Current trends in nontuberculous mycobacteria infections in Canadian children: A Pediatric Investigators Collaborative Network on Infections in Canada (PICNIC) study

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BACKGROUND: Nontuberculous mycobacteria (NTM) infections appear to be increasing in number and severity in developed countries worldwide. Surgical excision has been considered the standard treatment for NTM lymphadenitis, but the use of medical therapy seems to be increasing.

OBJECTIVE: To determine the disease characteristics as well as the current therapeutic management of NTM infections in Canadian children.

METHODS: Cases of definite or probable NTM infections were identified prospectively in children up to 18 years of age seen in 10 Canadian paediatric tertiary care centres from September 2005 to August 2006. Clinical, microbiological and pathological data were collected.

RESULTS: A total of 60 cases were identified. Data were complete for 45 patients, including 34 cases of lymphadenitis, four cases of skin and soft tissue infection, and seven cases of pulmonary NTM infection. Seventy-nine per cent of children (27 of 34) with lymphadenitis had an unsuccessful course of antibiotics before diagnosis. Sixty-eight per cent of purified protein derivative tests (15 of 22) were positive. NTM was detected in 76% of samples (29 of 38), of which 62% were *Mycobacterium avium* complex. All patients with lymphadenitis underwent surgical therapy and most patients (74%) also received antimicrobials.

CONCLUSIONS: Current trends indicate that the majority of the study centres are using medical therapy with variable regimen and duration as an adjunct to surgical excision in the treatment of NTM lymphadenitis. Larger numbers and longer follow-up times are needed to better evaluate the efficacy of medical therapy and outcome of disease. A randomized controlled study comparing surgical therapy alone and chemotherapy for NTM lymphadenitis is required.

Key Words: *Adenitis; Atypical mycobacteria; Management; Non-HIV; Nontuberculous mycobacteria; Treatment*

Les tendances actuelles d'infections à mycobactéries non tuberculeuses chez les enfants canadiens : Une étude du réseau coopératif de chercheurs pédiatriques sur les infections au Canada (PICNIC)

HISTORIQUE : Le nombre et la gravité des infections à mycobactéries non tuberculeuses (MNT) semblent augmenter dans les pays industrialisés. L'excision chirurgicale est perçue comme le traitement standard de la lymphadénite à MNT, mais le recours au traitement médicamenteux semble devenir plus fréquent.

OBJECTIF : Déterminer les caractéristiques de la maladie ainsi que la prise en charge thérapeutique actuelle des infections à MNT chez les enfants canadiens.

MÉTHODOLOGIE : Les auteurs ont repéré prospectivement les cas d'infections à MNT réels ou probables chez les enfants de 18 ans et moins vus dans dix centres pédiatriques canadiens de soins tertiaires entre septembre 2005 et août 2006. Ils ont colligé des données cliniques, microbiologiques et pathologiques.

RÉSULTATS : Les auteurs ont repéré un total de 60 cas. Les données étaient complètes à l'égard de 45 patients, y compris 34 cas de lymphadénite, quatre cas d'infections de la peau et des tissus mous et sept cas d'infection pulmonaire à MNT. Ainsi, 79 % des enfants ayant une lymphadénite (27 sur 34) avaient reçu une antibiothérapie en vain avant le diagnostic, et 68 % des tests dérivatifs à la protéine purifiée (15 sur 22) étaient positifs. De plus, 76 % des échantillons étaient positifs aux MNT (29 sur 38), dont 62 % correspondaient à un complexe *Mycobacterium avium*. Tous les patients ayant une lymphadénite ont subi un traitement chirurgical, et la plupart (74 %) ont également reçu des antimicrobiens.

CONCLUSIONS : Selon les tendances actuelles, la majorité des centres à l'étude recourent à un traitement médical aux posologies et aux durées variées pour compléter l'excision chirurgicale en cas de lymphadénite à MNT. Il faudrait un plus gros échantillon et un suivi plus prolongé pour mieux évaluer l'efficacité du traitement médical et l'issue de la maladie. Une étude aléatoire et contrôlée comparant le traitement chirurgical seul au traitement chirurgical accompagné d'une chimiothérapie de la lymphadénite à MNT s'impose.

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Nontuberculous mycobacteria (NTM) are ubiquitous in the environment and are frequently isolated from soil or water (1); however, they are still relatively infrequent human pathogens (2). More than 125 species of mycobacteria have been identified (3), with approximately 40% being potential human pathogens (4). Pulmonary disease, lymphadenitis, skin and soft tissue infection (SSTI), bone and joint infection, and disseminated infection in an immunocompromised patient are common clinical syndromes, with cervical lymphadenitis being the most common presentation in immunocompetent children.

Recently, an increase in both the incidence and severity of NTM infections, even in immunocompetent children, has been reported (5). This increase in incidence may be secondary to increased detection of NTM because of more rapid and accurate laboratory methods (6,7), the growing population of patients susceptible to NTM infections (such as patients with HIV, malignancy or cystic fibrosis) (4) and/or the discontinuation of universal Bacillus Calmette-Guérin vaccination, which is believed to provide some cross-protection against NTM infections (5). Bacillus Calmette-Guérin vaccination was discontinued in most Canadian provinces in the mid to late 1970s and more recently in 2005 to 2007 for First Nations communities. Because NTM infections are not reportable diseases to public health authorities, it is difficult to determine its true incidence (8). Moreover, although surgical excision has been considered the standard treatment for NTM lymphadenitis (9,10), the introduction of new macrolides has led to much more diversified treatment strategies (11-13). The objective of the present study was to describe the disease characteristics, and the current diagnostic and therapeutic managements of NTM infections in Canadian children.

METHODS

Study setting

A descriptive case series of NTM infection identified prospectively among Canadian paediatric tertiary care centres is reported. Only centres affiliated with the Pediatric Investigators Collaborative Network on Infections in Canada (PICNIC) were included. PICNIC brings together paediatric infectious disease specialists from the major Canadian paediatric teaching hospitals by encouraging regular collaboration on various research projects and protocols. There are 13 official PICNIC centres across Canada. All children aged 18 years or younger, seen at one of the PICNIC centres with a definite or probable case of NTM, were included in the present study.

Case definition

Subjects were defined as having 'definite NTM' when NTM species were identified from a clinical sample either by culture or polymerase chain reaction, with the treating physician considering NTM as the cause of disease. *Mycobacterium gordonae* is a frequent environmental contaminant and is seldom pathogenic (14). A case was considered to be 'probable NTM' if the child presented clinical features compatible with NTM, a positive result to at least one of the supportive investigations (see below), had no risk factors for *Mycobacterium tuberculosis* infection and had no alternative diagnosis. Compatible clinical features included lymphadenopathy not responding to standard antibiotic therapy for acute suppurative adenitis, pulmonary disease and SSTI. The supportive investigations included the presence of acid-fast bacilli (AFB) grown from a sample or biopsy tissue, or AFB grown from a nonsterile site sample; granulomatous reaction, caseous necrosis or AFB seen on a histopathological specimen; a tuberculin purified protein derivative (PPD) skin test of 5 mm or greater; and/or a negative *Bartonella* serology.

Study design

Cases were prospectively identified through microbiology and pathology laboratories in each participating centre. Monthly reminders were sent to investigators to report cases from their respective centres. All reported cases were recorded, and a detailed standardized questionnaire was sent to the reporting PICNIC investigator to collect clinical, microbiological and pathological data. The research ethics board in each centre approved the research protocol. Only anonymized data were sent.

Statistical analysis

Descriptive statistics, χ^2 tests and Student's *t* tests were used for univariate analyses. Risk factors associated with NTM recurrences were analyzed using logistic regression in a stepwise fashion (version 8.0, SAS Institute Inc, USA).

RESULTS

Ten of the 13 registered PICNIC centres participated in the present study from September 2005 to August 2006. A total of 60 cases were identified from participating centres, with the number of cases ranging from one to 19 in each centre during the one-year period. Data were complete for 45 cases. The remaining 15 questionnaires were not returned and, thus, were not included in the analysis.

Among the completed cases, 31 (69%) were definite NTM infection, including 34 children with cervical lymphadenitis, seven with pulmonary NTM and four with SSTIs. Table 1 describes the patient demographics. Children with lymphadenitis (median age of 2.8 years) were younger than patients with pulmonary NTM infection (median age of 14.5 years). The study cohort had a slight female predominance (64%), as observed in previous studies (15,16). Six patients had an underlying medical condition: four with cystic fibrosis and two with chronic lung disease. Of these six patients, five presented with pulmonary NTM. One patient described as having asthma developed a right submandibular lymphadenitis. Tables 2, 3 and 4 describe the characteristics of NTM lymphadenitis, pulmonary infections and SSTIs, respectively. The majority of cases (52%) were reported from the province of Quebec.

The time from onset of symptoms to diagnosis was, on average, 2.7 months (range 0.4 to 14.4 months) in the case of NTM lymphadenitis and four months (range 1.4 to

TABLE 1
Demographic characteristics of study patients (n=45)

Characteristic	Result	P
Age, years		
NTM lymphadenitis (n=34)		
Range	1.34–16.83	
Mean	3.42	
Median	2.82	
NTM pulmonary infection (n=7)		
Range	1.62–17.34	
Mean	12.08	
Median	14.52	
NTM skin and soft tissue infection (n=4)		
Range	1.94–16.83	
Mean	8.93	
Median	8.47	
Sex, n (%)		
Male	16 (36)	
Female	29 (64)	0.05
Area of residence, n (%)		
City, town or village	34 (75)	
Rural area	11 (35)	<0.01
Ethnicity, n (%)		
Caucasian	32 (71)	
Aboriginal	1 (2)	
Other	8 (18)	0.03
Specialist involved in cases, n (%)		
Infectious diseases	29 (64)	
Ear, nose and throat	20 (44)	
General surgeons	16 (35)	

NTM Nontuberculous mycobacteria

TABLE 2
Characteristics of nontuberculous mycobacteria (NTM) lymphadenitis

Characterisitics	Result, n (%)
Total number of cases	34 (100)
Site of NTM lesion	
Cervical	13 (38)
Submandibular	19 (56)
Axillary	2 (6)
Inguinal	1 (3)
Parotid	1 (3)
>2 sites	2 (6)
Definite NTM	20/34 (59)
Probable NTM	14/34 (41)
Fever related to NTM	4/34 (12)
Cough	1/31 (3)
Anorexia	2/29 (7)
Weight loss	1/29 (3)
Skin discolouration	20/34 (59)
URTI before presentation	10/25 (40)
Unsuccessful antibiotic trial	27/34 (79)
Purified protein derivative test	
0–5 mm	3/18 (17)
6–9 mm	4/18 (22)
>10 mm	11/18 (61)

URTI Upper respiratory tract infection

8.0 months) for pulmonary NTM. Children with lymphadenitis typically presented with a history of persistent lymph node swelling, mostly cervical or submandibular, without significant systemic symptoms. Seventy-nine per cent of these children (27 of 34) had received an unsuccessful course of oral antibiotics before diagnosis.

A tuberculin skin test (TST) using PPD was performed in 22 of 44 children (50%). In Canada, 0.1 mL of 5 tuberculin units of PPD is used (17). Among those tested, the mean TST result was 11.2 mm (median 11 mm, range 0 mm to 20 mm). Fifteen of the 22 children (68%) tested had a TST reading of 10 mm or greater (mean 14.2 mm). Two children had *Bartonella* serology tests (both were negative), and one patient had a basic immune workup that included lymphocyte subsets and phagocytic function, which were normal.

AFB were seen in biopsy or sputum specimens in 50% of lymphadenitis (n=17) and SSTI (n=2) cases, and in 43% of pulmonary cases (n=3). NTM was isolated in culture from 29 of 38 samples (76%), of which 18 (62%) were

TABLE 3
Characteristics of nontuberculous mycobacteria pulmonary infections

Age, years	Sex	Ethnicity	Underlying medical condition	Symptoms	PPD test, mm	Chest x-ray findings	Specimen obtained	AFB seen	Culture result	Treatment
1.6	Male	Canada	Scimitar syndrome	Cough, weight loss	N/A	Bilateral chest infiltrates	Lung biopsy	Yes	*M simiae* complex	No
8.7	Female	Canada	Cystic fibrosis	Cough, anorexia, weight loss	N/A	RML infiltrate, pulmonary nodules	Sputum	Yes	*M abscessus*	Clarithromycin, amikacin, cefoxitin, linezolid
14.5	Male	Canada	Cystic fibrosis	Cough	N/A	Normal	Sputum	No	*M avium* complex	No
16.8	Female	Canada	Cystic fibrosis	Fever, cough, weight loss	N/A	N/A	Sputum	Yes	*M saskatchewanense*	Clarithromycin, rifampin
16.9	Female	Israel	None	Cough, weight loss	15	Normal	Sputum	No	*M chelonae*	No
17.3	Female	Canada	Cystic fibrosis	Fever, cough, anorexia	N/A	New pulmonary nodules	Sputum	No	*M lentiflavum*	Clarithromycin, rifabutin
17.3	Male	Congo	None	None	11	Normal	Sputum	No	*M chimaera*	No

AFB Acid-fast bacilli; M Mycobacterium*; N/A Not available; PPD Purified protein derivative; RML Right middle lobe*

TABLE 4
Characteristics of nontuberculous mycobacteria skin and soft tissue infections

Age, years	Sex	Site of infection	Specimen obtained	Histopathology	Culture result	Medical treatment	Comment
1.9	Female	Left internal thigh, 2x1 cm	Excisional biopsy	Necrotizing caseating granuloma	*M avium intracellulare*	None	Resolution
4.0	Female	Soles of feet	Skin biopsy	Necrotizing granuloma with AFB seen	No growth	Clarithromycin for three months	Multiple cutaneous recurrences
7.2	Male	Left index finger	Skin biopsy	Lymphocytic and granulomatous infiltrate within the deep dermis, focal microabcess	*M marinum*	Clarithromycin for three months	Resolution on treatment
9.6	Male	Right hand nodule, 5 cm	Skin biopsy	Necrotizing granuloma	*M fortuitum*	Ethambutol TMP-SMX	Resistance to clarithromycin

AFB Acid-fast bacilli; M Mycobacterium*; TMP-SMX Trimethoprim-sulfamethoxazole*

Mycobacterium avium complex. The other species isolated were *Mycobacterium celatum* (n=2) and one each of *Mycobacterium chelonae*, *Mycobacterium abscessus*, *Mycobacterium simiae* complex, *Mycobacterium fortuitum*, *Mycobacterium chimaera*, *Mycobacterium interjectum*, *Mycobacterium lentiflavum*, *Mycobacterium saskatchewanense* and *Mycobacterium marinum*. Organisms were identified by 16S RNA in two cases. All of the excised lymph nodes were sent to pathology for evaluation. The majority of samples were described as ill-defined granuloma (44%), Langhans-type giant cells (45%) or noncaseating granuloma (32%). Subanalysis of the NTM species identified in Quebec did not reveal an unusual predominance of a specific NTM, which may have suggested an environmental source. Of the species identified, 58% were M *avium* complex.

All of the patients with lymphadenitis or SSTI underwent a surgical procedure: excisional biopsy (n=35), concomitant functional neck dissection (n=3) or incisional biopsy (n=2). Fine needle aspiration was not performed in any of the cases, whether for diagnostic or therapeutic purposes. Four of seven patients with pulmonary NTM were observed. Seventy-four per cent of patients with cervical lymphadenitis were treated with a course of antibiotic targeting NTM that was given either before surgery (32%), after (15%) or both (23%). Table 5 details the management and complications encountered. Table 6 shows the various antimicrobial regimens used. The duration of treatment was variable, ranging from 10 days to three months for lymphadenitis and four months to one year for pulmonary infection. Seven patients (21%) with lymphadenitis managed surgically experienced eight complications (Table 5). Nerve paresis was described in three patients, all of whom had mild residual facial asymmetry and weakness postoperation; none were considered severe. Two patients (8%) undergoing medical therapy experienced side effects, described as a rash in a patient taking clarithromycin and persistent headaches in a child taking clarithromycin and ethambutol.

There were 12 documented recurrences (27%) during the study period: 10 of 34 patients (29%) with lymphadenitis, one of four patients (25%) with SSTI and one of seven patients (14%) with pulmonary infection. Review of the initial management of these patients did not reveal any significant differences. All of the patients with lymphadenitis had undergone previous surgical excision and only one patient with recurrent lymphadenitis was treated initially with surgical excision alone. One patient with lymphadenitis who was treated with clarithromycin monotherapy had a recurrence. Otherwise, none of the factors evaluated, such as age, PPD reaction size, NTM species isolated or duration of symptom were predictive of recurrence of infection when analyzed by univariate and multivariate regression. The only patient with a pulmonary recurrence was a patient with cystic fibrosis infected with a

TABLE 5
Management of nontuberculous mycobacteria infection and complications of therapy

Management	Lymphadenitis, n (%)	SSTI, n (%)	Pulmonary infection, n (%)
Therapy			
No therapy	0	0	4 (57)
Surgery alone	9 (26)	1 (25)	0
Medical therapy alone	0	0	3 (43)
Combination therapy	25 (74)	3 (75)	0
Surgical therapy			
Excisional biopsy	33 (97)	2 (50)	N/A
Incisional biopsy	1 (3)	1 (25)	
Functional neck dissection	3 (9)	0	
Fine needle aspiration	0	0	
Timing of medical therapy			
Preoperation	11 (32)	0	N/A
Postoperation	5 (15)	3 (75)	
Pre- and postoperation	8 (23)	0	
Unknown	1 (3)	0	
Complications			
Surgical	7 (21)	0	0
Wound infection	3 (9)	0	0
Nerve paresis	3 (9)	0	0
Fistula formation	2 (6)	0	0
Medical	2 (6)	0	0
Recurrence	10 (29)	1 (25)	1 (14)
Management of recurrence			
Surgical	1 (10)	0	0
Medical	4 (40)	0	0
Combination	3 (30)	1 (100)	0
Observation	2 (20)	0	1 (100)

N/A Not applicable; SSTI Skin and soft tissue infection

TABLE 6
Medical therapy for nontuberculous mycobacteria (NTM) infections

	Medical therapy						
NTM infection	CL	CL + RFP	CL + RFB	AZT	Other	Non-NTM agents	Total
Lymphadenitis	15	5	1	2	0	3	26
Skin and soft tissue infection	2	0	0	0	1*	0	3
Pulmonary infection	0	1†	1	0	1‡	0	3

*Thirty-two patients were treated (29 with specific NTM treatment agents). *Clarithromycin (CL) plus ethambutol plus trimethoprim-sulfamethoxazole; †CL plus rifampin (RFP) plus ciprofloxacin; ‡CL plus amikacin plus cefoxitin plus linezolid. AZT Azithromycin; RFB Rifabutin*

multiresistant strain of M *abscessus* for multiple years. She was treated with a multidrug regimen that included clarithromycin (11 months), amikacin (four months) and cefoxitin (five months). The patient also received linezolid and inhaled amikacin. Symptoms recurred and the patient was scheduled to undergo surgical resection.

DISCUSSION

Children with NTM infections were found in various parts of Canada. The most common clinical syndrome in our Canadian paediatric cohort was lymphadenitis. Pulmonary NTM infection was also noted, including two patients with no known underlying disease. According to our cohort, lymphadenitis is mainly managed by surgical treatment, but an increasing number of children are being treated with antimicrobials. The medications used and the duration of treatment were variable, making it difficult to determine whether one regimen was superior to the others. In the present case series, the most commonly used regimen was clarithromycin with or without rifampin. Eleven cases of NTM lymphadenitis were treated with clarithromycin monotherapy. Retrospective studies show promising results with medical therapy alone (18-21). One study (22) suggested that in children with NTM lymphadenitis with unsuccessful surgical resection, chemotherapy should be considered before further surgery is undertaken. Lindeboom et al (23) from the Netherlands published a multicentre, randomized controlled trial that further addressed this question. A total of 100 children with microbiologically proven NTM cervicofacial lymphadenitis were randomly assigned to undergo surgical excision of the involved lymph node, or to receive antibiotic therapy with clarithromycin and rifabutin for at least 12 weeks. They concluded that surgical excision was more effective than antibiotic treatment alone, with cure rates of 96% and 66%, respectively, for children with NTM cervicofacial lymphadenitis. This study did not examine disease management consisting of a combination of surgery and chemotherapy, which appears to be the most common trend in our Canadian cohort. A recent study by Zeharia et al (24) described the outcome of 92 children with microbiologically confirmed NTM cervical lymphadenitis managed by observation alone following a diagnostic fine needle aspiration. These patients were diagnosed between 1990 and 2004, and were managed conservatively following parental request. Total resolution was achieved in 71% of patients within six months, and within nine to 12 months in the remaining patients. The majority of children had a draining lymph node for many weeks before resolution. The authors did not detail the proportion of children with NTM lymphadenitis followed at their centre who were actually observed; thus, we are unable to compare their patient population with ours. It is possible that those with more invasive or aggressive disease underwent surgery because of strong physician recommendation; therefore, the findings of the present study cannot be generalized to all children with NTM lymphadenitis.

The majority of patients with pulmonary NTM infections were not treated in our current study. Because most of these patients had an underlying pulmonary medical condition, the growth of NTM needs to be correlated with radiological and clinical findings before a decision regarding treatment is undertaken (12). However, the low incidence of pulmonary disease in our cohort is a significant limitation that does not allow us to comment on the efficacy of treatment.

Our study was also not designed to calculate incidence rate, because the distribution of NTM cases in our cohort is unlikely to be representative of the true incidence. The majority of surgeries in Canadian children occur in paediatric hospitals, which should allow us to record most of the cases of lymphadenitis requiring surgical excision in Canadian children. As mentioned previously, a significant proportion of the cases were identified in Quebec and, particularly, at the Centre Hospitalier Universitaire Sainte-Justine (Montreal, Quebec) – one of the largest children's hospitals in Canada. The high number of cases from Quebec may reflect the fact that the four hospitals that provide the vast majority of paediatric care services in Quebec participated in the study (Centre hosptialier universitaire Sainte-Justine, The Montreal Children's Hospital [Montreal, Quebec], Centre Universitaire de Santé de Sherbrooke [Sherbrooke, Quebec] and Centre Hospitalier de l'Université Laval [Quebec City, Quebec]). Therefore, the vast majority of cases seen in children were identified in Quebec, compared with other provinces. It is, therefore, likely that within the province of Quebec, most cases of NTM in children were identified. If this hypothesis holds true, the estimated incidence rate for all NTM infections in Quebec would be 2.15 per 100,000 children (95% CI 1.42 to 3.15), based on recent 2006 census population data (25), or 1.60 per 100,000 children (95% CI 0.98 to 2.46) for NTM lymphadenitis. Although our estimated incidence is likely to be an underestimate of reality, the incidence in Quebec is still statistically significantly higher than the one reported in the population-based prospective study (15) on NTM infections performed in the Netherlands, where the estimated incidence was 0.77 per

100,000 children. A similar prospective national epidemiological study (26) was also conducted in Australian children. The calculated incidence of NTM infection in that population was 0.84 per 100,000 children (95% CI 0.68 to 1.02). A national prospective registry of NTM infection in both adults and children would be helpful in determining the prevalence across Canada.

During the one-year study period, many cases were missed for the following reasons: six paediatric tertiary care centres did not participate in the present study, cases may have presented to peripheral community hospitals not affiliated with PICNIC, or samples may not have been appropriately sent to the microbiology and/or pathology laboratories. Moreover, the study was not designed to detect less severe cases that may have been treated solely with antibiotics or that would have resolved spontaneously.

A significant amount of PPD cross-reaction was noted, with TST being positive (10 mm or greater) in 68% of patients tested. These results are in accordance with previous studies in which 25% to 100% of TSTs were positive in the presence of NTM infection (15,16,27,28). Certain groups have advocated that the TST is a useful screening test in the evaluation of children with NTM lymphadenitis (29). The current TST cut-off in Canada (10 mm) for tuberculosis may need to be re-evaluated in the context of a low tuberculosis risk and a low incidence, as the American Thoracic Society did using a cut-off at 15 mm (30).

The Public Health Agency of Canada recently updated their recommendation regarding the use of interferon-gamma release assays (IGRA) in children for the diagnosis of latent and active tuberculosis infection. IGRA can be used as an adjunctive diagnostic method in children with suspected active tuberculosis and can also be used in children for confirmation of a positive TST. IGRAs are also recommended in immunocompetent adults and children with a positive TST and a relatively low risk of being infected with tuberculosis and of progressing to active disease (31). Although IGRA is more specific than TST, false-positive results may occur in individuals infected with the following NTM species: *Mycobacterium kansasii*, *Mycobacterium marinum*, *Mycobacterium szulgai* and *Mycobacterium flavescens*. In our series, we had only one infection caused by M *marinum*. Given this epidemiology, we should not expect too many false-positive IGRA results when confirming a positive TST result in children.

There is currently a lack of standardized treatment for NTM infection. Current trends indicate that the majority of study centres are using medical therapy as an adjunct to surgical excision in the treatment of NTM lymphadenitis, for which the regimen and duration chosen are variable. Larger numbers and longer follow-up periods are needed to better evaluate the efficacy of medical therapy and outcome of disease. A randomized controlled trial comparing surgical therapy alone and surgical therapy with chemotherapy would be required to answer these questions.

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