sensorineural)				
with recovery	3	1		4
without recovery[a]		1		1
Epidural abscess	2		1	3
Sub-periosteal abscess[b]	6		1	7
Extra-cranial soft tissue abscess[c]	2	1		3
Total number of complications	20	7	3	30

[a] Bilateral high-frequency, in a patient with bilateral mastoiditis
[b] Of the mastoid process
[c] E.g. in sternocleinomastoid or zygomatic muscle

bacteria recovered were *Streptococcus pyogenes* (seven patients, median age 5.1 years), *Streptococcus pneumoniae* (four patients, all isolates penicillin sensitive), *Pseudomonas aeruginosa* (4/6 patients as a single isolate) and *Staphylococcus aureus* (2/5 patients as a single isolate). Surgically confirmed coalescence was found in four of seven patients with *S. pyogenes*. Table 2 demonstrates culture results, sampling location and pre-treatment with per os and/or intravenously administered antibiotics. All patients received at least one intravenous dose of antibiotics prior to myringotomy or mastoid surgery. In total, 18 of 24 positive findings in bacterial cultures were obtained after per os or intravenous antibiotic therapy had been administered.

Table 3 demonstrates type of mastoiditis and presence of complications according to bacterium. *S. pyogenes* was more often (5/7) associated with complications than were the other most frequent bacteria.

Thirty-five patients underwent cranial CT and/or HR-CT of the temporal bone: both examinations were performed in 24 patients, HR-CT alone in seven patients, and cranial CT alone in three patients (reason for incomplete examinations: cranial CT or HR-CT unintentionally not ordered, respectively). Breach of protocol occurred additionally in one patient, in whom radiography was not performed until after surgery, and in three patients in whom neither cranial CT nor HR-CT was performed (reason: operation deemed too urgent to wait for CT).

In 21 of 29 patients who were treated by mastoid surgery, HR and/or cranial CT were performed and data concerning intra-operative findings were complete. When intra-operative findings were used as the gold standard, HR-CT was 100% sensitive and 38% specific in detecting coalescence. The positive predictive value (PPV) was 50% and the negative predictive value (NPV) 100%. Cranial CT was 80% sensitive and 94% specific in detecting intracranial extension. The PPV of cranial CT was 80% and the NPV 94%.

Table 2 Sampling location, antibiotic pre-treatment and results of bacterial cultures, n=33 (n = number of patients in whom bacteria were sampled)

Organism	Total no. of patients	Ear secretions and per os antibiotic pre-treatment[a]		Myringotomy aspirate[b]	Mastoid mucosa[b]
		with	without		
S. pyogenes	7[c]	2	2		3
S. pneumoniae	4[c]	3			1
P. aeruginosa	6[c,d]	2	3	1	
S. aureus	2	1	1		
Haemophilus influenzae, NT	2	1			1
Turicella otitidis	1	1			
Bacterioides sp.	1	1			
Escherichia coli + *Enterococcus sp.*	1	1			
Total	24	12	6	1	5

[a] In cases of existing tympanic membrane perforation, sample obtained at time of admission
[b] All patients received at least one intravenous dose of antibiotics before time of sampling
[c] Including one case in combination with *Staphylococcus aureus*
[d] Including one case in combination with *Burkholderia cepacia*

Table 3 Type of mastoiditis and presence of complications according to bacterium, n=24 [n = number of patients in whom bacteria were isolated , *(n)* = total number of patients in that category of mastoiditis, numbers in parentheses = number of cases with complications included in the total number of cases of that bacterium]

Bacterium	Acute mastoiditis (*n*=22)	Sub-acute mastoiditis (*n*=7)	Chronic mastoiditis (*n*=9)
S. pyogenes	7[a] (5)		
S. pneumoniae	2 (1)	1 (1)	1[a]
P. aeruginosa	3[a] (2)	1	2[b] (1)
S. aureus		1 (1)	1
H. influenzae, NT	1 (1)		1
T. otitidis	1 (1)		
Bacterioides sp.			1
E. coli + *Enterococcus sp.*			1 (1)
Total	14 (10)	3 (2)	7 (2)

[a] Including one case in combination with *S. aureus*
[b] Including one case in combination with *B. cepacia*

Patient treatment is shown in Table 4, and indications for mastoid surgery are shown in Table 5. The most common indication for mastoid surgery was the presence of a complication (15/29), followed by failure to improve with intravenous (i.v.) treatment with antibiotics (11/29).

Results of the histological examination of specimens obtained intra-operatively from the mastoid (or antrum) are depicted in Table 6. Predominantly acute inflammation was present in only two specimens. All other cases consisted of mixed acute/chronic inflammation or predominantly chronic inflammation. Figure 1 demonstrates examples of acute, chronic and mixed inflammation.

Discussion

The incidence of all forms of mastoiditis in our study reached an apparent peak during the study period. Studies of acute mastoiditis in children have shown incidences ranging from 1.2 per 100,000 per year [26] to 6.1 [11], with a peak of 13 in the year 2000 in southern Israel [11]. Taking into account only episodes of acute mastoiditis during our study period, we calculated an incidence of 12.2 per year, similar to the peak during the year 2000 in southern Israel. Although our study was not designed to answer questions concerning the epidemiology of mastoiditis, some potential causes of this surprising peak in mastoiditis in our region can be dismissed. There were no major demographic fluctuations, changes in day-care use, hospital referral, or antibiotic resistance during this time. We did not recover any isolates of resistant or intermediate resistant *S. pneumoniae*. Although the issue of prescribing antibiotics for AOM is controversial in Switzerland [13, 15], antibiotics were intentionally withheld in only four of our patients. The choice of per os antibiotic for AOM in our collective could be considered to have been appropriate in 13 of the 18 pre-treated cases for which an amino-penicillin was prescribed.

Table 4 Patient treatment, n=38 [*(n)* = total number of patients in that category of mastoiditis]

Treatment	Acute mastoiditis (*n*=22)	Sub-acute mastoiditis (*n*=7)	Chronic mastoiditis (*n*=9)	Total
Antibiotics alone	5	0	1	6
Antibiotics and myringotomy	2		1	3
Antibiotics and mastoid surgery	7	2	3	12
Antibiotics and mastoid surgery and myringotomy	8	5	4	17

Table 5 Indications for mastoid surgery, n=29 [n = total number of patients treated with mastoid surgery, *(n)* = total number of patients in that category of mastoiditis]

Indication	Acute mastoiditis (*n*=22)	Sub-acute mastoiditis (*n*=7)	Chronic mastoiditis (*n*=9)	Total
Severe general condition	2		1	3
Complication	9	5	1	15
No improvement on i.v. treatment with antibiotics	4	2	5	11
Mastoid surgery, total number	15	7	7	29

Table 6 Histology in patients treated by mastoid surgery, n=28, excluding one patient transferred to another hospital before surgery in whom histological examination was not performed [n = total number of patients in whom specimens were obtained, *(n)*) = number of patients in that category of mastoiditis]

Histology	Acute mastoiditis (*n*=22)	Sub-acute mastoiditis (*n*=7)	Chronic mastoiditis (*n*=9)	Total
Predominantly acute inflammation	2			2
Predominantly chronic inflammation		5	2	7
Mixed acute/chronic inflammation	12	2	5	19
Total number of histological specimens	14	7	7	28

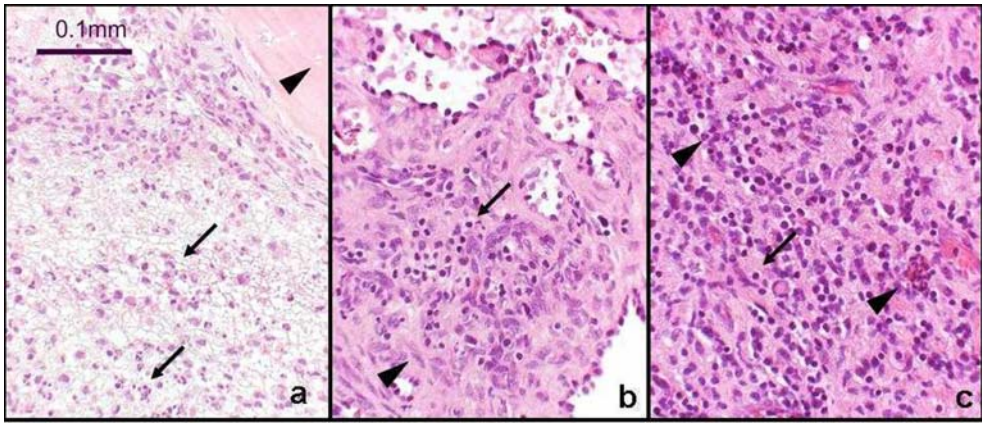

Fig. 1 Temporal bone histology, same scale in all frames. **a** acute inflammation in a patient with acute mastoiditis: neutrophilic granulocytes (*arrows*) predominate, well recognizable by their poly-lobulated nuclei. The cellular infiltrate is imbedded in a fibrin net. *Upper right corner* shows partially necrotic lamellar bone with one necrotic osteocyte (*arrowhead*). **b** Chronic inflammation in a patient with chronic mastoiditis: lymphocytes and plasma cells (*arrow*) predominate. Fibroblasts are abundant (*arrow head*) as well as pale pink collagen in the intercellular space. **c** Mixed acute and chronic inflammation in a patient with acute mastoiditis: lymphocytes and plasma cells (*arrow*) predominate, but there are also accumulations of neutrophils (*arrowheads*)

However adequacy of dosage and compliance were not assessed.

Our rate of complications (55%) at presentation is higher than that reported in other studies, although there is considerable variability, ranging between 6% and 43% [7–9, 12, 14, 24]. In these studies CT examination was not routinely performed. Complications were clinically silent and were detected by CT in only eight of our patients. Although clinically not apparent, these silent complications were significant. Five patients with sinus vein thrombosis (SVT) were treated with anti-coagulation for 6 months. Three patients with epidural abscesses required a change of antibiotic and a longer duration of treatment; in addition one of these patients required neuro-surgical drainage.

As most of the patients (18/24) in whom bacteria were recovered had been treated with antibiotics before the specimen was obtained, our bacteriology results are likely to be skewed, with over-representation of bacteria such as *P. aeruginosa* and *S. aureus*, which are often not sensitive to antibiotics commonly in use. This, however, is the case in many other studies of mastoiditis. A compilation of bacteriological results from 294 cases of acute mastoiditis occurring between 1955 and 2000, in which pre-treatment with antibiotics was frequent, showed a similar distribution of bacteria [27]. In light of its infrequency as a cause of AOM [4, 22], *S. pyogenes* has been disproportionately frequently found as a cause of mastoiditis in numerous studies [4, 7, 12, 14, 22, 23, 27]. The pronounced virulence of *S. pyogenes* [21] may explain its presence exclusively in acute mastoiditis and its association with severe forms of mastoiditis in our collective. Considering the fact that the majority of our patients received either per os or intravenous treatment with antibiotics before bacteriological sampling, and that *S. pyogenes* is uniformly sensitive to the most common antibiotics used (amino-penicillins), we suspect that our results under-represent the true presence of *S. pyogenes*.

Adherence to protocol was poor with regard to our obtaining complete radiological examinations. As all three of the patients in whom neither HR nor cranial CT was performed had acute mastoiditis and were treated by mastoid surgery (reason for breach of protocol: surgery deemed too urgent to wait for CT), we felt it legitimate to include them in the study. Missing data due to patients with incomplete radiological studies weaken the validity of our conclusions; nonetheless, we feel the available data were of sufficient quantity and interest to warrant analysis. Owing to the low specificity and PPV, our results show that temporal bone HR-CT is a poor indicator of coalescence. As the presence of coalescence is regarded as an indication for mastoidectomy [1, 7, 12, 27, 28], we conclude that HR-CT in isolation is not sufficient to predict whether surgery is necessary. However, because of its high sensitivity and NPV, it can be used reliably to rule out coalescence. In the absence of other indications, a negative HR-CT with regard to coalescence is sufficient to obviate the necessity of surgery. We therefore recommend HR-CT of the temporal bone, especially in the evaluation of patients under consideration for surgery.

Because of its high specificity and good PPV in detecting intra-cranial extension, cranial CT proved valuable in predicting when surgery was indicated. Owing to its good sensitivity and high NPV it could also be used to rule out intra-cranial extension. As intra-cranial involvement was often clinically silent in our collective, we recommend cranial CT with contrast in the initial examination of all

patients with mastoiditis. The use of contrast medium is essential in detecting intra-cranial involvement, in particular sinus vein thrombosis, the most common complication in our collective.

Our indications for mastoid surgery were similar to those reported in the literature. [2, 6, 7, 12, 14, 16, 18, 25]. Although our rate of surgery (76%) was high, it was within the range of that reported in other studies (9–88%) [14, 18, 25]. The main reason for this was the high rate of complications in our patients and the inclusion of patients with sub-acute and chronic mastoiditis.

Histological evidence of chronic inflammation in addition to acute inflammation in the majority (86%) of the surgically treated patients with acute mastoiditis suggests that the process was already sub-acute or chronic by the time of presentation. In light of this finding, the lack of history of a previous episode of AOM in 45% of patients with acute mastoiditis furthermore suggests that this process was initially clinically silent and therefore not detectable. Some cases may indeed have occurred rapidly. However, in our experience, this was less common, as demonstrated by the finding of predominantly acute inflammation in only two of the 14 surgically treated patients in the acute mastoiditis group.

The clinical and histological results of our study can be used to explain the continuum of manifestations seen in mastoiditis. Inflammation in acute otitis media extends to the mastoid cell system even before this involvement is clinically detectable [19, 20]. At some point in time the inflammation progresses enough to present classical local signs over the lateral mastoid cortex, thus becoming clinically recognizable [12, 27] as acute mastoiditis. However, some cases of AOM may evolve rapidly to overt acute mastoiditis without an intermediate phase of sub-clinical mastoid infection. This might occur when very virulent bacteria, such as *S. pyogenes*, perhaps in combination with individual anatomical or immunological factors, are involved [17]. We propose that these patients represent the only cases in which the process is truly, exclusively acute. In sub-acute mastoiditis persistent inflammation of the mastoid cell system does not break through externally to the lateral mastoid cortex [12]; rather, it proceeds internally to affect neighbouring intra-cranial structures [3, 10, 27], as emphasized by the high rate of complications in this group. In chronic mastoiditis, perforation of the tympanic membrane facilitates continual egress of inflammatory products out of the mastoid compartment from early on in the course of infection, permitting a tenuous, long-term stability until a new, acute inflammatory episode disturbs this equilibrium. This process is reflected in the histological picture of mixed acute and chronic inflammation.

In conclusion, our results provide histological evidence that not only sub-acute and chronic mastoiditis [5], but the majority of cases of acute mastoiditis as well, evolve in the framework of a sub-acute or chronic, clinically often initially undetected, infectious process within the mastoid cell system. This conclusion is compatible with the common finding of CT mastoid opacity in cases of uncomplicated AOM [3] and with previous studies on autopsy material presenting histopathological evidence of chronic infection in the middle ear cleft in patients without obvious clinical abnormality of the tympanic membrane [5, 19, 20].

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Appendix

Mastoiditis case inclusion criteria: concurrent or recent otitis media, presence of at least one of the following clinical characteristics, and at least one CT finding

Clinical characteristics

- typical specific local findings on physical examination (tender swelling or erythema over the mastoid, protrusion of the auricle)
- non-specific findings, such as failure to thrive, anaemia, fever of unknown aetiology, acute otitis media (in history or physical examination)
- one of the known complications of mastoiditis, as listed below
- suspected chronic secretory otitis media

CT findings

- opacity of the mastoid cell system (this alone, without at least one above-mentioned clinical criteria, does not suffice)
- mastoid coalescence: partial or complete loss of trabecular structure
- extra-cranial extension: periosteal thickening, subperiosteal abscess, disruption of the periosteum
- cortical involvement: destruction or irregularity of the mastoid cortex
- intra-cranial extension: epidural or temporal lobe abscess

Otogenic complications of mastoiditis

- facial or abducens nerve palsy
- vertigo
- sensorineural hearing loss
- meningitis
- sinus vein thrombosis
- pseudotumour cerebri
- epidural, sub-dural, temporal lobe abscess

- extra-cranial abscess: Mouret's, Bezold's
- Gradenigo syndrome (abducens palsy, trigeminal neuralgia, ear discharge)

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