



A Case Report

ISSN : 0975-7384
CODEN(USA) : JCPRC5

Lymphomatoid Granulomatosis

Fatemeh Niksolat¹, Hadi Majidi^{2*} and Siavosh Abedi³

¹Department of Rheumatology, Mazandaran University of Medical Sciences, Mazandaran, Iran

²Department of Radiology, Mazandaran University of Medical Sciences, Mazandaran, Iran

³Department of Pulmonology, Mazandaran University of Medical Sciences, Mazandaran, Iran

ABSTRACT

Lymphomatoid granulomatosis is a rare disorder and a form of non-Hodgkin's lymphoma with various presentations and it is difficult to diagnose. We present a patient with skin lesions, arthralgia and pulmonary nodules with diagnostic challenges.

Keywords: Lymphomatoid Granulomatosis, Pulmonary nodule, Arthralgia

INTRODUCTION

Lymphomatoid granulomatosis is a rare disorder and a form of non-Hodgkin's lymphoma. This disease engages the lung, skin, kidneys, liver, nervous system and adrenal gland. From a clinical and radiological perspective, it is similar to collagen vascular diseases, lung abscess, and metastatic disease and is difficult to diagnose. The present report introduces a case with diagnostic challenges.

Introducing the case

The patient was a non-smoker 63-year-old man referred from a skin clinic due to arthralgia. He complained of pain in elbow, wrist, and knee joints, intensifying at night times, with a non-inflammatory nature. He was complaining of skin lesions on his leg and arms. A skin biopsy was performed. He had a hospitalization record due to pulmonary problems two months earlier in another center, which was treated as pneumonia. He was under hydroxychloroquine treatment due to skin lesions. He did not mention a history of other diseases. A physical examination showed patch and plaques in the legs and arms, while other organs were normal. To rule out the collagen vascular diseases, the following laboratory tests were requested:

CBC diff, ANA, RF, Anticcp, ANCA, ACE Level, HBSAg, HCVAb, HIVAb, LFT, Cr, CPK, Aldolase, PSA, which were normal. LDH; 500U/L (NL;207-414)mg/L, ESR; 40mm/h, CRP; NL, Urine Analysis; NL.

The skin biopsy of leg lesions reported lymphohistiocytic infiltration in the upper and deep dermis and subcutis. Some histocytes in the upper dermis were surrounded by collagen fibers, and the final diagnosis of the skin lesions was granulomaannulare. Considering the recent pulmonary problems and the likelihood of paraneoplastic process, despite the normal results of the chest radiography, the CT scans of the chest, abdomen, and pelvis were requested. Numerous scattered interstitial nodules with distinct and smooth borders were observed in both lungs, with the biggest ones in the right and left lungs, 20×35 mm and 20 mm, respectively (figure 1,2,3). An adenopathy 15 mm in diameter existed in the middle mediastinum (figure 4).

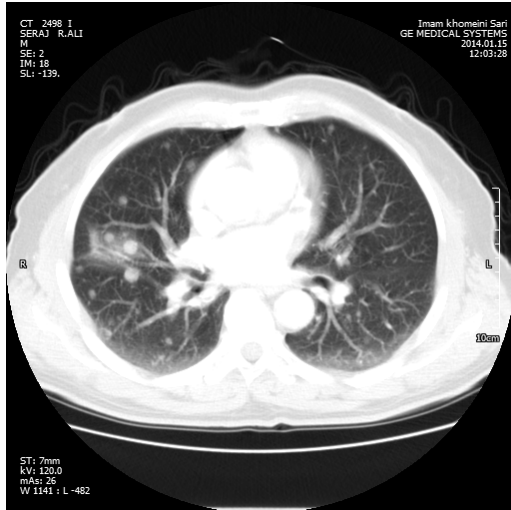


Figure 1: Pulmonary nodules

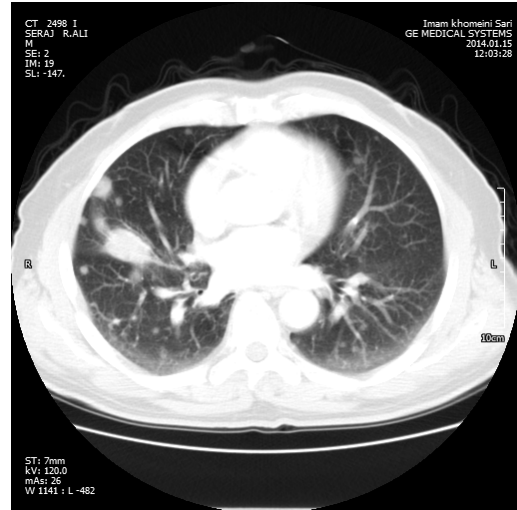


Figure 2: Pulmonary nodules

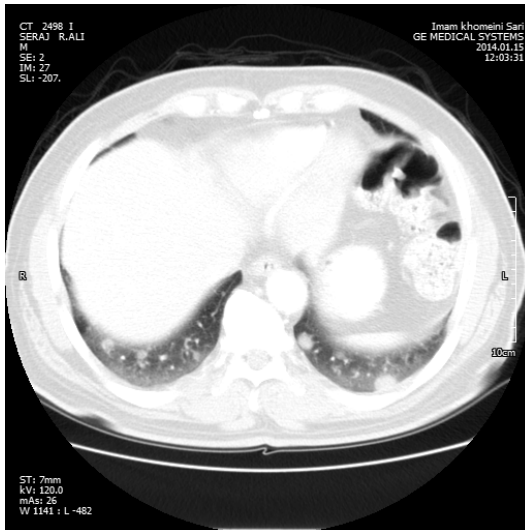


Figure3: Pulmonary nodules

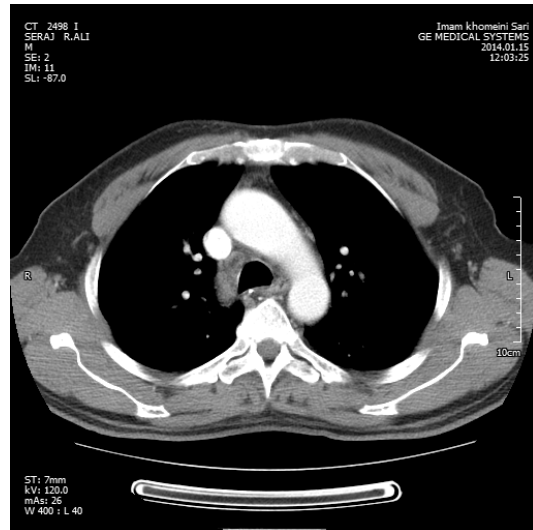


Figure4: Mediastinal adenopathy

An adenopathy 15 mm in diameter existed in the middle mediastinum (figure 4).

A solid heterogeneous mass with uneven and lobulated borders with the approximate size of 40×25 mm existed in the abdomen and pelvis inside the right adrenal gland (figure 5).

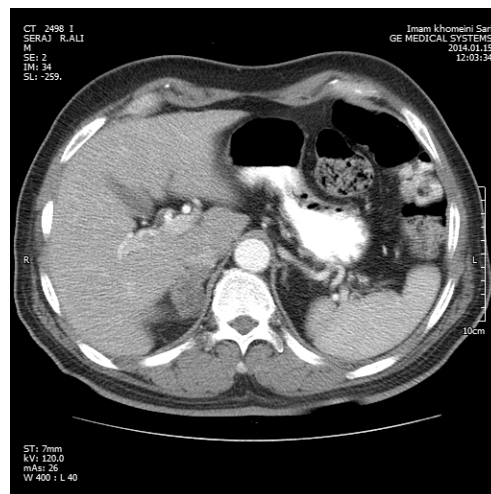


Figure 5: Right adrenal mass

To rule out gastrointestinal problems and malignancy, an endoscopy was performed, which showed normal results; so were the results of testes and ultrasonography of thyroid. To rule out endocarditis, the echocardiogram of the heart was showed no evidence for it. The probable diagnosis of lung cancer with metastasis was considered for which bronchoscopy and bronchoalveolar lavage (BAL) were performed. Bronchoscopy was normal, and in the BAL sample, an acute inflammatory process in the chronic inflammatory process was reported (the inflammatory cell included 75% macrophages and 15% lymphocytes and accessional PMN 10 %). Transthoracic CT- guided biopsy was performed on the biggest nodule of the right lung. Moderate multifocalin filtration of lymphocytes with the lesser degree of the infiltration of neutrophil and eosinophils along with carbon-laden macrophages were reported in the pathology report of chronic inflammation.

A whole body bone scan was performed due to joint pain, which did not show any evidence for malignancy or metastasis. As a result of failure to find a definitive diagnosis, the patient was recommended to perform an open lung biopsy, which was performed in another center. The section reveal fragments of tissue including pulmonary parenchyma with a lesion. It is composed of polymorphic infiltration predominantly small lymphoid cells at time with cleaved nuclei, mixed with scattered eosinophils and plasma cells. Lymphoid cells infiltrated into vessels wall, obliterated their lumens. They are more populated around vessels, and lesions contains extensive necrosis. IHC stains for CD20 in scattered follicular aggregates and for CD3 in intervening small lymphocytes and for ki67 in about 15%-20% in less active areas.

The pathology results indicated angiocentric immunoproliferative disorder, polymorphic type grade 1(Lymphomatoid granulomatosis).

Lung involvement

DISCUSSION

Lymphomatoid granulomatosis is a rare disease and a form of B-cell lymphoma associated with angiocentric lymphocytes and vascular damage, which usually engages the lung, as well as, skin, kidney, liver, spleen, adrenal, eyes, and central nervous system (1-2). This disease is a form of non-Hodgkin's lymphoma, involving men, two times as much as women, usually occurring in the 30-50 year age group (2).

The Epstein-Barr virus was found in most cases of Lymphomatoid granulomatosis, but the real etiology is unknown (1-3-4-5). The most common symptoms of the disease include cough, fever, and skin lesions. Patients might complain of weight loss, chest pain and dyspnea. Its most common radiological manifestation is multiple pulmonary nodules observed in 80% of cases.as these lesions can rapidly progress and cavitate, PLG often resembles granulomatosis with polyangitis (Wegener's granulomatosis) or metastasis. These nodules might disappear or migrate and cause the reversed halo sign with ground-glass opacities in the central part surrounded by a denser consolidation. Pleural effusion and mediastinal lymphadenopathy are observed in25% and 60% of CT scans respectively (6). Other less common radiological manifestations include coarse linear opacities in bronchovascular bundles and thin-wall cysts (7). Other features of this disease stated in articles include large necrotic tumor in the upper lobe of the left lung (8), idiopathic interstitial pneumonia (9), a nodule or single lung mass (10-11-12), and lung abscess (13). A biopsy is necessary for a definitive diagnosis. The classic biopsy triad is observed as mixed lymphoid infiltration, lymphoid infiltration in the artery wall and limited are as of necrosis.

IHC shows numerous reactive T-cells and different stages of malignant B-cells, which histologically come in three degrees as follows (2-6).

Grade 1: Few positive B-cell EBV are found

Grade 2: The number of positive B-cell EBV increases.

Grade 3: It is a form of diffuse large B-cell lymphoma

The treatment includes the following:

- 1- Systemic steroids with cyclophosphamide
- 2- Interferon alfa-2b
- 3- Combination CHOP chemotherapy regimen
- 4- Rituximab
- 5- Rituximab combined with CHOP chemotherapy regimen
- 6- Autologous bone marrow transplantation after high-dose chemotherapy

Prognosis

Spontaneous recovery is seen in 20% of patients (stage 1); the disease is progressive in other patients. The mortality rate has been reported 38%-88% during 5 years (2-7). The mean survival rate is 14-17 months. The prognosis is worse when the disease is in stages 2 and 3 or the nervous system is involved (2-7).

Regarding this recent case, given the rarity of the disease and available literature on the diseases, which have been all case reports, no cases of arthritis or arthralgia were reported. Also, joint and skin manifestations were primary features of collagen vascular diseases. As the patient had only a history of pulmonary disease and based on imaging findings, which were mostly in favor of metastasis, it might be proper to consider Lymphomatoid granulomatosis as the differential diagnosis of multiple pulmonary masses. It might also be necessary to take into account malignancies such as lymphoma in assessing joint diseases, especially in the elderly.

CONCLUSION

Malignancy specially lymphoma should be considered in differential diagnoses in elderly patients who present with musculoskeletal or atypical problems.

REFERENCES

- [1] WH Wilson, DW Kingma, M Raffeld, et al. *Bloodjournal. Hematology* **2014**;199687:4531-4537
- [2] C.CROFT, S.R. BENATAR, C.J.UYS. *SA medical journal* **1980**; 736-738
- [3] Ph. Taniere, F. THivolet-Bejui, D. Vitery.et al. *Eur respire J* **1998**; 12:102-106
- [4] Hiromasa Aria, Hisashi Oshiro, Sumitaka Yamanaka.et al. *J Clin Expheumatopathol* **2009**;49:39-44
- [5] Katzenstein AL, Doxtader E, Narendra S. *Am J Surgpathol* **2010**;34(12):35-48
- [6] Aanchalkapoor. *American college of chest physicians* **2011**;140
- [7] S. S. Hare, C. A. Souza, G. Bain, et al., *British Journal of Radiology* **2012**; 85(101): 848–864
- [8] W. Bartosik, A. Raza, S. Kalimuthu, and A. Fabre, *Interactive Cardio Vasc Thoracic Surgery* **2012**; 14(5):662–664
- [9] A. Makol, K. Kosuri, D. Tamkus, W. De M Calaca, and H. T. Chang, *Journal of Hematology and Oncology* **2009**; 2:39
- [10] T. Itoh, K. Umekawa, K. Rensha et al., *Nihon Kokyuki Gakkai Zasshi* **2008**;46(1): 50–54
- [11] P. S. Koh, A. H. C. Foyle, Y. Cartier et al., *Canadian Respiratory Journal* **2004**;11(1):51–54
- [12] F. Lou and Z. Xing, *Chinese Medical Journal* **1998**;101(9): 695–699
- [13] M. McCloskey, M. Catherwood, D. McManus, G. Todd, R. Cuthbert, and M. Riley, *Thorax* **2004**; 59(9): 818–819