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Cervicofacial nocardiosis in children

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APPROXIMATELY 500 to 1,000 nocardial infections are estimated to occur in the United States each year. *Nocardia* usually causes opportunistic infections in the compromised host; however, infection may occur in patients without a predisposing condition.¹ Most childhood infections are pulmonary or systemic²; skin or subcutaneous infections are infrequently reported.³⁻⁵

Recently, we have evaluated three children with cervicofacial nocardiosis. Their cases are summarized here to emphasize the unique clinical presentation, ease of diagnosis, and prompt response to appropriate therapy of this form of nocardiosis, as well as the lack of association with any immune deficiency.

CASE REPORT

Patient 1, a 22-month-old Caucasian girl, was hospitalized because of a pustular facial lesion and swelling in the left submandibular area. Two weeks before admission she received amoxicillin for ten days orally for a draining ear. The ear drainage ceased and two days before admission she developed a

pustule beneath the left naris. The patient received erythromycin orally; however, the pustule increased in size and the patient developed fever and a 2 × 4 cm red and tender submandibular lymph node, which prompted admission. Initially the patient was treated with methicillin parenterally, but the pustule and lymphadenopathy worsened and an incision and drainage was performed after three days. After 72 hours of incubation on the blood agar plate, *Nocardia brasiliensis* was isolated from the small amount of purulent material obtained at surgery. A culture of the pustule was reported as having no growth on blood agar after 48 hours. The patient was treated with trimethoprim/sulfamethoxazole orally with resolution of the pustule and lymphadenopathy. Quantitative immunoglobulin values were within the normal range.

Patient 2, a 5-year-old Caucasian boy, first developed an erythematous papule on his left cheek. Five days later he was given cephalexin orally after the lesion was cultured. The following day methicillin was given intramuscularly, but he developed a 3 × 3 cm tender left submandibular node and fever, and was hospitalized and given methicillin intravenously. His lymphadenopathy increased despite therapy. The culture of the cheek lesion grew *Nocardia brasiliensis* after 72 hours of incubation on blood agar. The patient received trimethoprim/sulfamethoxazole by mouth for four weeks and the submandibular lymph node enlargement resolved. The skin lesion on the cheek gradually improved after one month of therapy.

Patient 3, a 3-year-old Oriental girl, developed progressive swelling in the left submandibular area followed by a small draining pustule on the left naris. The following day she developed fever and was treated with penicillin. Because there was no response to treatment, she was hospitalized. A Gram stain

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of material from the nasal pustule and from an aspirate from the lymph node showed beaded, gram-positive, filamentous branching rods. Both cultures grew *Nocardia caviae*. She was treated for three months with trimethoprim/sulfamethoxazole by mouth and her skin lesion and lymphadenopathy resolved.

DISCUSSION

Primary cutaneous nocardiosis and the nocardial lymphocutaneous syndrome mimicking sporotrichosis have been described in adult patients.⁶⁻⁹ Among children, however, primary nocardial skin and lymph node infections have been reported infrequently,³⁻⁵ and *Nocardia* is unappreciated as an etiology of lymphadenitis. Common etiologies for cervical lymphadenitis in children include *Staphylococcus aureus*, Group A streptococci, and atypical mycobacteria. The presence of a pustule in association with cervical lymphadenitis suggests other potential etiologies as well, including tularemia, plague (*Yersinia pestis*), cutaneous diphtheria, cat scratch disease, cervicofacial actinomycosis, and sporotrichosis.

Among 347 nocardia isolates from man, 83.3% were *N. asteroides*, 6.9% were *N. brasiliensis*, 2.9% were *N. caviae* and 6.3% were identified as *Nocardia* sp.¹ *N. asteroides* isolates were associated with pulmonary, systemic, or primary central nervous system infections, whereas more than 50% of the *N. brasiliensis* isolates were from skin or soft tissue infection. *N. brasiliensis* can be associated with mycetomas, abscesses, pustules, and cutaneous abscesses, and over 90% of cutaneous disease with lymphatic involvement of an extremity in adults ("sporotrichoid" lymphocutaneous syndrome³) has involved this species. Nocardial isolates were speciated by the Houston City Health Department.¹⁰ *N. brasiliensis* was isolated from two of the three children reported here with the cervicofacial syndrome and from one of the two previously reported cases in the literature, thus supporting the observation that *N. brasiliensis* is the most common *Nocardia* sp. involving the skin, especially when lymph node involvement also is present.

A careful surveillance of *Nocardia* isolates from hospital laboratories and the Houston City Health Department (which serves as a reference laboratory for the city), and of cases referred to the Infectious Disease Services of the various hospitals has been maintained in Houston since 1975. During that time 20 cases of primary cutaneous nocardiosis were identified. Three of these were in children and these were the only cases that involved the face. During the same time period only two children were seen with pulmonary nocardia infection (R. J. Wallace, Jr., M.D., personal communication). A review of cutaneous isolates of *Nocardia* reported to the State Health Laboratory in Austin, Texas, over a three-year period revealed 24

additional cases of primary cutaneous disease, of which three were in children. Two of these involved the extremities; the third involved the face. As had been noted with the cases from Houston, none of the adult patients had cervicofacial involvement. (Joe Steadham, Ph.D., personal communication).

Nocardia sp are found in the soil worldwide, and no direct man-to-man or animal-to-man transmission has been documented. Although a history of trauma was not found in our patients (as it has been with most cases reported in adults), the isolation of *Nocardia* sp. from both pustule and regional lymph nodes suggests that the organism was introduced into the skin from the environment and involved the regional lymph nodes via lymphatic spread. The frequent involvement of the nose and cheek as the primary site of involvement in children but not in adults is unexplained. Perhaps the playing habits of children, contamination with soil, and the blood and lymphatic supply of this area contribute to this characteristic clinical picture.

Nocardia sp. grow well aerobically on blood or chocolate agar at 37°; however, it may take from two to five days for colonies to be visible. Gram stain is important since the presence of gram-positive, branching rods should alert the laboratory to hold the plates for one week rather than the standard 48 to 72 hours. Since the Gram stain is often negative, all plates should be held for one week.⁶

Each of our patients received trimethoprim/sulfamethoxazole orally for one to three months and had prompt resolution of fever and lymphadenitis, and gradual improvement in the pustule. Sulfonamides have been the drug of choice for nocardial infections. Recent clinical and laboratory assessment of trimethoprim/sulfamethoxazole indicates that this drug is highly effective for the treatment of nocardiosis; in vitro synergy between the two drugs is usually apparent when ratios of 1:5 trimethoprim/sulfamethoxazole or better are achieved.¹¹ Side effects are unusual but one patient developed a reversible leukopenia while receiving therapy.

All three patients were in good health prior to their infection and subsequently have remained well, with no unusual or recurrent infections. All patients had normal white blood cell function as determined by chemiluminescence. Thus, it appears that the development of cervicofacial nocardiosis can occur in normal children. It is not necessary to undertake an exhaustive evaluation of the patient's immunologic status if there is a prompt clinical response to therapy.

Pediatricians should be aware that *Nocardia* sp. in children may present as a cervicofacial syndrome and cause cervical adenitis. In particular, patients who are not

responding to "standard" therapy should be suspected of having a nocardial infection. Gram stain of pustules and aspirates, and incubation of material for culture on blood agar for one week will identify *Nocardia* sp. Trimethoprim/sulfamethoxazole given orally results in rapid clinical improvement. Prompt diagnosis and treatment will eliminate the need for inappropriate parenteral antibiotics, and should eliminate the need for surgical drainage.

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Transient T-cell depression in postoperative chylothorax

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THE CELLULAR COMPONENT of chyle contains predominantly lymphocytes of the T-cell type.^{1, 2} The removal of thoracic duct lymph has been shown to reduce cellular immunity in human beings^{3, 4} and to deplete thymic-dependent lymphoid tissues in calves.⁵ To establish if a deficiency in T-lymphocyte numbers occurs in patients with chylothoraces following thoracic surgery, we examined T-lymphocyte numbers in three patients who developed postoperative chylothoraces.

MATERIALS AND METHODS

Patients and controls. Three patients who developed transient chylothoraces following surgical correction of tracheoesophageal fistula, diaphragmatic hernia, and

transposition of the great vessels, respectively, were studied (Table). Patient 3 required a second surgical procedure for revision of the initial correction eight months after the first surgery. He again developed a postoperative chylothorax. Controls matched for age, surgical procedure, and postoperative time under similar stress as the patients were also studied.

Lymphocyte studies.

Peripheral blood. Absolute lymphocyte numbers were determined from the percentage of the total leukocyte count as seen on the complete blood count, using a Coulter electronic cell counter, and differential coatings of Wright-stained smears.⁶

Peripheral blood lymphocytes were isolated from venous blood on Ficoll-Hypaque gradients. T-lymphocyte numbers were determined by producing E-rosettes with sheep erythrocytes.⁷ B-lymphocyte numbers were determined by incubating the lymphocytes with fluorescein-labeled anti-Ig and determining the percentage of fluorescent cells.⁷

Chyle. Ten milliliters of chyle drainage were centrifuged at 900 g (200 rpm) for 25 minutes and washed four

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