A rare presentation of sarcoidosis with nasal bone involvement

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ABSTRACT

Background: Sarcoidosis is a multisystem granulomatous inflammatory disease that is induced by infectious or noninfectious environmental antigens in a genetically susceptible host. Tuberculosis and sarcoidosis are two diseases with similar clinical and pathologic findings. The link between these two diseases has been extensively studied.

Objective: Herein we describe a case of sarcoidosis associated with tuberculosis, treated for tuberculosis, and, 1 year, later presented with a nasal dorsal lump and skin lesions on the extremities.

Methods: Case report with clinical description.

Results: Our patient had a history of skin and cervical lymphadenopathy symptoms 1 year earlier and was treated with antituberculosis drugs in an outer medical center. Therapy had cured cervical lymphadenopathies, with no improvement in skin lesions. On appearance of the nasal dorsal lump, she presented to our outpatient clinic. We retrieved the previous specimens of the patient, which revealed coexistence of necrotizing granulomas with non-necrotizing granulomas, which was strongly indicative of the coexistence of tuberculosis and sarcoidosis. Radiologic, histopathologic, and microbiologic investigation revealed the diagnosis of sarcoidosis with nasal, cutaneous, and pulmonary involvement. Treatment with prednisolone and hydroxychloroquine resulted in dramatic improvement of nasal bone, pulmonary, and skin lesions within 2 weeks.

Conclusion: The clinical presentation of sarcoidosis can be complex, and the differential diagnosis from tuberculosis can be challenging. Atypical clinical pictures also can cause delays in diagnosis and proper management. In patients with granulomatous lesions that are unresponsive to antituberculosis therapy, physicians must be alerted to the possibility of coexistent sarcoidosis.

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lin skin test was also reported to be positive (10 mm) at that time. It was ascertained that the patient had been vaccinated. Unfortunately, no microbiologic analysis of the excised lymph node had been performed. Results of a sputum sample were negative for acid-fast bacilli. Based on the histopathologic finding of caseating granulomas, she was diagnosed as having tuberculosis of the skin and cervical lymph nodes, and received antituberculosis treatment (rifampicin 600 mg, isoniazid 300 mg, pyrazinamide 1500 mg, and ethambutol 1000 mg per day for 2 months, followed by 10 months of therapy with rifampicin 600 mg and isoniazid 300 mg per day). Cervical lymph nodes resolved, but no remission of skin lesions was reported by the patient, despite 1 year of therapy.

Results of a physical examination revealed diffuse nontender swelling over the nasal bones, which caused disfigurement of the bony nasal dorsum. There were no skin changes over the mass (Fig. 1). The nasal cavity and septum were normal except for mild crusting on the left inferior turbinate mucosa. There were no palpable lymph nodes in the neck, but there was a scar at the previous lymph node biopsy site. Results of the remainder of the head and neck examination were normal. Ultrasonography of the neck was also normal. There were multiple papular skin lesions on the upper and lower extremities (Fig. 2). Paranasal sinus computed tomography (CT) showed destruction of the nasal bones, with soft-tissue increase (Fig. 3). Because of her history, the patient was initially suspected to have tuberculosis that was affecting the nasal bones; however, skin lesions unresponsive to antituberculosis therapy and histopathologic demonstration of noncaseating granuloma in previous skin biopsy specimens raised the question about the former diagnosis of “skin tuberculosis.” We reevaluated the previous data of the patient. We obtained the pathologic slides of the excised cervical lymph node and stained for acid-fast bacilli; the results of staining were negative. Further workup was carried out for the differential diagnosis of sarcoidosis which is the major cause of noncaseating granuloma. A chest radiograph indicated bilateral hilar adenopathy, which was then confirmed by a CT of the chest. There also were parenchymal nodular lesions on a CT of the chest. She had no pulmonary symptoms. Pulmonary function test results also were within normal limits.

The patient was admitted with a presumptive diagnosis of sarcoidosis versus tuberculosis, and incisional biopsy was done transnasally through and intercartilaginous incision with the patient under general anesthesia. Histologic examination results showed noncaseating epithelioid cell granulomas. Tissue samples
also were provided for microbiologic assessment. Results of staining for fungi and acid-fast bacilli were negative. Results of a polymerase chain reaction test and culture for mycobacterium also were negative. Further workup for sarcoidosis revealed no ophthalmologic, renal, or cardiac involvement. Laboratory test results showed no specific evidence of any other disease. Serum and urine calcium and angiotensin-converting enzyme levels were normal. The patient was diagnosed with sarcoidosis and was started on prednisolone (40 mg/day) and hydroxychloroquine (400 mg/day). The therapy resulted in dramatic improvement of nasal bone, pulmonary, and skin lesions within 2 weeks (Fig. 4).

DISCUSSION

The clinical picture of sarcoidosis is usually complex and, combined with the rarity of the disease, can cause delays in the diagnosis and proper management. Sarcoidosis can involve any organ in the body. A recent study confirmed that 95% of patients had thoracic involvement, 50% had extrathoracic involvement, and only 2% had isolated extrathoracic sarcoidosis.\(^4\) Bilateral hilar adenopathy on chest radiograph indicates the diagnosis of sarcoidosis, especially in a patient who is asymptomatic. The most common extrapulmonary sites are eye and skin. Cardiac, neurologic, musculoskeletal, gastrointestinal, and renal involvement also can be seen. Skin is affected in 20 to 35% of patients. Skin manifestations of sarcoidosis are classified into two groups: specific (lesions that are associated with granuloma formation) and nonspecific (e.g., erythema nodosum, which shows no granulomas).\(^5\) Bone involvement is reported in 1–13% of patients with sarcoidosis, more often in African American patients. The most commonly affected bones are of the hands and feet. Other reported sites include vertebrae, skull, and nasal bones.\(^6\)

Sinosal sarcoidosis can be clinically classified into four groups: atrophic, hypertrophic, destructive, and nasal enlargement. Most of the patients with sinonasal sarcoidosis respond to medical therapy.\(^7\) No definitive specific diagnostic test exists for sarcoidosis. A diagnosis of sarcoidosis is based on three criteria: a compatible clinical presentation or consistent imaging; demonstration of noncaseating granulomas in tissue; and exclusion of other possible diseases, especially other granulomatous diseases, including tuberculosis, fungal infections (particularly coccidiomycosis), vasculitis, foreign body reaction, and lymphoma.

For the initial evaluation, laboratory tests include complete blood cell count, lung function tests, urinalysis, and electrocardiogram. Electrocardiogram is particularly important because it can be a clue for cardiac involvement, which may lead to life-threatening arrhythmias. A chest radiograph and/or CT of the chest also must be provided.\(^8\) Hypercalcemia, calciuria, and increased angiotensin-converting enzyme levels can be observed. Angiotensin-converting enzyme levels are elevated in 40 to 90% of patients with sarcoidosis. Elevations correlate with active pulmonary disease and normalize with successful therapy. Tissue biopsy is the criterion standard for confirming a clinical or radiographic diagnosis of sarcoidosis. Tissue biopsy should be obtained in patients with atypical presentation or before therapy to exclude infection or malignant disease. The specimen can be obtained from any clinically involved organ.\(^9\)

The relationship between sarcoidosis and tuberculosis can show three clinical patterns: patients with tuberculosis may later develop sarcoidosis; sarcoidosis and tuberculosis may coexist, as in our patient; and patients with chronic sarcoidosis can develop tuberculosis later as a result of immunosuppression. The role of mycobacteria in the etiology of sarcoidosis has been extensively studied in recent years. *Mycobacterium tuberculosis* DNA has been detected in tissue samples of patients with sarcoidosis.\(^10,11\) Results of a meta-analysis indicated a 30% prevalence rate of mycobacterial DNA in sarcoid samples.\(^12\) Similar blood transcriptional profiles, so called signatures, were demonstrated in both tuberculosis and sarcoidosis; however, the degree of their transcriptional activity was found to be different, which likely indicated the observed clinical differences.\(^13\) Mycobacterial antigens, such as heat shock proteins, have been proposed to induce different immune responses, which leads to the development of sarcoidosis or tuberculosis.\(^3\) Although sarcoidosis and tuberculosis have been considered as two extremes of
the same disease process, no epidemiologic similarities have been shown between sarcoidosis and tuberculosis in terms of incidence, sex, and geographic distribution.\(^\text{14,15}\) A limited number of cases have been reported, which showed the association of sarcoidosis and tuberculosis. With her atypical presentation, including nasal bone involvement and papular skin lesions, our patient was a rare example of tuberculosis and sarcoidosis association.

Sarcoidosis is a diagnostic challenge that has a great similarity with tuberculosis, particularly in countries where tuberculosis is prevalent. This was the situation with our patient. Despite the fact that biopsy specimens from skin lesions showed noncaseating granulomas, positivity of the tuberculin skin test results and histologic analysis of cervical lymph nodes consistent with caseating granulomatous inflammation led clinicians to diagnose the case as tuberculosis. The patient had been treated for tuberculosis for 1 year without any improvement of skin lesions. Six months later, she presented with a new finding of a nasal dorsal lump, and she was finally diagnosed as having sarcoidosis with pulmonary, skin, and nasal bone involvement. Symmetric bilateral hilar adenopathy with some form of paratracheal adenopathy is the classic pattern of sarcoidosis. Symmetrical involvement is helpful for a differential diagnosis because it is unusual in the major diagnostic alternatives, including tuberculosis or lymphoma. Our patient had bilateral hilar adenopathy and parenchymal nodules that were detected on a CT of the thorax.

A cervical lymph node biopsy that was performed at the initial presentation revealed granulomatous inflammation with necrosis. Notably, a few patients with sarcoidosis may have granulomas with some minor necrosis on a biopsy specimen; however, as a common opinion, granulomas with necrosis are more consistent with tuberculosis. Because the microbiologic confirmation was lacking, it was still obscure whether the patient had sarcoidosis misdiagnosed as tuberculosis or sarcoidosis with coexistent tuberculosis at the very first presentation. The absence of microbiologic investigation at the very first presentation in our case was a clear flaw. However we think that the presence of caseating granulomas in cervical lymph nodes but noncaseating granulomas in skin lesions and the disappearance of cervical lymph nodes but not the skin lesions after antituberculosis therapy support the coincidence of the two diseases.

Because the clinical presentation and outcome of sarcoidosis vary considerably, treatment strategies range from no treatment to a wide spectrum of agents, including glucocorticoids, cytotoxic drugs and anti–tumor necrosis factor \(\alpha\) agents. Patients who are asymptomatic and with acute disease, which is described as having a duration of \(<2–5\) years with no evidence of fibrosis, can be observed. Patients with symptoms and with acute disease that involves a single organ can be managed with topical steroid treatment. For extensive cutaneous disease, antimalarial agents have been reported to be useful.

Glucocorticoids are considered the first choice of treatment for patients with severe single organ disease, such as cardiac or neurologic disease, failed topical treatment, or multiorgan disease. In chronic cases or cases refractory to glucocorticoids, cytotoxic agents, including methotrexate, azathioprine, and leflunomide, are preferred. In cases with refractory disease, including fibrotic disease, secondary complications, and steroid resistance, use of anti–tumor necrosis factor treatments, including thalidomide and infliximab, have been suggested.\(^\text{16}\) Our patient had acute disease with multiorgan involvement, without fibrosis or pulmonary sequelae. So we preferred to use glucocorticoid plus hydroxychloroquine. Although osteosarcoidosis is reported to respond poorly to therapy,\(^\text{17}\) nasal swelling dramatically reduced 2 weeks after the treatment in our patient.

**CONCLUSION**

The clinical presentation of sarcoidosis can be complex, and the differential diagnosis from tuberculosis can be challenging. Combined with the rarity of the disease, atypical clinical pictures can also cause delays in diagnosis and proper management. In patients diagnosed as having tuberculosis and having lesions that do not respond to antituberculosis therapy, physicians must be alerted about the possibility of coexistent sarcoidosis. The importance of microbiologic investigation cannot be overemphasized in the differential diagnosis of granulomatous diseases. Even in a country with a high tuberculosis prevalence, the presence of granuloma does not mean “tuberculosis” all the time. The case presented here could be a part of data that support the association of tuberculosis and sarcoidosis.

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