CLINICAL NOTE

T-CELL LYMPHOBLASTIC LYMPHOMA DIAGNOSED WITH PLEURAL BIOPSY

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First award-winning clinical case at the 2017 Congress

Abstract:
We present the case of a 47-year-old male, without any significant history of disease, who was admitted to the pulmonology department with slowly progressing dyspnea. A left pleural effusion was observed.The patient's epidemiological background, clinical progress and the cytobiochemical analysis of the pleural fluid initially pointed towards a diagnosis of pleural tuberculosis (TB).However, the pleural biopsy done to complete the study confirmed a definitive diagnosis of t-cell lymphoblastic lymphoma.
The patient was transferred to the Hematology department, beginning a chemotherapy treatment after the completion of an extended study.After several complications that arose during said treatment, the patient was released and continues follow-up. He is currently in a state of complete remission.

Key words: lymphoblastic lymphoma, pleural effusion, pleural biopsy.

LINFOMA LINFOBLÁSTICO TIPO T DIAGNOSTICADO POR BIOPSIA PLEURAL

Resumen
Presentamos el caso de un hombre de 47 años, sin antecedentes patológicos importantes, que ingresa a cargo de neumología con clínica de disnea lentamente progresiva, objetivándose un derrame pleural izquierdo. Los antecedentes epidemiológicos del paciente, su evolución clínica y el análisis citobioquímico del liquido pleural, orientaban inicialmente al diagnóstico de tuberculosis (TBC) pleural. Sin embargo, la biopsia pleural realizada para completar el estudio confirmó el diagnóstico definitivo de Linfoma linfoblástico tipo T.
El paciente pasó a cargo del Servicio de hematología, comenzando tratamiento quimioterápico tras realizar estudio de extensión. Posteriormente a varias complicaciones que surgen durante dicho tratamiento, el paciente es dado de alta y continua en seguimiento, permaneciendo actualmente en estado de remisión completa.

Palabras clave: linfoma linfoblástico, derrame pleural, biopsia pleural.

INTRODUCTION

Under the WHO's classification system for hematologic neoplasms, lymphoblastic neoplasms, which can present as leukemia or lymphoma, are divided into two general categories: B-cell lymphoblastic leukemia/lymphoma, also called precursor B-cell acute lymphoblastic leukemia (precursor B-ALL) and T-cell lymphoblastic leukemia/lymphoma, also called precursor T-cell acute lymphoblastic leukemia (precursor T-ALL).

This is largely done because the prognosis and treatment differ between B-cell and T-cell neoplasms. These can be divided into lymphoblastic lymphoma or lymphoblastic leukemia. Clinically, a case is defined as lymphoma if there is a mass lesion in the mediastinum or another area and there are <25% blasts in the bone marrow. Leukemia is classified as >25% blasts in the bone marrow, with or without a mass lesion.

Although some patients present with predominantly lymphomatous involvement (for example, a mediastinal mass or other defined lesion), the majority later show medullary involvement. Similarly, patients presenting with leukemia may have or develop extramedullary tumors. As a result, acute

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lymphoblastic lymphoma and lymphoblastic leukemia should be considered the same disease with different clinical presentations.

A diagnosis is made based on an aspiration/biopsy of bone marrow and/or other involved tissues. In this paper, we present the case of a diagnosis made using pleural biopsy.

CLINICAL CASE

47-year-old Maghreb male, residing in Spain for 7 years, with no known allergies to medication or dangerous habits, who does not refer to any noteworthy preexisting pathology. No at-home treatment is provided. He has 9 siblings (4 male, 5 female) and 6 children. Family history of tuberculous lymphadenitis is unlikely. He has no oncological or hematological family history.

The patient goes to the hospital emergency department presenting with signs of progressively worsening dyspnea that has evolved over 2 months to the point of making minimal effort and suffering from pleurisy. No registered fever. No weight loss. No nausea or vomiting.

Physical examination: Glasgow Coma Scale: 15/15, with no neurological focality; no nuchal rigidity. No signs of dehydration and normal skin and mucus coloring.

Lung auscultation: reduced vesicular murmur in the left lung base, with no other pathological sounds. Cardiac auscultation: normal intensity tones without bruit.

Abdomen: soft, no tenderness, splenomegaly unlikely and positive peristalsis.

Extremities: no edema or deep vein thrombosis; no peripheral perfusion deficit.

Left submandibular, bilateral cervical and inguinal lymphadenopathies of about 4-5 cm can be felt.

Complementary tests:

1. *Analysis:* Hemogram. Slight leukocytosis without other notable changes. Serum iron, coagulation study, basic biochemistry and immunoglobulins: normal. Proteinogram: slightly elevated alpha-2. HIV, cytomegalovirus, Epstein Barr virus, syphilis, and hepatitis B serology: negative for active infection. Hepatitis C virus antibody: negative.
2. *Chest x-ray:* practically complete opacification of the left hemithorax, with right displaced cardiomediastinal structures; the presence of the polylobulated surface observed in the small area of this hemithorax with air density suggests an extensive and very thick, mesothelioma-type pleural mass.
3. *Chest CT:* marked nodular thickening of the left pleural cavity and mediastinal masses and lymphadenopathies, findings very likely caused by neoplasm. Initially assessed as mesothelioma or adenocarcinoma (Figure 1. Admission chest CT).
4. *Thoracic ultrasound:* moderate left pleural effusion. Linear images with "snowy" interior, suggesting partitioning. Marked parietal and visceral pleural thickening. Subjacent lung with mamelonated pleural thickening. It was not possible to clearly view the pulmonary echostructure. Diagnostic thoracentesis was done and 20 cc. of blood tinged fluid was extracted, which was sent to Cytobiochemisty, Microbiology and Anatomic Pathology. After studying the pleural fluid, a lymphocyte-predominant exudate with elevated ADA was observed. Pleural fluid cytology: highly cellular smear made up of limited reactive mesothelial cells and primarily by an intense population of small lymphocytes, heterogeneous without cellular atypia. Said findings were nonspecific, including the differential diagnosis of different infectious and inflammatory processes such as tuberculosis. Negative for neoplastic cells. Microbiological study of pleural fluid: negative. A pleural biopsy to confirm pleural TB and resistance study were also done. The biopsy confirmed the definitive diagnosis of t-cell lymphoblastic lymphoma
5. *Pleural biopsy:* after signing the informed consent, a pleural biopsy (x3) with Tru-cut (18G) using ultrasound was done without immediate complications and thoracentesis was done with Abbocath Nº16, draining 850 cc of serosanguinous fluid without immediate complications. Result: infiltration of the pleural wall by a population of small cells with limited cytoplasm and a round nucleus with dense chromatin, which appear to correspond to small lymphocytes and have the following profile:

Chromogranin: negative.
CD10: negative.
CD20: negative.
CD79a: barely positive.

CD3: positive.
CD5: positive.
CD23: negative.
CD56: negative.
Ki 67: near 99%.
Pleural wall with T-CELL LYMPHOBLASTIC LEUKEMIA/LYMPHOMA INFILTRATION.

6- *Medullary aspiration:* bone marrow with representation of all cell lines in which 2% immature cells are observed, lymphomatous bone marrow infiltration is ruled out.
Bone marrow biopsy: bone cylinder that shows general conserved architecture with a good relationship between hemopoietic tissue and adipose tissue, conserving all series, with no observed neoplastic lymphoid infiltrate. Bone marrow within normal limits.

7- *Spine-chest-abdominal CT:* marked left pleural thickening associated with pleural effusion and atelectasis of the left lung. Mediastinal adenopathy masses and hilar, cervical, supraclavicular and, to a lesser extent and less likely significance, abdominal and axillary adenopathies.

8- *Echocardiogram:* inconclusive study from the cardiological perspective with imaging of the parasternal region and an apical dense mass over fluid background, with good edge motility, suggesting a mediastinal mass.

Definitive diagnosis: stage IV-a lymphoblastic lymphoma with bulky mediastinal mass.

Once the diagnosis was established, staging was determined with an extended study and chemotherapy treatment was then started with the hyper-CVAD regimen (Cycle A: cyclophosphamide, vincristine, doxorubicin, Adriamycin and dexamethasone; Cycle B: methotrexate and cytarabine) after signing the informed consent. The third day of the cycle, an alteration was seen in urea, creatinine, uric acid, calcium and phosphorus amounts, a sign compatible with tumor lysis syndrome, which required increased hydration, intensifying diuresis, and substituting allopurinol with Rasburicase, as well as maintaining close analytical control. There were also isolated episodes of bradycardia, chest pain and dyspnea. All of these symptoms were quickly controlled with the measures taken. After one month of hospitalization and in light of favorable clinical evolution, the patient was released for outpatient monitoring.

Patient evolution.

After diagnosis, the patient received chemotherapy treatment with the hyper-CVAD regimen (4 cycles), achieving partial remission. As a result, he underwent 6 additional cycles. At 7 months, he shows disease progression, and thus begins a 2nd line treatment with nelarabine (4 cycles) and local mediastinal radiation therapy, achieving partial remission. Hematopoietic stem cell transplantation (HSCT) was not done due to the patient presenting with febrile neutropenia after induction with the DHAP regimen (cisplatin, cytarabine, dexamethasone).

To date, the patient has suffered several post-chemotherapy complications: tumor lysis syndrome; hospitalization for toxic hepatopathy; neutropenic fever; esophageal candidiasis; cytomegalovirus infection with gastric, pulmonary, retinal and hepatic involvement; and septic shock from pneumococcal pneumonia that required admission to the Intensive Care Unit.
The patient continues to undergo periodical examinations at hematology clinics and is currently in a state of complete remission (Figure 2. Chest CT after chemotherapy).

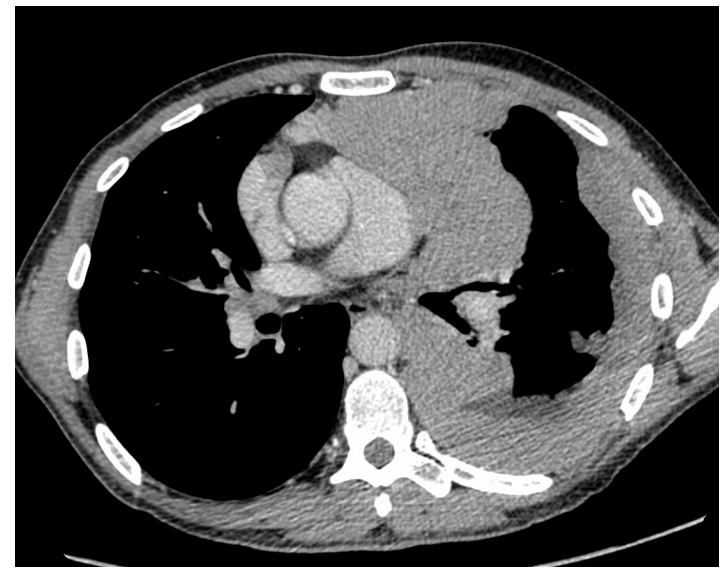

Figure 1.

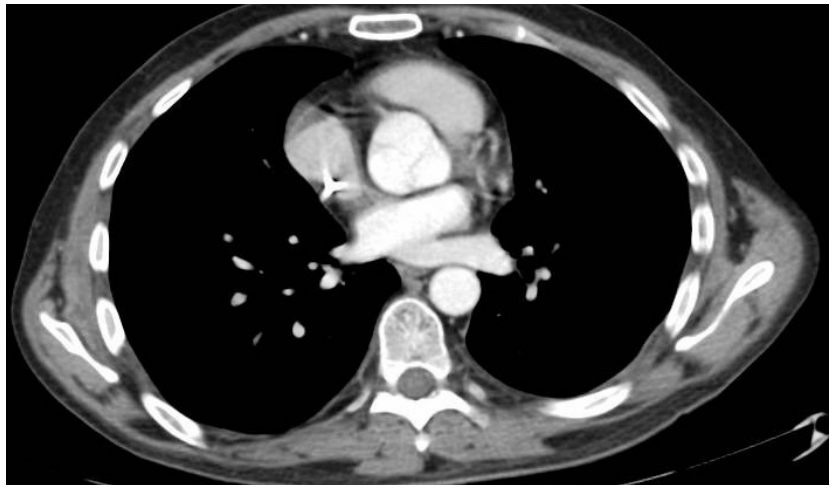

Figure 2.

DISCUSSION

T-cell lymphoblastic lymphoma most often affects adolescents and adults, primarily males at a ratio of 2:1 and accounts for 2% of adult non-Hodgkin lymphomas[1]. Incidence in the United States is approximately three cases per one million people a year and does not vary according to ethnicity[2].

Patients are usually male, in their early 20s, and present with cervical, supraclavicular and axillary lymphadenopathies (50%) or a mediastinal mass (50-75%)[3].

In most patients, the mediastinal mass is anterior, bulky and associated with pleural effusions. These masses can cause complications like superior vena cava syndrome, tracheal obstruction and pericardial effusions (with or without tamponade). The evolution of the disease can vary, with some patients showing symptoms which slowly progress over weeks or months and others present with more acute symptoms[4].

Less commonly, patients present with extranodal disease (for example, cutaneous, testicular or bone involvement). Abdominal involvement is very infrequent, but when it does occur, it is mainly found in the liver and spleen[5].

More than 80% of patients with the disease are stage III or IV and almost 50% of all patients have B symptoms. In the majority, lactate dehydrogenase (LDH) serum levels are elevated. Although the bone marrow often appears normal, approximately 60% of patients develop bone marrow infiltration and subsequent leukemia[6].

Evaluation of cerebrospinal fluid is essential to rule out central nervous system (CNS) involvement which is often observed. Patients with bone marrow involvement show a particularly high incidence of CNS infiltration[7].

A diagnosis of T-cell lymphoblastic leukemia/lymphoma is made by performing a bone marrow aspiration and/or biopsy and/or aspiration with or without biopsy of other involved tissues, such as the mediastinum. In addition to histological analysis, portions of the aspirated material or the biopsy sample must be sent for flow cytometry and cytogenetic evaluation[8].

The term T-cell acute lymphoblastic leukemia is used when there are more than 25% blasts in bone marrow, with or without a mass lesion. In cases with a mass lesion and less than 25% bone marrow involvement, the term T-cell lymphoblastic lymphoma is used[9].

Our clinical case confirms the importance of pleural biopsy in patients with suspected pleural TB.

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