Tanaffos (2010) 9(3), 80-83

A 25-Year-Old Woman with Cough, Constitutional Symptoms and Lymphadenopathy

Ilad Alavi Darazam [1], Seyed Davood Mansouri [1,2], Shirin Karimi [1], Alireza Nadji [3], Ahmad Reza Moradi [3], Majid Marjani [1,2], Nahal Mansouri [1]

[1] Mycobacteriology Research Center, [2] Department of Internal Medicine, Division of Infectious Disease and Clinical Immunology, [3] Virology Research Center, NRITLD, Shahid Beheshti University M.C., TEHRAN- IRAN.

WHAT IS YOUR DIAGNOSIS?

A 25-year-old woman was admitted with malaise, mild fever, night sweats and intermittent non-purulent cough since six months ago. Her symptoms gradually progressed during the previous weeks and recently she experienced nausea and mild dyspnea on exertion. On physical examination, she was ill and pale with stable vital signs. There was a mobile, elastic and non-tender lymph node in right neck base near a previous lymphadenectomy scar. Cardiopulmonary examination revealed a systolic III/VI murmur. Mild splenomegaly, clubbing, multiple Beau's lines on her fingernails and mildly destroyed left fungal toenails were also found. She was a rural married housewife with one healthy child. Her husband had no significant medical history. She had a few thallasemic relatives in her both parental families. In her past medical history she complained of painful oral aphthous lesions occurring 3-4 times a year and denied morning stiffness in her joints, photosensivity or other rheumatologic symptoms. She had undergone cervical lymphadenectomy and thoracotomy 2 months ago. Histopathological examination revealed a reactive lymphadenitis and hyperplasia, plasmacytosis and vascularization in cervical and mediastinal lymph nodes, respectively. Laboratory test results are demonstrated in Table 1.

Table1. Laboratory findings

Analysis	Result	Analysis	Result
WBC	28010	Sodium	142 meq/L
Neutrophil	77%	Potassium	4.3 meq/L
Lymphocyte	10%	Urinalaysis	normal
Monocyte	6%	Calcium	7.3 mg/dl
Band cell	3%	Phosphorus	4.2 mg/dl
Basophil	1%		
Lymph varients	3%	Wright	negative
Hemoglobin	10.6 mg/dl	Coombs Wright	negative
MCV	76.6fL	Cholestrol	90 mg/dl
MCH	23.1pg/cell	Triglyceride	74 mg/dl
RDW	19.2	High density lipoprotein	10 mg/dl
Platelet	540 x10^9/L	Low density lipoprotein	65 mg/dl
Erytherocyte sedimentation rate	125mm	Serum Iron	10µg/dl
Urea	35 mg/dl	Total iron binding capacity	262 µg/dl
Creatinin	0.8ng/ml	Ferritin	700 µg/L
Aspartate aminotransfrase	10U/L	Fibrinogen	390mg/dl
Alanin aminotransfrase	16U/L	Nitroblue tetrazolium test	99%
Alkaline phospatase	205 U/L	Angiotensin convertase enzyme	65U/L
Lactate dehydrogenase	333 U/L	Human immune deficiency virus antibody	Negative

Hemoglobin electrophoresis was normal and protein electrophoresis revealed a polyclonal gammopathy and hypoalbuminemia. (Albumin 35.3%, α1: 2.8%, α2:10.2, β: 2.2, γ: 49.5). Cytomegalovirus (CMV), Epstein - Barr virus (EBV), and human herpes virus 8 (HHV-8) were not detected in the plasma sample by nested-PCR (Polymerase Chain Reaction) method. Figures 1 and 2 show the chest-X-ray and chest computed tomography (CT) scan of the patient. Abdominopelvic CT-scan demonstrated mild hepatosplenomegaly with homogenous density without lymphadenopathy. Pelvic cavity was normal. ***(Tanaffos 2010; 9(3): 80-83)***

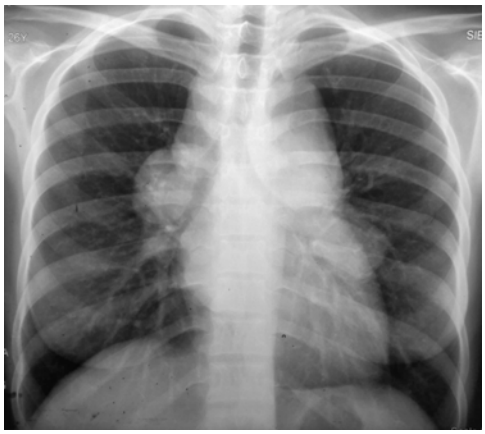

Figure 1. Chest x-ray of the patient.

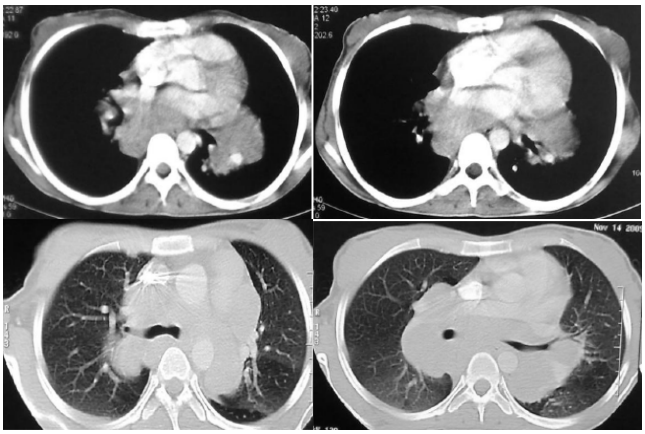

Figure 2. Lung CT-scan of the patient.

Correspondence to: Mansouri SD
Address: NRITLD, Shaheed Bahonar Ave, Darabad, TEHRAN 19569, P.O:19575/154, IRAN
Email address: dmansouree@yahoo.com

Diagnosis: Multicentric plasma cell type Castleman's disease

Histopathological revision of lymph nodes revealed lymph node structure with mild architectural alternation and obliteration of some of the subcapsular sinusoids due to extensive increase of lymphoid follicles both in cortical and medullary areas. In addition to above morphologic findings, the interfollicular areas were loaded with sheets of plasma cells. On immunohistochemistry staining, CD20 highlighted the localization of B cells in germinal centers. The CD31 also highlighted the rich vascularization of the lymph node. On serial sections, there was no evidence of any CD30 positive atypical lymphocytes.

The above morphological findings were not characteristic and could be seen in a variety of diseases, like lymphoma, collagen vascular disorders, infections (especially HIV) (1) and Castleman's disease.

Physical examination and serologic tests for rheumatologic diseases, HIV and other suspected etiologies like EBV, CMV and HHV-8 were negative. For further evaluation we examined lymph node biopsy with PCR to identify HHV-8. The positive HHV-8 PCR of lymph node sampling, with exclusion of other differential diagnoses and suggestive pathologic features resulted in diagnosis of Castleman's disease.

Castleman's disease (CD) was introduced in 1956 as a localized mediastinal lymph node hyperplasia resembling thymoma (2). Since 1956, multiple cases of CD have been reported and new data about its presentations, localization, etiology and treatment have been collected. However, it is a rare entity and a mimicking disease. At present, two distinct pathologic types (hyaline vascular pattern and plasma cell type) and also two distinct clinical manifestations (localized versus multicentric) are well known (3). Before 90s, HHV-8 had been named Kaposi's sarcoma associated herpes virus (KSHV) (4), but after identification of its role in pathogenesis of other conditions we also consider HHV-8 as one of multiple etiologies of Castleman's disease (4-6).

Identification of HHV-8 in tissue in this case is the first report in this respect from Iran.

Recently, valganciclovir has been used in a randomized clinical trial for reducing HHV-8 shedding. Limiting HHV-8 replication appears to control some cases of Castleman's disease (7). We initiated prednisolone as the first line regimen, but considering the persistent mediastinal lymphadenopathy and since the symptoms remained unchanged after 45 days, she is supposed to take valganciclovir and will probably be treated by chemotherapeutic agents (8).

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