Objective: To review the treatment and outcome of patients with nontuberculous mycobacterial (NTM) cervical lymphadenitis.

Design: Retrospective chart review.

Setting: Tertiary care children’s hospital.

Patients: Thirty consecutive immunocompetent patients (median age, 32 months; age range, 11-147 months) diagnosed as having NTM cervical lymphadenitis over a 77-month period.

Interventions: Primary therapy for 34 foci of NTM cervical lymphadenitis in 30 children consisted of excisional biopsy (n=8), incision and drainage procedures (n=14), fine-needle aspiration biopsy (n=7), observation only (n=4), and antimycobacterial chemotherapy only (n=1).

Main Outcome Measures: (1) Time to cure, (2) recurrent adenitis, and (3) complications associated with therapy were determined for each therapeutic option. The average duration of follow-up was 32 months (range, 6-78 months).

Results: Nearly all patients (97%) were cured of their disease regardless of which therapeutic option was used. Excisional biopsy, while associated with transient marginal mandibular nerve injury in 1 patient, typically resulted in the most rapid resolution of disease. Observation alone did result in eventual cure, although the disease course was protracted. Simple incision and drainage without curettage was associated with prolonged postoperative wound discharge and hypertrophic scarring.

Conclusions: A variety of therapeutic options were used in children with NTM cervical lymphadenitis. Resolution of infection was an eventual outcome regardless of treatment option, although duration of disease, potential for facial nerve injury, and incidence of hypertrophic scarring varied among the different treatments. An individualized management approach is recommended, with excisional biopsy as the preferred option when feasible.


Prior to the 1950s, mycobacterial cervical lymphadenitis was a common childhood disease that was almost exclusively ascribed to Mycobacterium tuberculosis and Mycobacterium bovis. However, nontuberculous mycobacteria (NTM) are now the most frequent cause, accounting for up to 95% of cases.

In 1981, Saitz described the typical clinical course of NTM cervical adenopathy. A regional lymph node begins to enlarge. Early during the course, the overlying skin adheres to the underlying tissues. In weeks to months, the node develops fluctuance, with thinning and violaceous discoloration of the skin. Spontaneous drainage may then occur, continuing for months until medical or surgical intervention or natural resolution occurs. The proportion of infected lymph nodes that may resolve spontaneously is not known.

Surgical excision has been regarded widely as the treatment of choice for NTM cervical adenitis. However, a variety of other treatment options have been attempted in our hospital, with varying results. The purpose of the present study was to review the treatment and outcome of patients diagnosed with NTM cervical adenitis at a tertiary care children’s hospital.

Methods: Outpatient and inpatient records were retrospectively searched using International Classification of Diseases, Ninth Revision (ICD-9), codes 031.8 (mycobacterial disease not elsewhere classified) and 031.9 (mycobacterial disease not otherwise specified). Also, the hospital microbiology database was searched for
positive NTM specimens obtained from abscess contents or lymph node tissue. The search period ranged from May 1, 1995 (the earliest date the computerized databases could track records), to October 22, 2001 (the actual date the computerized records were queried). Patients with evidence of immunodeficiency, NTM infection of a noncervical site, or incomplete medical records were excluded from further analysis. This study was determined to be exempt from hospital Human Rights Committee review under 45 Code of Federal Regulations 46.101(b)(4).

The information sought via chart review included demographic data; medical history; physical examination and clinical test results; treatment administered; time to cure; disease recurrence; and complications associated with therapy. Clinical material submitted to the microbiology laboratory was routinely inoculated into commercially available mycobacteria growth indicator tubes (Becton Dickinson, Cockeysville, Md). As soon as any mycobacterial growth was identified, the specimen was assayed for the presence of Mycobacterium avium complex and M tuberculosis using a commercially available single-stranded DNA probe with a chemiluminescent label that is complementary to the target organism ribosomal RNA (GenProbe Inc, San Diego, Calif).

RESULTS

CLINICAL FEATURES

Thirty-nine patients who had been diagnosed as having NTM infection were identified over the 77-month study period. Nine patients were excluded because of pulmonary NTM infection (n=3), immune deficiency (n=2), NTM adenitis of the groin (n=2), postoperative NTM infection of the soft tissue of the foot in an adult (n=1), and cervical NTM adenitis with incomplete documentation of treatment (n=1). The remaining 30 patients were diagnosed as having NTM cervical adenitis, and chart documentation was complete. The average age at the time of diagnosis was 36 months (median age, 32 months; age range, 11-147 months). There were 16 girls and 14 boys. Four patients (13%) had experienced recent constitutional symptoms at the time of diagnosis.

Nontuberculous mycobacterial adenitis was diagnosed within 6 months of presentation (median, 4 weeks) in all but 1 patient, who was initially presumed to have adenitis due to M tuberculosis. Twenty-eight patients (93%) received at least 1 course of antibiotic directed against gram-positive organisms before the diagnosis was made. A single mass was identified on clinical examination in 25 patients (83%). Two masses were present in 4 patients (13%), and multiple adenopathy was found in 1 patient (3%). Overall, there were 34 discrete foci of NTM adenitis in the 30 patients. The masses were found in the following anatomic regions: submandibular (n=17, 50%), anterior cervical (n=6, 18%), preauricular/parotid (n=5, 15%), submental (n=3, 9%), and posterior cervical (n=3, 9%).

Nontuberculous mycobacterial adenitis was diagnosed in the following manner: (1) positive results on DNA probe testing for M avium complex in 14 (56%) of 25 patients tested with this technique, or (2) "typical clinical picture" with positive acid-fast bacilli on tissue staining, a reactive tuberculin skin test, and/or characteristic histological findings. Staining for acid-fast bacilli was positive in 22 (92%) of 24 tissue specimens. The results of tuberculin skin testing in 21 patients were "intermediate" (7-15 mm of induration) or negative in 8 (38%) and 9 (43%) patients, respectively. Routine cultures were negative for bacteria and fungi in all cases.

The size of the neck mass based on clinical examination ranged from 1 to 6 cm (mean, 2.5 cm). Mild tenderness was present in only 4 patients. Two patients presented with pain, fever, and an elevated white blood cell count. Defervescence after intravenous antibiotic therapy directed against gram-positive organisms suggests that a conventional bacterial pathogen may also have been present. Overlying skin changes were described at presentation in 17 (50%) of 34 masses, and typically involved bluish purple discoloration or erythema with frequent thinning, peeling, and scaling.

LABORATORY EVALUATION

Computed tomography with intravenous contrast was performed in 16 patients (53%). Although multifocality of lymphadenopathy was appreciated on clinical examination in only 5 patients (17%), computed tomographic images demonstrated clusters of lymph nodes, some with central areas of low attenuation suggestive of necrosis, in 10 (63%) of 16 disease foci. Plain chest radiographs were obtained in 13 patients (43%); no pulmonary disease was detected. Bartonella and Epstein-Barr virus titers were frequently obtained and were negative in each case. Tuberculin skin testing of parents and close contacts was performed in 9 cases (30%); all results were negative.

White blood cell counts were obtained in 16 patients (53%) and were abnormal only in the 2 patients with NTM adenitis who originally presented with an acute pyogenic abscess (21800 mm3 and 20500 mm3, respectively). Levels returned to normal after the patients underwent antibiotic therapy directed against gram-positive organisms.

TREATMENT

Twenty-two foci of NTM adenitis were treated with a neck incision and either excisional biopsy (n=8) or incisional biopsy with or without curettage (n=14). Another 12 foci were treated with other techniques, including fine-needle aspiration (FNA) (n=7), clarithromycin therapy alone (n=1), and observation only (n=4). Average follow-up time for all patients was 32 months (range, 6-78 months).

Of the 8 patients who underwent excisional biopsy, 7 healed within 2 to 3 weeks after surgery with a small linear scar, and 1 experienced 13 months of postoperative scab formation and violaceous skin discoloration. One patient experienced weakness of the right side of the lower lip that required 4 months to resolve, while another patient developed a postoperative seroma that required surgical drainage. Of the 14 patients who had masses that were treated with "incision and drainage" procedures with either incisional biopsy or curettage, 8 had postoperative drainage from the incision site that persisted for 2 1/2 to 12 months, and 5 who underwent simple incision and drainage without extensive tissue biopsy or...
curettage had long-term hypertrophic, erythematous scarring. Disease resolution was ultimately confirmed in 21 of the 22 patients who were treated with a neck incision, while 1 patient with a persistent fluctuant mass after incision and drainage was unavailable for follow-up at 6 months.

Seven foci of NTM cervical adenitis were initially managed with FNA. Drainage from the biopsy site occurred in 3 patients (43%), persisting for 6 weeks to 5 months. In 2 patients, the disease eventually resolved completely after FNA. However, because of progression of disease, 5 patients underwent further open surgical procedures an average of 5 months after FNA, with all patients eventually cured.

One patient with NTM adenitis of the preauricular region directly adjacent to the parotid gland was treated with a 10-week course of clarithromycin. The lesion drained spontaneously during the first 2 weeks of therapy, but had resolved with a residual reddish skin tint by 8 months.

Four foci of NTM adenitis were simply observed, with an average follow-up of 52 months (range, 36-71 months). Spontaneous drainage occurred from 2 masses during the observation period. In all cases, the disease ultimately resolved, after an average of 20 months (range, 5-34 months). The final results were similar: a small pockmark or dimple of the skin, with normal skin color and no mass.

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**COMMENT**

The ubiquitous presence of NTM organisms in the environment, along with the propensity for toddlers to put objects in their mouth, may account for the typical age group (age range, 1-5 years) and location (submandibular and anterior cervical) in which NTM cervical adenitis is often found. The differential diagnosis of NTM cervical adenitis includes tuberculosis (scrofula), cat-scratch disease, pyogenic abscess, histoplasmosis, toxoplasmosis, infectious mononucleosis, parotitis, salivary duct stone or tumor, branchial cyst, and lymphoma.

The diagnosis can be difficult to make definitively, as a positive culture for NTM is generally obtained from only 40% to 50% of lymph nodes that are suspected to be infected with NTM. The most common isolate in recent years has been M. avium complex. Other typical findings in patients with NTM adenitis, in addition to the clinical features described above, include intermediate induration (6-14 mm) after Mantoux testing, presence of acid-fast bacilli on tissue staining, and histological identification of caseating granulomas. Use of computed tomographic scanning may not be indicated on a routine basis for NTM cervical adenitis, but may be helpful when other diseases (eg, lymphoma or branchial cyst) are being considered in the differential diagnosis.

Excisional biopsy is widely regarded to be the treatment of choice for NTM cervical adenitis, with complete resolution of disease reported in 80% to 96% of patients. Local drainage lasting from 1 to 6 months after excision has been reported in up to nearly 10% of patients, and transient facial paresis has been reported in 3% to 50% of patients.

Because of persistent drainage from the incision site (73% to 100% of cases), low cure rates (no higher than 40%), and a high incidence of secondary surgical procedures (in up to 90% of patients), incision and drainage alone without complete excision of the infected disease focus has generally been discouraged as a treatment option for patients with NTM cervical adenitis. Incision and curettage has been suggested as an appropriate treatment for NTM cervical adenitis when fluctuance, skin necrosis, and/or close proximity to the facial nerve is present. High cure rates, with excellent cosmetic results and rapid healing (2-4 weeks), have been reported, although delayed healing (up to 5-7 months) can occur. Recurrence rates of 10% to 20% have been described. Facial nerve injury has not been reported with this technique.

The role of FNA in the diagnosis and management of NTM cervical adenitis is not clear. Some authors advocate routine use of FNA to obtain diagnostic material in patients with NTM adenitis. Others have promoted FNA as a therapeutic technique, claiming FNA results in no facial nerve injury, acceptable scarring, and disease resolution within 1 year. Detractors of FNA in NTM cervical adenitis report an increased risk of chronic draining sinuses, scattering, and failure to heal after the procedure.

Although most NTM organisms cultured from infected cervical lymph nodes have shown resistance to treatment with all the usual first-line antituberculous drugs, such as isoniazid, ethambutol, pyrazinamide, streptomycin, and rifampin, several recent case reports have suggested that NTM lymphadenitis in immunocompetent children may be effectively treated with macrolide antibiotics such as clarithromycin or azithromycin. The cure rate in a series of 10 patients treated with a macrolide regimen was 50%; complete resolution of disease was noted within 3 to 7 months. The appropriate duration and established efficacy of macrolide therapy are not known.

The use of observation as a management option for patients with adenitis caused by NTM has been infrequently explored. Concerns regarding local drainage, persistent adenopathy, and spontaneous enlargement after a period of quiescence have been cited. However, in a study of 5 children with cervicofacial NTM adenitis, all 5 patients had resolution with observation alone in 8 to 27 months, although residual irregular scarring was noted.

Based on the results of the present study and literature review, it is recommended that treatment of NTM cervical adenitis should be individualized. We have identified the following factors that influence decision making: (1) potential for facial nerve injury, (2) cosmetic results, (3) parental tolerance for a protracted clinical course, and (4) status of the lesion (eg, skin loss and active drainage). It should be explained to parents that spontaneous resolution will eventually occur, but may require time (average of 20 months, up to 34 months). If the diagnosis is uncertain, FNA may be considered to obtain a tissue specimen, but one should be prepared for the possibility of persistent drainage from the aspiration site and the potential need for definitive surgery. If the
mass is in an accessible location and the overlying skin is intact, excisional biopsy with skin preservation, if possible, is recommended. For masses in the submandibular region, the surgical risk of marginal mandibular nerve injury should be discussed preoperatively. If a focus of NTM adenitis is present within the parotid gland, observation is recommended; treatment with a macrolide antibiotic and/or incision and curettage may also be considered. In the presence of significant fluctuance, skin breakdown, or spontaneous drainage, either incision and curettage or observation with or without macrolide therapy is recommended. A simple incision and drainage procedure without curettage is discouraged, as it may lead to prolonged drainage and unsightly scarring.

Accepted for publication August 8, 2002.

This study was presented as a poster at the 17th Annual Meeting of the American Society of Pediatric Otolaryngology, Boca Raton, Fla, May 13-14, 2002.

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REFERENCES