Sarcoidosis is a multiorgan granulomatous disease, the most common head and neck manifestation of which is cervical lymphadenopathy. Only the presentation of sarcoidal granuloma in cervical lymph nodes without typical manifestations of systemic sarcoidosis poses a diagnostic difficulty. We describe the case of a 39-year-old male who had a 2-month history of a progressively increasing mass with soreness in his right neck. The biopsy from the neck mass demonstrated non-caseating epithelioid cell granuloma of the lymph nodes. The differential diagnoses of mycobacterial or fungal infections were excluded. Thoracic evaluations, including chest X-ray and high-resolution computed tomography, revealed no abnormal findings. Treatment with systemic corticosteroids resulted in improved clinical symptoms. No recurrence of the neck mass or other signs of systemic sarcoidosis were noted during 1.5 years of follow-up. Although our patient’s definitive diagnosis could not be determined, the case highlights important issues: sarcoidal granuloma in lymph nodes may be a precursor of sarcoidosis, even in the absence of pulmonary or other systemic involvement; and regular follow-up is recommended in such cases. [J Chin Med Assoc 2005;68(7):339–342]

Key Words: granuloma, lymph node, neck, sarcoidosis

Introduction

Sarcoidosis is a multisystemic granulomatous disorder of unknown cause that is characterized by non-caseating epithelioid cell granulomas in affected organs, particularly the lung, hilar lymph nodes, skin and eyes. While the diagnosis of sarcoidosis depends on clinical manifestations and histopathologic findings, the presence of sarcoidal granuloma is not specific for sarcoidosis. Clinically, there are many conditions resulting in sarcoid-like granulomas that may be interpreted either as a local reaction to a malignancy, or as a non-caseating reaction to a focus of cavitating tuberculosis or other inflammatory disease. These known granulomatous diseases should be excluded in patients without typical symptoms of sarcoidosis.

Sarcoidosis has various presentations, such as bilateral hilar lymphadenopathy, pulmonary infiltration, and cutaneous and ocular lesions. Bilateral hilar lymphadenopathy is the earliest and most common intrathoracic manifestation of sarcoidosis. Although peripheral lymphadenopathy is also observed during the course of sarcoidosis, it is an uncommon initial presentation. The presentation of sarcoidal granuloma in peripheral lymph nodes, without clinical findings suggestive of sarcoidosis elsewhere, poses a diagnostic problem. Our patient had a sarcoidal granuloma restricted to cervical lymph nodes and a suspected diagnosis of sarcoidosis. It should be emphasized that in patients who present with sarcoidal granuloma in peripheral lymph nodes, a diagnosis of sarcoidosis may only be made months or years later. This report discusses the possibility of sarcoidal granuloma becoming true sarcoidosis, and the importance of follow-up in patients with sarcoidal granuloma in peripheral lymph nodes.

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Case Report

A 39-year-old male had suffered from a progressively increasing mass and soreness in the right neck for 2 months. He had no symptoms of dyspnea, chest pain, fatigue, fever or weight loss. Four years previously, he had undergone excision biopsy at the same site in the right neck; the diagnosis, at another hospital, had been pseudotumor. The patient’s medical records revealed no tuberculosis or sexually transmitted diseases, and no significant family history.

Physical examination revealed a scar over the right upper neck skin, and multiple palpable, non-tender, firm and mobile lymph nodes in both sides of the neck. The largest node was about 2.0 × 1.5 cm in the posterior triangle of the right neck. There was no enlargement in either parotid gland, and no splenomegaly or hepatomegaly. Magnetic resonance imaging indicated multiple, bean-shaped, homogeneous lymph nodes about 1.0–1.5 cm in size in both sides of the neck (Figure 1). Preoperative chest X-ray and electrocardiography were normal. Laboratory data, including complete blood cell counts, erythrocyte sedimentation rate, liver function, renal function, serum calcium, and urinalysis, were within normal limits. Incision biopsy of the neck mass was performed. Histology revealed a typical non-caseating epithelioid cell granuloma in the lymph nodes that was compatible with sarcoidal granuloma (Figure 2). Stains for acid-fast bacilli and fungi were negative, and a polymerase chain reaction (PCR) of the biopsy tissue was negative for mycobacteria.

Further evaluation with computed tomography of the chest revealed no enlarged lymph nodes or lung infiltration. As the patient’s neck soreness had become worse with time, treatment was started with low-dose prednisolone 20 mg/day. After 1 week of treatment, the patient’s neck soreness had improved dramatically, and the remaining enlarged lymph nodes had resolved almost completely. The dosage of prednisolone was tapered to 10 mg/day for another week; the drug was then discontinued in the third week. According to the histologic examination and clinical response to treatment, a suspected diagnosis of sarcoidosis was considered. No recurrence of the neck mass, or signs of other systemic sarcoidosis, were found in the follow-up period of 1.5 years.

Discussion

Lymphadenopathy in the head and neck often results from nonspecific inflammation, common hyperplasia,
Sarcoideal lymph nodes

Sarcoideal lymph nodes are a manifestation of sarcoidosis, a multisystem disease characterized by the development of non-caseating epithelioid granulomas. The diagnosis of sarcoidosis is based on physical examination, radiologic and laboratory findings, and histologic examination. Most patients present with constitutional symptoms, such as cough, dyspnea, fever, fatigue, arthralgias, or ocular and cutaneous symptoms; more than 90% have abnormal chest radiography. Laboratory findings include an elevated level of angiotensin-converting enzyme, hypercalcemia, hypercalciuria, hypergamma globulinemia, increased erythrocyte sedimentation rate, and positive Kveim test. Histologic examination of biopsied tissue from the affected organ will show typical non-caseating epithelioid granuloma.

Although the cause of sarcoidosis remains unknown, immunologic mechanisms, genetic susceptibility, and infectious and environmental agents have all been implicated as possible factors. An antigen-driven, cell-mediated immune response in tissues affected by sarcoidosis leads to a cytokine cascade and to granuloma formation that is thought to be mediated by stimulation of CD4 T lymphocytes/T helper cells through macrophage-presented antigen. Sarcoideal granuloma in the cervical lymph nodes is genetically a complex disease, the most prominent finding of which is a link to a region containing the major histocompatibility complex on the short arm of chromosome 6. A positive association with human leukocyte antigen-B8 and -DR3 has also been reported. Various infectious and environmental agents may be causative factors of sarcoidosis, but such agents have not yet been definitively identified or proven.

Since many clinical conditions can result in sarcoideal granuloma, the diagnosis of sarcoidosis is also established by exclusion of other granulomatous diseases such as Wegener’s granulomatosis, lymphoma, carcinoma, fungal disease, foreign-body reaction, berylliosis, syphilis, and infection with Mycobacterium tuberculosis. The latter infection is the most likely differential diagnosis, and some authors think that M. tuberculosis may play a role in the pathogenesis of sarcoidosis. The detection of DNA from M. tuberculosis by PCR has been described as a highly specific and sensitive method for diagnosing tuberculosis; this method can also be used to exclude M. tuberculosis as the cause of sarcoidosis.

Most patients with sarcoidosis have spontaneous remission, and the disease is self-limiting. Notably, about 10–20% of patients have chronic and progressive disease, with a mortality rate of about 1–5%. Treatment is recommended to preserve organ function, relieve symptoms, or both, and corticosteroids are currently the treatment of choice. Antimalarial drugs, immunosuppressant drugs, immunophilins, and anti-tumor necrosis factor drugs have recently shown some success in the treatment of sarcoidosis. During follow-up, clinicians should assess the involvement of critical organs, such as the lungs, heart, brain, liver and kidneys, and should provide routine evaluations every 2–4 months according to clinical need. Such evaluations should include chest X-ray, pulmonary function tests, electrocardiogram, blood counts, 24-hour calciuria determination and urinalysis, and serologic tests for liver function, renal function, and calcemia. Recent promising studies of serum levels of interleukin and tumor necrosis factor demonstrate a correlation with sarcoidosis progression and activity.

Known granulomatous diseases were excluded in our patient, but a definitive diagnosis could not be made because sarcoidosis is, by definition, a multisystem disease. Although many patients with lymphadenopathy may respond to corticosteroids, the abovementioned findings in our patient led us to suspect that sarcoideal granuloma in the cervical lymph nodes may have been an early sign of systemic sarcoidosis. This notion was supported by data from case reports and several studies. For example, Rizzato and Montemurro studied 43 patients with an initial presentation of sarcoideal granuloma in peripheral lymph nodes. A definitive diagnosis of sarcoidosis was made in 33 patients after a median time from presentation of 5 years; in the remaining 10 patients, the diagnosis was categorized as idiopathic granulomatosis of the lymph nodes. The authors concluded that, in patients presenting with sarcoideal granuloma in peripheral lymph nodes, sarcoidosis may be diagnosed months or years later when characteristic manifestations appear. Apparently, patients with sarcoideal granuloma in the peripheral lymph nodes have a high risk of developing systemic sarcoidosis.

In summary, sarcoidosis should be included in the differential diagnosis of cervical lymphadenopathy. Sarcoideal granuloma in peripheral lymph nodes may precede a diagnosis of systemic sarcoidosis, and regular follow-up of patients with such granuloma is highly recommended.
References