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Original article

Cervicofacial non-tuberculous mycobacteria: A report of 30 cases

P. Rives[a], M. Joubert[b], E. Launay[c], A. Guillouzouic[d], F. Espitalier[a,d], O. Malard[a,*]

[a] Service d'ORL et chirurgie cervico-faciale, CHU de Nantes, 1, place Alexis-Ricordeau, 44000 Nantes, France
[b] Service d'anatomopathologie, CHU de Nantes, 1, place Alexis-Ricordeau, 44000 Nantes, France
[c] Service de pédiatrie, HME de Nantes, 1, place Alexis-Ricordeau, 44000 Nantes, France
[d] Service de bactériologie, CHU de Nantes, 1, place Alexis-Ricordeau, 44000 Nantes, France

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ABSTRACT

Background: Mycobacterial infection is the most common cause of cervical granuloma, implicating either a tuberculous or a non-tuberculous mycobacterium (NTM). NTM is a ubiquitous organism, found in soil, water, food, etc. The most frequently implicated is *Mycobacterium avium*-intracellular. Most authors agree that NTM is increasingly isolated, due to a decrease in vaccination rates. Initial diagnosis is difficult and management is not clearly codified.
Methods: A retrospective study conducted in the University Hospital of Nantes, France, between 2005 and 2014, included all patients treated for head and neck NTM lymphadenitis. The research was conducted on the database of the institution's bacteriology department. Population, history, symptoms and diagnostic features were noted. Treatment, surgical complications, adverse reactions to antibiotics, patient adherence, antibiotic therapy duration, time to remission and prognosis were analyzed.
Results: Between 2005 and 2014, 30 patients were diagnosed with head and neck NTM lymphadenitis: 17 female, 13 male; mean age at diagnosis, 4.5 years. Locations were submandibular ($n=16$), parotid, ($n=7$), cervical ($n=5$), parapharyngeal ($n=4$) and, for 1 patient, in the auricle concha. Eight patients received first-line surgical treatment, which was effective in 75% of cases, 2 patients requiring additional antibiotic therapy. Twenty-two patients were treated with first-line antibiotherapy, which was effective in 90% of cases. There were no relapses at a mean 32 weeks' follow-up.
Conclusions: Total resection of all affected nodes and infiltrated subcutaneous fatty tissue is the treatment of choice. Drug therapy (including at least a macrolide) seems indicated only in case of incomplete resection or if surgery would entail functional and/or esthetic risk. Increased incidence, since BCG vaccination was stopped, will continue to confront the practitioner with an infantile disease in which management must be multidisciplinary.

1. Introduction

Mycobacterial infection is the most frequent cause of cervical granuloma, and may implicate tuberculous (*Mycobacterium tuberculosis*, *Mycobacterium bovis*, *Mycobacterium africanum*) or non-tuberculous mycobacteria (NTM) [1]. NTM is a ubiquitous organism, found in soil, water and certain foods.

Cervical lymphadenitis is the most frequent form of NTM infection in non-immunosuppressed children.

Overall, most authors agree that NTM is increasingly frequently isolated [1]. Initial diagnosis is difficult and management is not clearly codified.

A retrospective study conducted in the University Hospital of Nantes, France, between 2005 and 2014, included all patients treated for or diagnosed with NTM head and neck adenitis.

The study objective was to describe clinical features and to study treatment options, in order to improve management.

2. Patients and methods

The research was conducted on the database of the institution's bacteriology department.

The inclusion criterion was head and neck adenitis implicating NTM on bacteriological analysis.

* Corresponding author. Service d'ORL et de chirurgie cervico-faciale, CHU Hôtel-Dieu, 1, place A.-Ricordeau, BP 1005, 44093 Nantes cedex 01, France.
Tel.: +33 2 40 08 34 75; fax: +33 2 40 08 34 77.
E-mail address: omalard@chu-nantes.fr (O. Malard).

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Incidence was recorded by year of diagnosis. Patient age and gender, history, immune status and Bacillus Clamette-Guérin (BCG) vaccination status were noted.

Functional signs, clinical presentation (adenopathy size, general clinical aspect) and general signs were recorded. Initial lesion location was described in terms of head and neck topography.

Isolation was performed on aspiration and biopsy samples for direct examination and culturing. Pathologic examination screened for epithelial and giant-cell granuloma and acid-alcohol-resistant bacilli (AARB).

Treatment methods were analyzed as surgical (adenectomy, dermo-hypodermal resection), medical (antibiotic therapy: type and duration), or mixed.

Side-effects, prognosis, results and sequelae were recorded.

3. Results

Between 2005 and 2014, in the University Hospital of Nantes, France, 30 patients had positive bacteriological diagnosis of head and neck NTM infection: 17 female, 13 male; mean age, 4.5 years. Immune deficiency screening was systematically negative, and no patients had relevant history. Regarding BCG vaccination status: 4 patients were vaccinated, 20 not, and status was unrecorded for 4 (Table 1).

At diagnosis, fluctuating tumefaction was observed in 42% of cases, firm lymphadenopathy in 35% and cutaneous fistulae in 10%.

Locations were submandibular ($n = 16$), parotid, ($n = 7$), cervical ($n = 5$), parapharyngeal ($n = 4$) and, for 1 patient, in the outer ear.

Sampling methods are presented in Table 2. Bacteriology found positive samples on direct examination in 51% of cases and after culture in 49%. Culture identified *M. avium*-intracellular ($n = 20$), *Mycobacterium lentiflavum* ($n = 9$) *Mycobacterium malmoense* and *Mycobacterium scrofulaceum* ($n = 1$). Pathologic examination was performed in 22 patients and found giant-cell granuloma without casseous necrosis in 86% of cases, associated with AARB. Antibiograms were performed on 21 samples (17 *M. avium*, 4 *M. avium*-intracellular) found 100% clarithromycin susceptibility. Mean interval between first consultation and bacteriological identification was 52 days.

Regarding treatment modalities (Table 3), 22 patients received first-line antibiotic therapy: 14 isolated clarithromycin, 5 clarithromycin-rifampicin, and 3 clarithromycin-rifampicin-ethambutol.

Table 1
Demographic data ($n = 30$).

	$n = 30$
Gender	
Female	17
Male	13
Mean age (years)	4.5 (2–28)
BCG vaccination status	
Vaccinated	4
Non-vaccinated	20
Not known	4

Table 2
Sampling methods. Positive culture, $n = 30$ (100%).

Sampling methods	$n = 30$
Fine-needle aspiration under local anesthesia, n (%)	5 (16)
Sampling under general anesthesia, n (%)	25 (84)
Curettage, *n*	8
Abscess drainage, *n*	9
Resection biopsy, *n*	8

Table 3
Known BCG status ($n = 28$).

Medical treatment, n (%)	22 (73)
Clarithromycin	14
Clarithromycin + rifampicin	5
Clarithromycin + rifampicin + ethambutol	3
Complete recovery, *n* (%)	20 (90)
Salvage surgery, *n* (%)	2 (10)
Surgical treatment, n (%)	8 (27)
Complete recovery, *n* (%)	6 (75)
Second-line antibiotic therapy, *n* (%)	2 (25)

Twenty of the 22 patients (90%) showed complete remission under antibiotic therapy; the other 2 underwent complementary surgical resection.

Mean antibiotic therapy duration was 2.45 months. Three patients showed adverse effects such as intolerance: two under monotherapy and 1 under bitherapy. Three patients showed defective adherence.

The other 8 patients underwent first-line surgery. Six showed complete remission with surgery alone; 2 received secondary drug treatment. There were no postoperative complications.

4. Discussion

Clinical diagnosis of NTM lymphadenitis is difficult, and definitive confirmation on positive culture involves delay.

Diagnosis may be suspected clinically on several grounds. Infection generally occurs in 1–5-year-old children, with female predominance [1–3]; the present series had a mean age of 4.5 years, and female predominance. Locations are mainly cervical and submandibular, and more rarely parotid [3], although in the present series rates of cervical and parotid involvement were the same. The initial presentation is generally a painless cervical adenopathy resistant to standard antibiotic therapy [1,3]; in the present series, adenopathies were fluctuating in 42% and firm in 35% of cases. Progression to a purplish coloration in adjacent skin or to fistulization is generally late [4], although 10% of the present series already showed such an aspect at their first consultation.

The interval between symptom onset and diagnosis ranges from 4 to 12 weeks [4,5], with a mean 7 weeks in the present series.

Definitive diagnosis on positive culture can be long to obtain; results may indeed remain negative for a long time, given the difficulty of ensuring growth in NTM, which is an intracellular bacterium that is fragile ex vivo.

Several sampling methods may be used: fine-needle aspiration, curettage, drainage, or complete resection. There are no studies defining optimal sampling. In the present series, 80% of positive cultures were based on deep sampling under general anesthesia.

These findings seem to argue for deep sampling (curettage, drainage, under general anesthesia to facilitate the procedure) which optimizes identification in culture by providing a larger sample than aspiration or minimal sampling, without leading to more fistulization than fine-needle aspiration [1].

Identification in culture can exclude differential diagnoses. Culture media may be solid (Löwenstein-Jensen) or liquid. Incubation lasts 45–60 days. A liquid medium (Bactec MGIT 960) allows earlier diagnosis, with faster bacterial growth (1–2 weeks) [2].

New genotype amplification techniques by polymerase chain reaction (PCR) allow early diagnosis, differentiating between tuberculous and non-tuberculous strains with more than 95% specificity [2,5].

However, these techniques are available only in certain centers. Culture in the present study was exclusively on solid medium.