A Sixty-four Years Old Woman with Febrile Syndrome and Generalized Lymphadenopathy

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Abstract

Generalized lymphadenopathy could be involved by metastatic carcinoma, Hodgkin lymphoma, tuberculosis, systemic fungal infections, infectious mononucleosis, or sarcoidosis. We report a case of a 64-year-old woman, who presented febrile syndrome and generalized lymphadenopathy (hilar, mediastinal and retroperitoneal regions). The diagnosis was made by biopsy of a retroperitoneal lymph node showing nodular sclerosis Hodgkin lymphoma after multiple diagnostic tests. The differential diagnosis was established between lymphoproliferative syndrome and sarcoidosis, sharing many clinical features, and laboratory and histological findings. In conclusion, clinicians should be aware of the potential risks of lymphoproliferative syndrome or other malignancy processes in patients with lymphadenopathy, even though a diagnosis of sarcoidosis seems reasonable.

Keywords: Lymphadenopathy, sarcoidosis, lymphoma

Introduction

The term of lymphadenopathy refers to abnormal enlargement of lymph nodes. In the case of intra-abdominal or intra-thoracic localization, a lymph node is accepted as pathological if it exceeds 1.5 cm in diameter. Lymphadenopathy may be a primary or secondary manifestation of many diseases. Although it sometimes may be caused by a nonspecific etiology, lymphadenopathy can also be a manifestation of serious diseases, which need clinical evaluation and specific diagnostic tests including lymph node biopsy (this procedure sometimes will provide the final diagnosis). Lymphadenopathy can be detected by imaging or suspected by symptoms resulting from compression of adjacent structures. The most common etiologies of lymphadenopathy are secondary to metastatic carcinoma (bronchial, pleural, breast, etc.), Hodgkin lymphoma, tuberculosis, systemic mycotic infection, infectious mononucleosis, and sarcoidosis (1).

Case Report

We report a case of a 64-year-old woman with no relevant medical history or toxic habits, who was referred to internal medicine clinic by her primary care physician. She presented constitutional symptoms, recurrent fever up to 38.5 °C and bilateral hilar lymphadenopathy on chest radiography and computed tomography (CT). Her vital signs were normal and she was in a good general condition and presented normal cardiac and pulmonary auscultation on physical examination. There was no peripheral lymphadenopathy, palpable organomegaly nor abdominal masses. No rash was observed. In blood tests, we observed normocytic-normochromic anemia (hemoglobin, 10.5 g/dl; normal value (NV), 12-16), but it was normal for absolute reticulocytes as well as leukocyte count (4000 /ml) and formula. The erythrocyte sedimentation rate was 66 mm/h; C-reactive protein, 15.8 mg/l (NV, <3); angiotensin converting enzyme (ACE), 152 IU/l (NV, 8-52); and corrected calcium, 10.5 mg/dl (NV, 8.4-10.2). The other biochemistry and coagulation values were normal. In electrophoretic spectrum, no monoclonal bands were observed. The tumor markers (CEA, CA 19.9, CA 125, CA 15.3, beta-2 microglobulin, chromogranin A) and autoimmunity tests (Rheumatoid factor, anti-cyclic citrullinated peptides (CCP), antinuclear antibodies (ANA), anti-double-stranded DNA (dsDNA), anti-Smith (Sm),anti- Scl-70 (topoisomerase I), anti-Ro/SSA, anti-La/SSB, anti-RNP, anti Jo-1, antiribosomal P, anti-RNA polymerase III antibody, anticitrulline antibody (ACA), antineutrophil cytoplasmic antibody (ANCA), antiphospholipid antibodies, C3 and C4) were all negative.

The microbiologic study showed negative Mantoux, and blood and urine culture. Virus serology demonstrated: positive VCA-IgG, negative VCA-IgM, and negative Ig anti-EBNA for Epstein-Barr virus; positive IgG and negative IgM for cytomegalovirus and varicella-zoster virus; and negative for HIV-1, Rickettsia, Borrelia, Brucella, Rubella, Syphilis and...
Toxoplasma. Blood smear study showed rouleaux, and bone marrow biopsy was normal without significant alterations.

Thoraco-abdomino-pelvic CT scan showed enlargement of multiple mediastinal and retroperitoneal lymph nodes, suggesting a lymphoproliferative process. We proposed differential diagnosis between lymphoma and sarcoidosis, and performed chest high resolution computed tomography (HRCT). HRCT revealed a small focus of peripheral parenchyma infiltrates as ground-glass opacity in the apical region of the right upper lobe as well as mediastinal lymphadenopathy. The findings of pulmonary infiltrates, bilateral hilar lymphadenopathy and elevated ACE could be compatible with the diagnosis of sarcoidosis.

Figure 2: PET-CT scan of the chest, showing bilateral mediastinal and hilar lymphadenopathies.

The bronchoscopy showed a tumoral lesion with vascular proliferation in the right bronchial system, and biopsy of the lesion was consistent with carcinoid tumor (removed with bronchoscopy) (Figure 1). With transtracheal puncture of an enlarged lymph node, and the lymph node biopsy did not show malignancy. The bronchoscopy showed a tumoral lesion with vascular proliferation in the right bronchial system, and biopsy of the lesion was consistent with carcinoid tumor (removed with bronchoscopy) (Figure 1). With transtracheal puncture of an enlarged lymph node, and the lymph node biopsy did not show malignancy.

All tests for lymphoma were negative and the patient's evolution was fine, without clinical deterioration. Because of that, we assumed the diagnosis of atypical sarcoidosis and prednisone treatment was started. However, the patient had persistent high fever, shiver, and general malaise; the signs of chronic inflammation continued; LDH was raised to 690 IU/l (NV: 240-480); and beta-2 microglobulin was increased to 4.3 U/l (NV: 1 - 2.2). As a result of no response to treatment, tests were repeated: thoraco-abdominal CT showed enlargement of the lymph nodes; and biopsy of the bone marrow demonstrated no specific findings. We further performed biopsy of retroperitoneal lymph nodes with the findings of nodular sclerosis Hodgkin lymphoma (Figure 4). Currently, the patient has been accepting chemotherapy with improvement of her general condition and no new symptoms appeared.

Discussion

This case describes a patient with lymphadenopathy syndrome and requiring differential diagnosis between sarcoidosis and lymphoma. At first, there was nothing suggestive of lymphoma and a diagnosis of sarcoidosis was made. We started treatment with corticosteroids, but there was no response. Therefore, the case was reevaluated and we made the final diagnosis of Hodgkin lymphoma. Sarcoidosis is an idiopathic multisystem granulomatous disease and the diagnostic criteria are: clinical and radiology support, nodal biopsy compatible (noncaseating granulomas) and absence of an alternative diagnosis (2-3).

Noncaseating granulomas typical of sarcoidosis can occur in different types of diseases: infection, Crohn’s disease, drug reaction, lymphoma, and metastatic carcinoma (4). We are able to detect noncaseating granulomas in cancer patients who do not have a diagnosis of systemic sarcoidosis (sarcoid-like reaction). Sarcoid-like granulomas may occur in association with Hodgkin lymphoma (13.8%) or non-Hodgkin lymphoma (3.6%), or can be so extensive that may hide the diagnosis of malignancy; it usually occurs in patients with a diagnosis of carcinoma (4.4%) (4-5). For our case, we observed existence of a carcinoid tumor in the lung and the lymph node biopsy findings (epithelioid granulomatous lymphadenitis) could be reactive to the presence of carcinoid tumor. In the absence of other findings that would justify the clinical manifestations, the diagnosis of sarcoidosis was established at the first time. There are some cases described in which sarcoidosis and carcinoid tumor coexists (6).

The differential diagnosis between sarcoidosis and lymphoma is often complicated. Sarcoidosis and some lymphomas share several clinical, analytical and even histological findings. Sarcoidosis-lymphoma syndrome was first described in 1986 by Brincker, in a group of 46 cases with a relationship between sarcoidosis and lymphoproliferative syndrome (7). In some cases, sarcoidosis is added to lymphoma and sarcoidosis may precede lymphoma or vice-versa (5).

In our case, the diagnosis of sarcoidosis was made based on the pathological findings, radiology support, ACE elevation, and absence of an alternative diagnosis despite multiple biopsies. Hypercalcemia and the increase in ACE are associated to, but are
not diagnostic criteria of sarcoidosis; they have also been described in patients with lymphoma (4). In our case, the final diagnosis was Hodgkin lymphoma (with mild hypercalcemia and elevated ACE).

In summary, for a patient with lymphadenopathy syndrome, we should rule out the lymphoproliferative syndrome, even though a diagnosis of sarcoidosis seems safe. The possibility that atypical manifestations of lymphoma could simulate sarcoidosis should be considered and multiple diagnostic biopsies may be necessary to rule out malignancy.

Conflict of Interest:

The authors declare no conflict of interest.

References: