Case In Point: A case of bilateral hilar lymphadenopathy

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The authors describe a rare cause of diffuse thoracic lymphadenopathy—Cogan syndrome. This case was remarkable for the temporal development of extensive lymphadenopathy independent of other hallmark symptoms and signs of this syndrome. In the appropriate clinical setting, Cogan syndrome should be considered in the differential diagnosis of thoracic lymphadenopathy.

Case report

A 38-year-old woman was referred to a clinic for evaluation of newly recognized bilateral hilar lymphadenopathy. She denied any pulmonary or systemic symptoms, including recent fevers, chills, weight loss, dyspnea, cough, and chest pain. Fifteen years earlier, the patient suffered from acute interstitial keratitis and acute hearing loss. A diagnosis of Cogan syndrome was made based on the clinical presentation, an audiogram showing sensorineural deafness, and a negative rapid plasma reagin test for syphilis. Her chest radiograph was normal at that time. Although her symptoms resolved with a course of oral prednisone, she subsequently experienced episodic photosensitivity and blurred vision that responded to treatment with topical corticosteroids.

The patient's medical history also included a positive purified protein derivative test result, chronic sinusitis with repeated sinus surgeries, and controlled hypothyroidism. She was an ex-smoker who had smoked cigarettes for 10 years. She had lived in Arizona before moving to California. One year ago, the patient underwent removal of a malignant melanoma. Evaluation at that time included a chest radiograph, which was normal. However, the chest radiograph obtained just before her clinic visit demonstrated new bilateral hilar lymphadenopathy (Figure 1). CT of the chest confirmed bilateral lymphadenopathy in the paratracheal, pretracheal, subcarinal, and hilar regions without parenchymal infiltrates (Figure 2).

On physical examination, the patient appeared well with normal vital signs and no fever. There were no palpable supraclavicular or axillary lymph nodes. Examination of the chest, abdomen, and skin did not reveal any abnormalities.

Based on the patient's history and age, our greatest concern was for disseminated malignant melanoma or lymphoma. Other likely possibilities included reactivation tuberculosis, pulmonary coccidioidomycosis (because of her residence in the southwestern United States), and pulmonary sarcoidosis (Table). White blood cell count; hemoglobin, calcium, albumin, transaminase, and angiotensin-converting enzyme (ACE) levels; and urinalysis results were all normal. Coccidioides titers indicated no previous exposure. The patient was unable to produce any sputum.

Given the absence of pulmonary or systemic symptoms, we decided to obtain nodal tissue for analysis. Mediastinoscopy was performed, and 2 paratracheal lymph nodes were obtained. Noncaseating granulomatous lymphadenitis with giant cells was identified in both lymph nodes (Figure 3). No acid-fast bacilli, fungi, or bacteria were found. A presumptive diagnosis of benign lymphadenopathy secondary to Cogan syndrome was made. The patient continued to do well clinically without treatment 1 year after mediastinoscopy.

Discussion

Cogan syndrome is a rare disease of young adults that was first defined in 1945 as a clinical entity of audiovestibular symptoms and ocular inflammation. Since its first description, 2 clinical presentations have been recognized. Typical Cogan syndrome, Cogan syndrome I, is characterized by acute interstitial keratitis with audiovestibular dysfunction (acute bilateral hearing loss, vertigo, tinnitus, nausea, and vomiting).

Atypical Cogan syndrome, Cogan syndrome II, is characterized by audiovestibular dysfunction with inflammatory eye lesions in addition to or instead of interstitial keratitis. Systemic involvement has been observed in 20% to 50% of patients with Cogan syndrome. Lung involvement is very uncommon. Pleuritis (cough, chest pain) and transient chest radiographic...
infiltrates are among the more commonly observed pulmonary abnormalities. Dyspnea and hemoptysis have also been reported. Diffuse thoracic lymphadenopathy is even less common than pulmonary involvement and may suggest an alternative diagnosis.

Generalized lymphadenopathy has been described, with a frequency of 7% to 18%. However, the degree of lymph node enlargement and the specific lymph node stations involved have not been well described. Our case suggests that thoracic lymphadenopathy can be striking and may not parallel the course of other symptoms associated with the disease. It is interesting that our patient had diffuse thoracic lymphadenopathy in the absence of either ocular or auditory symptoms. Her lymphadenopathy may reflect underlying systemic inflammation not revealed by her symptoms. In determining the cause of lymphadenopathy in our patient, the identification of histologic findings compatible with Cogan syndrome was important. The noncaseating granulomas and the lymphocytic and giant cell infiltrates observed in multiple lymph node biopsy specimens are consistent with previously described findings in Cogan syndrome. Of 10 lymph nodes described by Vollertsen and associates, contained mild granulomatous inflammation, giant cells, and macrophages, while others had nonspecific nodal inflammatory hyperplasia. The lack of evidence of a causative infectious agent in the patient's biopsy specimens is also consistent with previous reports.

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In considering the differential diagnosis for our patient's thoracic lymphadenopathy, most causes were easily eliminated. For example, the lymph node pathology excluded disseminated malignant melanoma and lymphoma. Various infections, including reactivation tuberculosis and coccidioidomycosis, are associated with different symptoms, and the results of special stains for organisms and cultures were negative. However, differentiating this presentation from sarcoidosis was less straightforward, because Cogan syndrome and sarcoidosis are both diagnoses of exclusion. Several features make sarcoidosis a less likely diagnosis in this patient. First, she had an established diagnosis of Cogan syndrome, which could explain the hilar adenopathy. Also, the ACE level was normal. Although ACE levels can be normal in sarcoidosis, the combination of a normal ACE level with atypical clinical features makes the diagnosis less likely.

It is possible that her previous ocular findings and sensorineural hearing loss were caused by sarcoidosis. However, bilateral hearing loss and simultaneous interstitial keratitis are highly atypical for sarcoidosis, and yet they are the classic symptoms of Cogan syndrome. The more common ear, nose, and throat manifestations of sarcoidosis include bilateral facial paralysis and Heerfordt syndrome, which were not seen in this patient. Her history and clinical course strongly suggest that her adenopathy was secondary to long-standing Cogan syndrome, rather than a new or an extraordinary presentation of sarcoidosis.

Although the cause of Cogan syndrome is unknown, the acute onset of this disease is commonly preceded by an upper respiratory tract infection. This has led investigators to postulate that Chlamydia infection is a possible cause. Attempts to isolate causative agents, however, have been disappointing. Other data suggest Cogan syndrome is a cell-mediated autoimmune disorder. Several reports have described positive rheumatoid factor antibodies and antineutrophil cytoplasmic antibodies (ANCA) (p-ANCA and myeloperoxidase-ANCA) in patients with Cogan syndrome. Lunardi and associates identified 4 autoantibodies that were found in all patients with Cogan syndrome in their study. Mice injected with these autoantibodies demonstrated a clinical picture that mimics Cogan syndrome. Consistent with their data, the authors postulated that an infectious agent stimulates the production of antibodies that attack inner ear cells and ophthalmic membranes.

Cogan syndrome may represent an excellent clinical model of molecular mimicry between exogenous infectious particles and human cell antigens.

References:

REFERENCES


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