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CASE REPORT

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25 Years Old Women With Inflammatory Low Back Pain

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ABSTRACT

Introduction: Diffuse large B-cell lymphoma (DLBCL) is the most frequent histological type of malignant lymphomas (approximately 30% of cases). DLBCL is highly curable through chemotherapy. Rituximab in combination with CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) chemotherapy as the most frequent of care for first - DLBCL therapy, improves long-term survival of patients effectively. **Case report**: A young female (25 years old) complained about pain in her right back for two years. She was suffering from backache with priority in the right and contracture in mornings. Sacroiliac joint seemed normal but lytic and sclerotic lesions and also density changing of L5 and humerus head was revealed by CT scan. Biopsy was taken from the iliac bone and diffuse large B cell lymphoma was diagnosed. **Conclusion:** Chronic pains especially in axial skeleton, pelvis area and main joints must be taken seriously and examined by CT scan and MRI. If no particular issue was reported primarily while the pain was remained, a complete diagnosis BMB associated with PET must be applied. Despite of dependency on diagnosis the treatment by CHOP in association with rituximab is the most recommended chemotherapy alternative for patients with DLBCL.

Key words: diffuse large B-cell lymphoma, iliac bone, lytic and sclerotic, lesions and biopsy.

1. INTRODUCTION

Diffuse large B-cell lymphoma (DLBCL or DLBL) is a cancer of B cells, a type of white blood cell that produces antibodies against external agents or internal agents in self immune cases. DLBCL is the most common sort of non-Hodgkin lymphoma among adults (1) 7-8 cases per 100,000 people are got involved with DLBCL annually according to literature (2, 3). It is the most frequent histological type among malignant lymphomas, accounting for approximately 30% of cases. DLBCL is highly chemosensitive and curable. The use of anti-CD20 antibody in addition to chemotherapy has significantly improved outcomes in patients with DLBCL. Rituximab in combination with CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) chemotherapy has emerged as the standard of care for first-line DLBCL therapy, which can improve long-term survival (4).

This cancer occurrence in older individuals is more often, with an average of approximately 70 years of age diagnosis (3). It is reported that almost one-third of newly diagnosed patients are over the age of 75 (5). Though it can also occur in children and young people in rare cases. DLBCL is an aggressive tumor which can arise in any part of the body (6), and the first sign of this illness is typically the observation of a rapidly growing mass, sometimes the swelling is associated with fever, weight loss, and night sweats. The most typical symptom at the time of diagnosis is a mass that is rapidly developing which is located in a part of the body that includes multiple lymph nodes (7).

Lymphoma can occur in many parts of the body, but only rarely in the soft tissues such as breast or adrenals (8).

The reasons of why diffuse large B-cell lymphoma occurs are remained unknown so far. DLBCL usually is derived from normal B cells, however it can also represent a malignant transformation of other sorts of lymphoma or leukemia.

An underlying immunodeficiency and infection with Epstein-Barr virus are putative candidates as significant risk factors and could contribute the development of some subgroups of DLBCL (9). DLBCL probably arises via a stepwise process of somatic mutations, particularly chromosomal translocations involving oncogenes and, often, promoter regions of the immunoglobulin genes (10).

Diagnosis of DLBCL is usually made by removing a part of the tumor through a biopsy,

Then examine futures of the taken tissue such as it's morphology by microscope. Usually the diagnosis is made by an experienced hematopathologist (11). Positron emission tomography (PET) that takes advantage of ^{18}fluoro-2-deoxyglucose (FDG), has become a standard clinical tool for staging and response assessment in aggressive lymphomas. But in most cases a combination of PET and biopsy evidence improves prognostic prediction in diffuse large B-cell lymphoma (12).

Several subtypes of DLBCL have been identified and described by relevant organizations such as WHO so far. Although any of which have a different clinical presentation and prognosis, chemotherapy often in combination with an antibody targeted at the tumor cells are the most recommended treatment for all of them (11). With standard therapy, including rituximab and an anthracycline-containing regimen, approximately 67% of patients in a population-based registry are alive without lymphoma with a median follow-up of 4 years.

a) Therefore, despite the improvements in overall survival (OS) of patients with DLBCL with the routine addition of rituximab therapy,

b) One-third of patients have disease that is either refractory to initial therapy or relapses after standard therapy.

Although the majority of relapses occur early, a recent series has emphasized that late relapses (after 5 years) are possible, and may be associated with initial localized stage, favorable International Prognostic Index (IPI) score, and extranodal involvement at diagnosis (13).

Detecting changes in the genetic pattern of diffuse large B cell lymphoma by rapid emergence of molecularly based techniques, including gene expression, DNA and RNA sequencing, and epigenetic profiling, has significantly influenced the understanding and therapeutic targeting of DLBCL (14).

Historically, DLBCL has been thought to involve recurrent translocations of the IGH gene (immunoglobulin heavy chain) and the deregulation of rearranged oncogenes, including *BCL2*, *BCL6*, or *MYC*. More recently, the molecular heterogeneity of DLBCLs has been deciphered by gene expression profiling, and DLBCLs have been divided into three main molecular subtypes: the germinal center B-cell like (GCB) subtype, the activated B-cell like (ABC) subtype, and the primary mediastinal B-cell lymphoma (PMBL) subtype. These subtypes arise from distinct B cells at separate stages of differentiation and maturation, leading to well-defined gene expression profiles (GEPs) and different clinical outcomes and responses to immunochemotherapy (15).

Bone marrow (BM) examination is considered essential in evaluation and staging of non-Hodgkin lymphoma (NHL) at the time of initial diagnosis as well as after therapy. Bilateral iliac crest BM biopsies and step sections for morphological view are advocated for optimal specimen and detection of small focal lesions accompanied by fibrosis that may not be readily detected in aspirate smear preparations, thereby increasing the yield of possible diagnosis and becoming superior to aspiration study (6).

It is an important part of the routine staging of Hodgkin's disease (HD) and non-Hodgkin's lymphoma (NHL). Two factors make the marrow trephine biopsy an unsatisfactory diagnostic test: it is a painful and invasive procedure and, even if the volume of the biopsy is adequate, focal lesions can be missed (16).

Unilateral blind biopsy of bone marrow of the posterior iliac crest is routinely performed during bone marrow evaluation. It is recommended to perform bone marrow biopsy for all patients with NHL (17).

2. CASE PRESENTATION

The case report is describing a 25 years old housekeeper married female that complained about functional inflammatory issues for 2 years with priority in the right side and morning contraction for more than 1 hour. It was recognized as AS (Ankylosing spondylitis) primarily and treatment by 150 mg of indomethacin daily was applied which no clinical response was observed for it. Fever, night sweating and weight loss were not occurred as well. During examinations there was not any particular point but tenderness in the right sacroiliac (Figure 1).

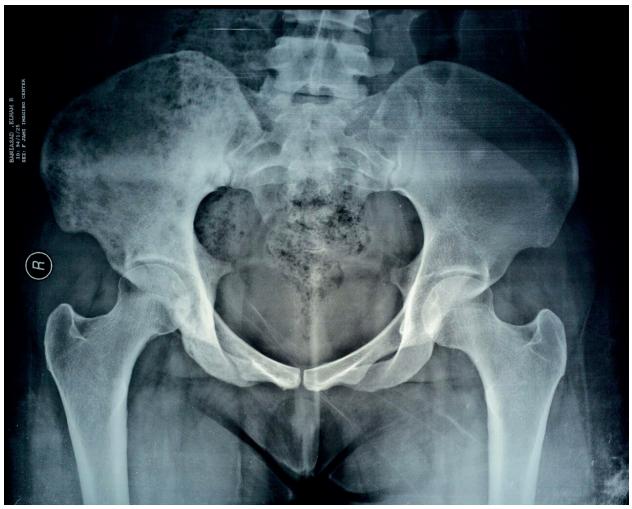

Figure1. Pelvis Xray, Sclerolytic Lesion in Right Illiac.

During the checkups it was demonstrated sacroiliac joint is normal. However lytic and sclerotic lesions in right iliac and density changing of L5 vertebra and humerus head have been revealed by CT scan. It has to be mentioned that all of clinical experiments were considered as normal including CBC, ESR, LDH and LFT. Primary diagnosis was Paget's and the then open biopsy was taken from the iliac bone. The morphological results revealed of diffuse large B cell lymphoma.

3. DISCUSSION

Ankylosing spondylitis (AS) is a chronic inflammatory disease characterized by disabling rheumatic disease characterized by inflammatory back pain, restricted spinal mobility, and frequently peripheral arthritis, enthesitis, and acute anterior uveitis, inflammation of the axial skeleton and enthuses, causing pain, stiffness, and occasionally progressing to joint ankylosis (18, 19)

AS is associated with disability comparable to that of rheumatoid arthritis. Diagnosis should first focus on nocturnal back pain, diurnal variation in symptoms with prolonged morning stiffness, and a good response to Non-steroidal anti-inflammatory drugs (NSAID) therapy. Physical examination is often unrevealing. Pelvic x-ray results are often normal in early disease. Magnetic resonance imaging is the most sensitive imaging technique for detecting early inflammatory lesions and should be considered (20).

Based on mentioned studies the primary diagnosis for the patient was AS. Indomethacin as a common anti-inflammatory drug was prescript.

Indomethacin is a non-steroidal anti-inflammatory drug that has been discovered in 1963 (21). It is utilized for reducing pain, fever, swelling and stiffness. It has been used by both oral capsules and injecting serum. Large dose of Indomethacin (100 to 200 mg), taken at night, could effectively relieve morning pain and stiffness which is known as a treatment for diseases such as rheumatoid arthritis and ankylosing spondylitis (22).

Diffuse large B-cell lymphoma (DLBCL) as the most frequent subtype of high-grade non-Hodgkin lymphoma, is the sixth most common cause of malignant tumor incidence and mortality in Europe and the United States. It shows a 150% increase in incidence in the past decades, which makes it a major public health problem (23).

Similar to AS symptoms of DLBCL are pain in the back, swelling, knight sweating and stiffness that of which confused us at the first place. Sometimes multiple focal lesions in the spine, pelvis, and femurs are accompanied with necrosis in the marrow space are probably observed (24).

DLBCL involves the bone marrow in up to 27% of cases that has been assessed by iliac crest bone marrow biopsy (25).

Utilizing of bilateral BM biopsies to assess BM involvement in patients with NHL is recommended mostly. It increases the positive yield of BM involvement by 10% to 22%.

As the size of the sample affects the yield with as well as the number of the samples, the total length of the biopsy should be at least 2.0 cm in order to evaluate BM involvement.

However obtaining adequate amounts of specimens in clinical situations is not always possible. This could cause false negative evaluation of BM involvement. Meanwhile, it would rather be difficult to distinguish benign lymphocytic aggregates from focal lymphomatous involvement of the BM (26).

So biopsy was taken from patient iliac bone to diagnose the illness.

DLBCL has a variable pattern, characterized by paratrabecular, nodular, sinusoidal or diffuse infiltration. The cancer cells immunophenotype depends on the DLBCL variants, subgroups and subtypes (27).

Besides BMB, other methods have been reported to diagnose and examine DLBCL such as CT scan, PET and combinations of mentioned methods. It has been demonstrated that either bone marrow histology or PET alone is not a reliable indicator of poor risk marrow disease and the most consistent indicator is marrow involvement that is identified by both PET and histology. It should be mentioned when the BM involvement is negative on staging PET a solitary positive marrow biopsy dose not consist of adequate information for treatment planning or outcome prediction (28).

Also the iliac BM is not the only candidate for lymphoma that should be examined. As a reported case of one patient who had an initial negative iliac crest biopsy that followed by a positive biopsy from a focal "hot spot" within the left humeral head it is assumed that bone marrow in other important organs should be assessed as well in suspicious cases (16).

It is remarkable that despite the pain and missing focal lesions it has been reported that marrow biopsy causes hemorrhagic or compartmental complications during iliac crest bone biopsy procedures (29).

Based on literature most common treatment for DLBCL is chemotherapy in which taking CHOP and rituximab is frequently used. It is reported that patients receiving chemotherapy generally survived for a longer time in comparison with those did not (median 34 months versus 14 months) (30).

4. CONCLUSION

Any type of chronic pain of axial skeleton, pelvis area and main joints must be taken seriously. For primary examinations CT scan and MRI is strongly recommended. If nothing is observed and issue goes on, for a complete diagnosis BMB associated with PET is a wise choice. Treatment is directly depend on the diagnosis but CHOP in association with rituximab is a good chemotherapy alternative for patients with DLBCL.

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