Differential Diagnosis of Cervical Mycobacterial Lymphadenitis in Children

Anna C. C. Carvalho, MD, PhD, Luigi Codecasa, MD,† Gabriele Pinsi, MD,‡ Maurizio Ferrarese, MD,† Chiara Fornabaio, MD,* Viviana Bergamaschi, MD,* Carla Lacchini, MD,† Giorgio Ekema, MD,§ Stefania Stefini, MD,¶ Mario Comelli, MD, PhD,‖ and Alberto Matteelli, MD**

Background and Aims: The differential diagnosis between tuberculosis (TB) and lymphadenitis caused by nontuberculous mycobacteria (NTM) in children is often based on epidemiologic and clinical data. The aim of this study was to identify epidemiologic and clinical variables associated with TB lymphadenitis in children attending 2 TB out-patient clinics in northern Italy during a 10-year period.

Patients and Methods: All children less than 16 years of age attending the study sites suspected of mycobacterial disease from 1999 through 2008 were included in the analysis. Logistic regression was used to evaluate the variables independently associated with TB lymphadenitis.

Results: From 299 children diagnosed with mycobacterial disease 121 children (40%) had a clinical diagnosis of cervical mycobacterial lymphadenitis: 38 TB (31%) and 83 NTM lymphadenitis (69%) cases. Increasing age (OR, 1.29; 95% CI, 1.02–1.69; $P = 0.04$), being foreign born (OR, 11.60; 95% CI, 1.37–114.20; $P = 0.02$), and having an abnormal chest radiograph (OR, 18.32; 95% CI, 2.37–201.68; $P = 0.008$) were independently associated with TB lymphadenitis. In the selected model, a 5-year-old foreign born child with cervical lymphadenitis and abnormal findings on chest radiograph has an estimated 0.90 probability of having TB disease. On the other hand, an Italy born child of the same age with cervical lymphadenitis and normal chest radiograph has a 0.04 probability of having TB.

Conclusion: Epidemiologic and clinical data are useful tools in the differential diagnosis between TB and NTM lymphadenitis when etiologic diagnosis is not available.

Key Words: Tuberculosis, nontuberculous Mycobacteria, lymphadenitis, children and adolescents

(*Pediatr Infect Dis J* 2010;29: 629–633)

Tuberculosis (TB) has re-emerged as a public health concern in developed countries in recent years.[1–3] TB notification rates in the 25 European Union countries decreased by 4% each year between 1999 and 2003, but Italy and the United Kingdom registered an increase in TB rates mainly because of TB cases among immigrants.[3] Increasing TB rates in children born abroad or with immigrant parents have also been described in other low prevalence European countries.[4–6] Children represent a vulnerable population for TB, they are more likely to have a rapid progression from infection to disease and they develop more frequently extrapulmonary and disseminated forms.[7,8] Cervical lymphadenitis is a frequent clinical presentation of TB in children and these cases must be differentiated from lymphadenitis caused by nontuberculous mycobacteria (NTM), a more common cause of mycobacterial lymphadenitis among children in non endemic TB countries.[9–12]

Differential diagnosis between TB and NTM lymphadenitis is based on mycobacterial identification in lymph node samples obtained by fine-needle aspiration or by surgical biopsy. Culture and molecular tests for mycobacteria identification are not always available or are not included in the diagnostic procedure because mycobacterial lymphadenitis is initially not suspected. Histologic characteristics of NTM lymphadenitis are similar to those found in lymph node disease caused by *Mycobacterium tuberculosis* (MTB); therefore, when specimen identification is not available the definitive differential diagnosis between NTM and TB disease cannot be done. In these circumstances, the choice of treatment is based on epidemiologic and clinical characteristics. This decision is critical, as the management of NTM and TB lymphadenitis differs significantly: in NTM cases treatment is based on surgical excision of involved lymph nodes, while children with TB require treatment with antimycobacterial drugs, considering the increased risk of disseminated disease, in particular among the youngest.[7,13]

We report the results of a retrospective investigation on children with mycobacterial disease that is intended to provide epidemiologic and clinical data useful to differentiate TB lymphadenitis from NTM when etiologic diagnosis is not available.

PATIENTS AND METHODS

Study Design

A retrospective study was done involving all children less than 16 years of age with a final clinical diagnosis of mycobacterial lymphadenitis who sought care at TB out-patient clinics of the Institute of Tropical and Infectious Diseases, Spedali Civili, Brescia and at the TB Reference Centre and Laboratory of Villa Marelli Institute, Milan, between January 1999 and January 2009. These centers are responsible for the care of approximately 500 patients with mycobacterial disease per year, representing 50% of mycobacterial cases notified in the Lombardy Region, North Italy.

A definitive diagnosis of TB lymphadenitis was based on the presence of a positive culture for MTB or a positive polymerase chain reaction (PCR) for MTB complex species from lymph

Accepted for publication December 29, 2009.

From the *Institute of Infectious and Tropical Diseases (IITD), University of Brescia, Spedali Civili di Brescia, Italy; †TB Reference Centre and Laboratory, Villa Marelli Institute/Niguarda Hospital, Milan, Italy; ‡U.O. Microbiology and Virology, Spedali Civili di Brescia, Brescia, Italy; §Clinic of Pediatric Surgery; ¶Department of Pediatric Otology and Laryngology, Spedali Civili di Brescia, Brescia, Italy; and ‖Dipartimento di Scienze Sanitarie Applicate e Psicocomportamentali, University of Pavia, Pavia, Italy.

We confirm that all the authors do not have any possible conflicts of interest (including financial and other relationships).

Address for correspondence: Anna C. C. Carvalho, MD, PhD, Institute of Infectious and Tropical Diseases, University of Brescia. Piazza Spedali Civili, 1. 25125, Brescia, Italy. E-mail: a.carvalho@libero.it.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's Web site (www.pidj.com).

ISSN: 0891-3668/10/2907-0629
DOI: 10.1097/INF.0b013e3181d1fdcd

node specimen (by biopsy or fine needle aspiration) in a child with lymph node enlargement. A probable TB case was defined as a positive result for acid fast bacilli (AFB) or a histologic finding of granulomatous disease from lymph node in a child with clinical improvement after standard antituberculosis therapy. A definitive diagnosis of NTM lymphadenitis was based on a positive culture for NTM from a lymph node specimen. A probable diagnosis of NTM lymphadenitis was accepted when granulomatous lymphadenitis or AFB was observed in a lymph node sample of a child without epidemiologic data for TB (negative history of contact with TB patients, born in Italy).

Laboratory Procedures

Samples of lymph node tissue obtained by surgical biopsy or fine needle aspiration were sent to the Microbiology Laboratories of Spedali Civili and Niguarda hospitals for AFB microscopic examination and mycobacterial cultures. Slides were prepared and stained with rhodamine-auramine flurochrome dye and examined by fluorescence microscopy. Culture was performed on MGIT960 (Becton Dickinson Microbiology Systems, Cockeysville, MD) automated system in agreement with the manufacturer's instructions. Species identification was performed by molecular techniques using AccuProbe *M. tuberculosis* complex culture identification test (Gen-Probe Incorporated, San Diego, CA) and INNO LiPA Mycobacteria v2 (Innogenetics Inc., Alpharetta, GA). Identification of species within the MTB complex was done by biochemical testing for niacin and nitrate production. MTB isolates underwent drug susceptibility testing by Bactec MGIT 960; drug susceptibility testing for NTM isolates were done with Bactec 460 radiometric culture system. PCR for the identification of MTB complex rRNA using Amplified MTB direct test (Gen-Probe Inc., San Diego, CA) was done in the Reference laboratory of Niguarda Hospital directly on tissue sample or pus aspiration from lymph node.

Tuberculin skin testing (TST) and chest radiograph were offered to all children with suspected mycobacterial disease. The TST was performed by trained, experienced nurses and consisted of 5 tuberculin units of purified protein derivative standard applied by the Mantoux method. TST results were read after 48 to 72 hours by a health care provider and the skin induration was registered in millimeters. Children with cervical lymphadenitis were evaluated initially by a pediatrician or by a specialist in otolaryngology or surgery and all received an initial full course of antistaphylococcal/antistreptococcal therapy. Serologic tests for Epstein Barr virus, cytomegalovirus, *Toxoplasma gondii* and *Bartonella* species were often done and resulted negative for acute infection in all children included in the analysis. HIV testing was not routinely performed.

Chest radiographs were read by pneumologists (Villa Marelli Institute) or radiologists (Spedali Civili) and the findings were considered abnormal and suggestive of mycobacterial disease in the presence of hilar, mediastinal or subcarinal adenitis and/or parenchymal infiltrate, miliary infiltrate, or pleural effusion.

Statistical Analysis

Univariate analysis of the association of clinical and epidemiologic categorical variables with the type of mycobacterial lymphadenitis was performed using the χ^2 test. The crude odds ratios (OR) with their respective 95% confidence intervals (CI) are presented. The Student t test was used to analyze continuous variables. All 2-tailed P values are shown. Only the variables with a significance level of at least 0.05 in the univariate tests were considered for the successive multivariable analyses.

Logistic regression was used to estimate the ability of the clinical and sociodemographic variables for independent prediction of TB lymphadenitis. Only children with a definitive diagnosis of mycobacterial lymphadenitis were included in the univariate and in the logistic regression analysis. The predictors which remained statistically significant in the multivariable analysis were retained in the final selected model (P-values shown).

Patients clinical and laboratory data were entered into specific TB database files (Microsoft Access 2000 and Excel 2000; Microsoft Corp, Redmond, WA). SPSS 12.0 for Windows (SPSS, Inc., Chicago, IL) and R version 2.8.1 were used for statistical analyses.[14]

RESULTS

During the 10-year period 299 children with a diagnosis of mycobacterial disease were evaluated in the 2 clinical sites (94 children in Brescia and 205 in Milan); from these, 121 (40%) had a clinical diagnosis of cervical mycobacterial lymphadenitis: 38 TB (31%) and 83 NTM (69%) cases. Table, Supplemental Digital Content 1, http://links.lww.com/INF/A372, reports the sociodemographic and clinical characteristics of children with mycobacterial lymphadenitis. Sixty percent (23/38) of TB children were foreign born or had immigrant parents; Asia (Philippines, Pakistan, China, and India), Latin America (mainly Peru), and North Africa (most of all from Morocco) were the regions of birth frequently represented among children with TB (19/38; 50% of total). A TST induration $\geq$10 mm was registered in 83% (24/29) of TB children and in 40% (20/50) of children with NTM. History of contact with a TB patient was reported for only 5% (2/38) of TB children, but this history was negative for all children with NTM disease. Children with a definitive diagnosis of TB lymphadenitis were older and had more frequently abnormal chest radiograph findings when compared with children with a probable diagnosis of TB lymph node disease. We did not observe statistically significant differences regarding children with probable or definitive diagnosis of NTM lymphadenitis.

A definitive diagnosis of mycobacterial disease was available for 75 (62%) cases of lymphadenitis: 16 (21%) were TB and 59 (79%) were NTM cases. Culture isolation of MTB was achieved in 15 cases of TB lymphadenitis; 1 child had the definitive diagnosis based on a positive PCR result. In total 10 children had PCR test done; the test was negative for 7 children (5 cases of definitive NTM lymphadenitis and 2 cases of TB, one of them had a positive culture for MTB) and positive in 3 cases (in 2 of them the culture for MTB was positive). Drug sensitivity results were available for 93% (14/15) of cases of definitive TB lymphadenitis. Drug resistance to at least one first line drug was identified in 3 (21%) patients: 2 MTB strains were resistant to isoniazid (one of which was also resistant to streptomycin) and 1 was resistant to pyrazinamide and streptomycin.

Species identification was possible for 56 (95%) cases of NTM lymphadenitis. *Mycobacterium avium* was the most frequently identified strain (91%; 51/56); in 2 children *Mycobacterium scrofulaceum* was isolated, followed by single cases of *Mycobacterium malmoense*, *Mycobacterium chelonae*, and *Mycobacterium fortuitum*; in 3 cases the species of NTM could not be identified. Children with NTM lymphadenitis were not evaluated routinely for immunodeficiency disorders; however, none of them had a history of associated diseases suggestive of decreased immunity or had a severe clinical presentation indicative of underlying immunosupression.

The children with definitive cervical mycobacterial lymphadenitis diagnosis were included in the analysis for variables

TABLE 1. Sociodemographic and Clinical Characteristics Associated With TB Lymphadenitis

Variables	Tuberculosis N = 16 (%)	Atypical Mycobacteria N = 59 (%)	Crude OR (95% CI)*; *P*	Adjusted OR (95% CI)*; *P*
Female	6 (37.5)	33 (55.9)	2.1 (0.68–6.58); 0.26	
Mean age (±SD)†	10.1 (±4.96)	3.7 (±2.54)	<0.005	1.29‡ (1.02–1.69); 0.04
Foreign born	12 (75.0)	5 (8.5)	32.4 (7.55–138.95); <0.005	11.60 (1.37–114.20); 0.02
Contact with TB patient	1 (14.3)	0 (0)	NA§; 0.21	
Abnormal chest radiograph	9 (56.3)	5 (8.5)	13.9 (3.6–53.4); <0.005	18.32 (2.37–201.68); 0.008
Tuberculin skin test	n = 14	n = 38		
≥5 mm	14 (100.0)	27 (71.1)	NA; 0.02	
≥10 mm	14 (100.0)	18 (47.4)	NA; <0.005	

*OR (95% CI) indicates odds ratio (95% confidence interval).
†Student *t* test.
‡For each year of life.
§NA indicates not applicable.

TABLE 2. Predictive Models for TB Lymphadenitis

Type of Child With Lymphadenitis	Formula
Probability of TB lymphadenitis for a foreign born child with abnormal chest radiograph	$[\exp(0.9324 + 0.2528 \times \text{age})]/[1 + \exp(0.9324 + 0.2528 \times \text{age})]$
Probability of TB lymphadenitis for a foreign born child with normal chest radiograph	$[\exp(-1.9758 + 0.2528 \times \text{age})]/[1 + \exp(-1.9758 + 0.2528 \times \text{age})]$
Probability of TB lymphadenitis for an Italian child with abnormal chest radiograph	$[\exp(-1.5183 + 0.2528 \times \text{age})]/[1 + \exp(-1.5183 + 0.2528 \times \text{age})]$
Probability of TB lymphadenitis for an Italian child with normal chest radiograph	$[\exp(-4.4265 + 0.2528 \times \text{age})]/[1 + \exp(-4.4265 + 0.2528 \times \text{age})]$

predictive of TB disease (Table 1). By univariate analysis a statistically significant association of age and nationality with an increased risk for lymph node TB was observed, ie, patients with TB were more frequently older and foreign born than children with NTM lymphadenitis. Only one child with TB lymphadenitis was reported to have a previous contact with a TB patient. TST response among TB patients was ≥10 mm induration for all children and 47% of NTM cases had similar reactions ($P < 0.005$). For 56% of children with TB lymphadenitis the chest radiograph had abnormal findings (mainly mediastinal lymph node enlargement) versus 8.5% among children with NTM lymph node disease. Logistic regression models were built to control possible confounding of variables associated with TB lymphadenitis in the univariate analysis. Increasing age, being foreign born and having an abnormal chest radiograph turned out to be independently associated with TB lymphadenitis in the final model.

We also evaluated the ability of the selected model to predict the diagnosis of TB in a child with cervical lymph node enlargement. For example, a 5-year-old foreign born child with cervical lymphadenitis and abnormal findings on chest radiograph has an estimated 0.90 probability of having TB disease. On the other hand, a child born in Italy of the same age with lymphadenitis and normal chest radiograph has a probability of having TB as low as 0.04. The model had a sensitivity of 87.5% and a specificity of 88% when using, as a discriminating cut-off, the estimated probability of TB lymphadenitis ≥0.22. The predictive formulas for the 4 relevant types of patients are presented in the Table 2.

DISCUSSION

The main objective of our study was to evaluate the usefulness of a model, based on easily available information, for the differential diagnosis of mycobacterial lymphadenitis in settings where TB is an increasing concern, as observed in many industrialized cities of Western Europe. The strength of our results is that it quantifies in a mathematical model what had been previously described by several authors.[9–12,15–17]

Suspicion of TB in otherwise healthy children can cause great anxiety for the parents; on the other hand, the delay in diagnosing and treating a case of TB in a young patient can lead to disease progression, more severe clinical presentation and worse prognosis. The process for the etiologic diagnosis of lymph node TB in children may be slow and insensitive. The sensitivity of mycobacterial culture varies depending on the sample method (tissue biopsy or fine-needle aspiration) and on microbiologic techniques used; it is usually less than 50%.[18–20] The use of new molecular tests like nested PCR may increase the yield of specimen identification in lymph node samples up to 96%, as described by Portillo-Gómez et al.[21] Similarly, culture identification of NTM varied from 20%[15,22] to a maximum of 75% under study conditions.[12]

The availability of a score system based on easily obtainable clinical-epidemiological and laboratory information may be of value. Algorithms have always been used to diagnose TB in children. Data on previous contact with a TB patient and a positive TST, associated with suggestive signs and symptoms of TB disease, are important tools that improve the accuracy of diagnosis, especially in resource limited countries where diagnostic resources are limited.[23] An abnormal chest radiograph is frequently found in primary TB and, when available, should be included in the algorithms for TB diagnosis in children. In our study, abnormal findings on chest radiograph in children with TB lymphadenitis was identified in 56% of patients, a higher frequency than that previously described by Marais et al (35%).[13] In our study the presence of abnormal findings on chest radiograph, being foreign born and increasing age were all variables independently associated with TB diagnosis in children with lymphadenitis.

Infectious diseases are a diagnostic dilemma in children with cervical lymphadenitis when malignancies have been ruled out. Acute localized cervical lymph node enlargement in children is mainly caused by pyogenic bacteria as *Staphylococcus aureus* and *Streptococcus pyogenes*. Some virus (cytomegalovirus, Epstein-Barr virus, adenovirus) or *Toxoplasma gondii* can also cause acute cervical lymphadenitis in children. There has been recent evidence of the increasing importance of *Bartonella* infections as cause of lymph node enlargement in children; *Bartonella* species may cause suppurative lymphadenitis associated with granulomatous lesions.[24–26]

Mycobacterial lymphadenitis has a more insidious onset and an indolent course when compared with lymph node enlargement caused by other infective agents. NTM lymph node disease in immunocompetent children is associated with painless lymph node enlargement that frequently evolves to abscess formation, causing a swollen fluctuant area and fistula formation in absence of systemic symptoms.[10,11,17] In United States and Western Europe NTM are responsible for the majority of cases of mycobacterial lymphadenitis among children, causing disease limited to lymph nodes of cervical and submandibular chains although involvement within the parotid gland is not infrequent.[9,12,17] Pulmonary or disseminated disease caused by NTM in children are frequently associated with immunodeficiency disorders although cases of pulmonary disease in immunocompetent children has already been reported.[9,27,28] Surgical excision of the affected lymph nodes is the therapy for choice for NTM lymphadenitis since antibiotic regimens are of limited efficacy due to natural resistance of most NTM; moreover, the use of antibiotics in young children is frequently associated with drug intolerance.[29] In our study, NTM were a minor cause of mycobacterial disease as a whole (83 cases, 28% of total), but it was the main etiologic agent of lymphadenitis, being responsible for 56% of lymphadenitis cases in Milan and 82% in Brescia.

TB lymphadenitis, on the other hand, is a common disease in endemic TB countries, being the most frequent site of extrapulmonary disease in children. The clinical course of TB lymphadenitis is usually similar to that of NTM, with subacute lymph node enlargement and, in absence of therapy, fistula formation ("scrofula"). Cervical lymph nodes are the most frequent site of disease but other lymph node chains (supraclavicular, axillary) may also be involved.[13,30,31] The treatment of TB lymphadenitis requires a 6-month course of therapy, with an initial 2-month course of rifampin, isoniazid, pyrazinamide, and ethambutol followed by a continuation phase of rifampin and isoniazid for 4 months.[8,32]

Our study has some limitations, mainly related to its retrospective design. Although performed by trained nurses the TST results were not regularly controlled for intra and interobserver variability and many children did not return to TST result reading. Some clinical and laboratory characteristics might have been missed in the analysis as they were not prospectively collected. For instance, the information regarding previous contact with a TB patient might be underestimated due to incorrect questioning or to limited information. Moreover, the small size of our sample of confirmed mycobacterial lymphadenitis limited the precision of our estimates, therefore the ability of the model to predict TB lymphadenitis should be validated by other studies involving larger samples. On the other hand, the differences found between probable and definitive cases of TB lymphadenitis in our study reinforce the need of culture confirmation and in its absence, the utility of probability models to increase the diagnostic accuracy.

REFERENCES

1. Brudney K, Dobkin J. Resurgent tuberculosis in New York City. HIV, homelessness, and the decline of tuberculosis control program. *Am Rev Respir Dis*. 1991;144:745–749.
2. Broekmans JF, Migliori GB, Rieder HL, et al. European framework for tuberculosis control and elimination in countries with a low incidence. *Eur Respir J*. 2002;19:765–775.
3. Falzon D, Ait-Belghiti F. What is tuberculosis surveillance in the European Union telling us? *Clin Infect Dis.* 2007;44:1261–1267.
4. Eriksson M, Bennet R, Danielsson N. Clinical manifestations and epidemiology of childhood tuberculosis in Stockholm 1976–1995. *Scand J Infect Dis*. 1997;29:569–572.
5. Rosenfeldt V, Paerregaard A, Fuursted K, et al. Childhood tuberculosis in a Scandinavian metropolitan area 1984–1993. *Scand J Infect Dis*. 1998;30: 53–57.
6. Walls T, Shingadia D. The epidemiology of tuberculosis in Europe. *Arch Dis Child*. 2007;92:726–729.
7. Newton SM, Brent AJ, Anderson S, et al. Paediatric tuberculosis. *Lancet Infect Dis*. 2008;8:498–510.
8. World Health Organization (WHO). Guidance for national tuberculosis programmes on the management of tuberculosis in children. Available at: http://whqlibdoc.who.int/hq/2006/WHO_HTM_TB_2006.371_eng.pdf.
9. Lincoln EM, Gilbert LA. Disease in children due to mycobacteria other than Mycobacterium tuberculosis. *Am Rev Respir Dis*. 1972;105:683–714.
10. Spark RP, Fried ML, Bean CK, et al. Nontuberculous mycobacterial adenitis of childhood. The ten-year experience at a community hospital. *Am J Dis Child*. 1988;142:106–108.
11. Hazra R, Robson CD, Perez-Atayde AR, et al. Lymphadenitis due to nontuberculous mycobacteria in children: presentation and response to therapy. *Clin Infect Dis*. 1999;28:123–129.
12. Haverkamp MH, Arend SM, Lindeboom JA, et al. Nontuberculous mycobacterial infection in children: a 2-year prospective surveillance study in the Netherlands. *Clin Infect Dis*. 2004;39:450–456.
13. Marais BJ, Gie RP, Schaaf HS, et al. The natural history of childhood intra-thoracic tuberculosis: a critical review of literature from the pre-chemotherapy era. *Int J Tuberc Lung Dis*. 2004;8:392–402.
14. R Development Core Team. R: A language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing, 2008. ISBN 3-900051-07-0. Available at: http://www.R-project.org.
15. Margileth AM, Chandra R, Altman RP. Chronic lymphadenopathy due to mycobacterial infection. Clinical features, diagnosis, histopathology, and management. *Am J Dis Child*. 1984;138:917–922.
16. Evans M, Smith NM, Thornton C, et al. Atypical mycobacterial lymphadenitis in childhood–a clinicopathological study of 17 cases. *J Clin Pathol*. 1998;51:925–927.
17. Wolinsky E. Mycobacterial lymphadenitis in children: a prospective study of 105 nontuberculous cases with long-term follow-up. *Clin Infect Dis*. 1995;20:954–963.
18. Starke JR, Taylor-Watts KT. Tuberculosis in the Pediatric Population of Houston, Texas. *Pediatrics*. 1989;84:28–35.
19. Khan RA, Wahab S, Chana RS, et al. Children with significant cervical lymphadenopathy: clinicopathological analysis and role of fine-needle aspiration in Indian setup. *J Pediatr*. 2008;84:449–454.
20. Jindal N, Devi B, Aggarwal A. Mycobacterial cervical lymphadenitis in childhood. *Indian J Med Sci*. 2003;57:12–15.
21. Portillo-Gómez L, Murillo-Neri MV, Gaitan-Mesa J, et al. Nested polymerase chain reaction in the diagnosis of cervical tuberculous lymphadenitis in Mexican children. *Int J Tuberc Lung Dis*. 2008;12:1313–1319.
22. Schaad UB, Votteler TP, McCracken GH Jr, et al. Management of atypical mycobacterial lymphadenitis in childhood: a review based on 380 cases. *J Pediatr*. 1979;95:356–360.
23. Hesseling AC, Schaaf HS, Gie RP, et al. A critical review of diagnostic approaches used in the diagnosis of childhood tuberculosis. *Int J Tuberc Lung Dis*. 2002;6:1038–1045.
24. Chow AW. Infections of the oral cavity, neck, and head. In: Mandell GL, Douglas RG, Bennett JE, et al, eds. *Mandell, Douglas, and Benett's Principles and Practice of Infectious Diseases*. 6th ed. Philadelphia: Elsevier Churchill Livingstone; 2005.
25. Bass JW, Vincent JM, Person DA. The expanding spectrum of Bartonella infections: II. Cat-scratch disease. *Pediatric Infect Dis J*. 1997;16:163–179.

26. Massei F, Gori L, Macchia P, et al. The expanded spectrum of bartonellosis in children. *Infect Dis Clin North Am*. 2005;19:691–711.
27. Nolt D, Michaels MG, Wald E. Intrathoracic disease from nontuberculous mycobacteria in children: two cases and a review of the literature. *Pediatrics*. 2003;112:434–439.
28. Wong KS, Lin TY, Huang YC, et al. Nontuberculous mycobacterial pulmonary disease in an immunocompetent adolescent. *Respir Care*. 2008; 53:908–911.
29. Lindeboom JA, Kuijper EJ, Bruijnesteijn van Coppenraet ES, et al. Surgical excision versus antibiotic treatment for non tuberculosis mycobacterial cervicofacial lymphadenitis in children: a multicenter, randomized, controlled trial. *Clin Infect Dis*. 2007;44:1057–1064.
30. Narang P, Narang R, Narang R, et al. Prevalence of tuberculous lymphadenitis in children in Wardha District, Maharashtra State, India. *Int J Tuberc Lung Dis*. 2005;9:188–194.
31. Shingadia D, Novelli V. Diagnosis and treatment of tuberculosis in children. *Lancet Infect Dis*. 2003;3:624–632.
32. Donald P, Maher D, Maritz S, et al; World Health Organization. Ethambutol efficacy and toxicity 2006. Available at: http://whqlibdoc.who.int/hq/2006/WHO_HTM_TB_2006.365_eng.pdf.