

Atypical Mycobacterial Cervical Lymphadenitis Associated with Sweet's Syndrome

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We report the case of a 52-year-old woman with a non-tuberculous (atypical) mycobacterial cervical lymphadenitis, caused by *Mycobacterium fortuitum*, in association with Sweet's syndrome. The cervical lymphadenitis was resistant to medical treatment, and the Sweet's syndrome occurred intermittently. Systemic steroid treatment was required to control the cutaneous symptoms.

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Mycobacterial lymphadenitis is still a common and often poorly treated disease. Cervical lymph nodes are most frequently involved. Although non-tuberculous mycobacterial cervical lymphadenitis is frequently seen in children, it is only rarely encountered in adults, in whom *Mycobacterium tuberculosis* clearly preponderates as the cause of mycobacterial cervical lymphadenitis. Most recently, reviews have concentrated on the best means to differentiate between tuberculous and atypical mycobacterial infections of the cervical nodes, since both diagnostic methods and treatment choices differ for these two groups of diseases. Multidrug antituberculous (antiTB) chemotherapy is the mainstay of treatment in tuberculous lymphadenitis; most of these drugs offer little for treatment of patients with atypical mycobacterial lymphadenitis, and surgical intervention to remove all involved nodes is usually indicated.

Sweet's syndrome (acute febrile neutrophilic dermatosis) was first described in 1964. Many etiologic factors, including various infectious, inflammatory, neoplastic and miscellaneous disorders, have been reported to be associated with the syndrome. However, to our knowledge, no case of atypical mycobacterial infection has been reported in association with Sweet's syndrome in the English literature. This report concerns an adult patient presenting with *Mycobacterium fortuitum*-induced cervical lymphadenitis in association with Sweet's syndrome. A brief review is also presented.

CASE REPORT

A 52-year-old woman began to experience recurrent, painful skin eruptions in December 1991. The skin lesions were mainly composed of reddish papules and nodules of various sizes. They occasionally disappeared but then returned, and either relieved spontaneously or by alternative medical treatments. Left neck lymphadenopathy was found in May 1992. A lymph node biopsy, performed at a local medical institution, revealed granulomatous inflammation and caseous necrosis, with acid-fast stain positive organisms. A culture of the lymph node biopsy specimen was done and sent to a reference laboratory, but the result was not available. Tuberculosis of the lymph nodes was assumed and three combined antiTB regimens (isoniazid, rifampin and ethambu-

tol) were then initiated. However, episodes of rapid enlargement of the preexisting neck mass, accompanied by simultaneous development of generalized painful skin lesions, were still noted despite vigorous antiTB treatment. Constitutional symptoms, such as fever, joint pain and sore throat, were other complaints.

The patient visited the Department of Dermatology at the National Taiwan University Hospital in January 1993. At presentation, physical examination showed one hen egg-sized, lobulated, elastic-firm subcutaneous mass with overlying erythematous plaques located over the left submandibular area. Some discrete smaller nodules were noted at the lower part of the left side of the neck. Many edematous, erythematous papules, plaques and nodules of various sizes were distributed over the trunk and extremities (Figs. 1 and 2). Some of these were studded with pustules. Small ulcers following rupture of the pustules were also seen. In addition, typical pustular formation (pathergy phenomenon) over venipuncture and biopsied sites was noted. No oral ulcer, genital ulcer, scar or eye lesions were found. Transient fever (37.4°C) and mild leukocytosis (13,730/ul) were noted. Laboratory findings as well as special diagnostic procedures revealed no evidence of underlying autoimmune and immunodeficiency disorders (including HIV infection), internal malignancies or other infectious foci, except old fibrotic lesions over the right upper lobe and lymphadenopathy in anterior mediastinum and right tracheobronchial region. One skin biopsy and one lymph node biopsy specimen were obtained. Histologically, the skin lesion showed marked edema in the upper dermis, and dense polymorphous cellular infiltration in the middle to lower dermis. The infiltrate extended somewhat into subcutis and was mainly composed of neutrophils and, to a lesser extent, eosinophils (Fig. 3). Vascular changes, such as endothelial swelling, perivascular neutrophil infiltration and some nuclear dust were noted; however, no frank vasculitis developed. No acid-fast organisms were found. Mycobacterial culture from skin lesions was also negative. The lymph node biopsy specimen yielded granulomatous inflammation, caseous necrosis, scattered neutrophil infiltration as well as nonspecific reactive sinus histiocytosis. Langhans' giant cells were also seen. In the subcutaneous tissue adjacent to the lymph node, there was septal and lobular infiltration of many neutrophils.

Prophylactic antibiotics, including erythromycin and cephalixin, and a fourth antiTB agent, pyrazinamide, were added, but without clinical improvement. Dapsone 100 to 150 mg per day was tried, but only a temporary effect was noted. A systemic steroid, prednisolone 15 mg three times a day, was then given, under the coverage of four combined antiTB regimens, and both the cutaneous lesions and the lymphadenopathy improved dramatically. The skin eruption began to resolve within a few days and was almost cleared away after 2 weeks, leaving no scars. The enlarged, swollen cervical lymph nodes diminished in size at first and then remained stationary. The patient was discharged and regularly followed-up by the Out-Patient Department. When oral prednisolone was tapered to 20 mg per day, another episode of rapid enlargement of the neck mass with simultaneous development of similar skin lesions was noted. The skin lesions were well controlled again by systemic steroid treatment (prednisolone 60 mg per day), and the lymph nodes returned to their original sizes. During the tapering course, no recurrence of skin lesions was noted; however, the cervical lymphadenopathy persisted. Later, *Mycobacterium fortuitum* was isolated from the lymph node biopsy specimen, proving to be resistant to all antiTB drugs tested, including isoniazid, ethambutol, rifampin, pyrazinamide, para-aminosalicylic acid, kanamycin, streptomycin and enviomycin (tuberactin). The culture result, from a reference laboratory, of the lymph node biopsy specimen obtained in the aforementioned medical institution also revealed the same organism. A diagnosis of *Mycobacterium fortuitum*-induced cervical lymphadenitis was confirmed. AntiTB



Fig. 1. Many edematous, erythematous papules and nodules can be noted over the extremities.

Fig. 2. One erythematous, edematous small plaque with an "illusion of vesiculation".

Fig. 3. Marked edema in upper dermis and an infiltrate composed predominantly of neutrophils and, to a lesser extent, eosinophils in mid-lower dermis. (H&E, 40x).

treatment was discontinued. The patient has experienced many similar attacks subsequently, and the symptoms were relieved by systemic steroids. Because of the relatively low cure rate by medical treatment for atypical mycobacterial lymphadenitis, surgical management to remove the involved lymph nodes was suggested but refused by the patient. Ofloxacin, amikacin, cefoperazone and minocycline were later tried but proved useless. In April 1994, severe pleural effusions, interstitial pneumonitis, cervical lymphadenitis and painful skin lesions developed. She received a combination of ciprofloxacin and imipenem. Short-term systemic steroid was used, and skin lesions resolved. The infiltrative pulmonary disorder improved gradually, and neck lymph nodes not only returned to their original sizes but diminished further in size. Unfortunately, progressive headache and consciousness changes were noted, and eventuated in severe subarachnoid and intracranial hemorrhage. *Candida albicans* was isolated from blood cultures. The patient's general condition deteriorated, and she died in June 1994. Autopsy was refused by the family.

DISCUSSION

In this patient, metastatic tuberculous abscess and tuberculid were taken into account at first. However, the painful and non-scarring characters of skin lesions, the poor responses to anti-TB regimen, lack of granulomatous reaction and/or vasculitis as well as absence of causative organisms, *Mycobacterium tuberculosis*, told against such a diagnosis. In addition, the use of steroids in active mycobacterial infection does constitute a dilemma. To our belief, steroids can be used, with caution, if steroid therapy is indicated and is under the coverage of an anti-mycobacterial regimen. The use of systemic steroids in similar situations, such as sepsis, reactional states of leprosy and tuberculous meningiomyeloradiculitis (1) for limitation of severe inflammatory sequelae, has also been reported.

In 1986, Su & Liu reviewed five cases of Sweet's syndrome

with typical clinical and histological features (2), suggesting that it was a reactive phenomenon. Many etiologic and pathogenetic factors had been speculated, indicating that Sweet's syndrome was an unusual inflammatory manifestation of cutaneous hypersensitivity to antigens from various infectious, inflammatory, neoplastic and miscellaneous disorders (3). In the presented case, the diagnosis of atypical mycobacterial cervical lymphadenitis and Sweet's syndrome was confirmed on the basis of characteristic clinical, histologic and laboratory findings. Some facts have suggested a close, even causal, association rather than a coincidental link between these two disorders. First, exacerbation and amelioration of skin lesions are always accompanied by enlargement and shrinkage of involved nodes. Second, although the skin lesions responded to systemic steroid, the involved nodes merely returned to their original sizes and never disappeared. Third, when the involved nodes improved further after initiation of ciprofloxacin and imipenem, no more new skin lesions recurred elsewhere, even without the anti-inflammatory effect of systemic steroid. The skin manifestations and the enlargement of preexisting lymphadenopathy might result from distant and local inflammatory reactions to chronic and episodic release of mycobacterial antigens from involved nodes. This could be explained by accumulation of neutrophils in skin lesions and around lymph nodes. On the other hand, the persistence of lymphadenopathy can be attributed to a multidrug-resistant *Mycobacterium fortuitum* infection. Pulmonary manifestations were probably caused by infectious or reactive processes, since no causative organisms were identified.

Up to 1993, various infectious diseases, including salmonellosis, streptococcosis (URI), urinary tract infection (*E. coli*), leprosy, tuberculosis, yersiniosis, histoplasmosis, toxoplasmosis and BCG or tuberculin reaction-related conditions, have been reported to be associated with Sweet's syndrome (37). To our knowledge, this is the first case report in the English literature of atypical mycobacterial infection in association with Sweet's syndrome.

Diseases caused by atypical mycobacterium have become increasingly frequent as tuberculosis incidence has declined.

With regard to mycobacterial infection of lymph nodes, in most patients younger than 12 years, the cause is non-tuberculous mycobacteria; older patients had tuberculous lymphadenitis. *Mycobacterium scrofulaceum* has been reported as the most common world-wide etiologic agent of atypical mycobacterial lymphadenitis, while *Mycobacterium avium-intracellulare* complex appears to cause the majority of cases in the United States (8, 9). In the presented case, the infection was caused by *Mycobacterium fortuitum*, a relatively uncommon causative agent. The infection is initially confined to cervical lymph nodes, with intermittent cutaneous reactions. After repeated episodes of similar attacks, pulmonary manifestations supervened and the patient eventually died of hemorrhagic complications of the central nervous system. The importance of early recognition and prompt treatment of this infection are emphasized, in the hope that this approach might reduce complications and improve survival chances.

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