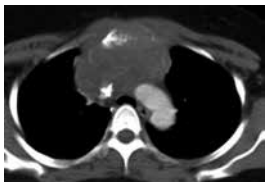

PRIMARY MEDIASTINAL LYMPHOMA (THYMIC): A CASE REPORT

Linfoma primario del mediastino (tímico): Presentación de caso

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Summary

Anterior mediastinal lymphomas may be part of systemic lymphoma and they comprise approximately 50 % of mediastinal neoplasms. Primary non-Hodgkin's lymphoma of the mediastinum is a subtype with lower prevalence, representing 10 % of all cases; it has two histologic subtypes that include T-cell lymphoblastic lymphoma and diffuse large B-cell lymphoma. The latter is an aggressive neoplasm that tends to infiltrate the pleura, bone structures and the lung; it originates from thymic medullary B cells. This article presents a case of primary non-Hodgkin's lymphoma of the mediastinum with diffuse large B-cell subtype, its radiologic findings, pathology and a brief review of the literature.

Resumen

Los linfomas mediastinales anteriores pueden hacer parte del linfoma sistémico y comprenden aproximadamente el 50 % de los tumores mediastinales. El linfoma no Hodgkin primario del mediastino es un subtipo de menor prevalencia, representando un 10 % de los casos; este tiene dos subtipos histológicos que son el linfoma T linfoblástico y el linfoma B difuso de célula grande. Este último es agresivo y tiende a infiltrar la pleura, las estructuras óseas y el pulmón; se origina de las células B de la médula del timo. En este artículo se describe un caso de linfoma no Hodgkin primario del mediastino del subtipo B difuso de células grandes, sus hallazgos por imágenes, patología y una breve revisión de la literatura.

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Introduction

Anterior mediastinal lymphoma type lesions generally make part of systemic lymphoma; however, a subtype with lower prevalence is the primary non-Hodgkin's thymus lymphoma. This last one is a low frequency entity, described in 1970 by Van Heerden and collaborators (1) that is characterized by an aggressive behaviour with tendency for local invasion.

The two histological subtypes of primary non-Hodgkin's mediastinal lymphoma are T-cell lymphoblastic lymphoma and diffuse large B-cell lymphoma. This last one represents only 6-10% of non-Hodgkin's lymphomas. Next we describe the case of a 24 year old patient with primary non-Hodgkin's lymphoma of the mediastinum with diffuse large B-cell subtype and its findings by images

Clinical case

Female patient is of 24 years of age, without relevant clinical history, who consults emergency services given a clinical picture of 2 months of evolution of thoracic pain and dyspnea associated to constitutional symptoms. The physical exam finds a sternal mass of 8 cms × 6 cms, painful, with no inflammatory or compressive signs. The para-clinical exams discard infection.

In the thorax radiography (figure 1) a mediastinal engrossing was identified, for which a computerized tomography (CT) of the thorax (figure 2) was performed, where an anterior mediastinal mass could be observed with infiltration to the thoracic wall and with compressive effect over the superior cava vein and trachea.

A biopsy was performed that revealed a malignant tumour constituted by large pleomorphic cells, with oval nuclei and clear cytoplasm (figure 3a). In the immunohistochemistry studies reactivity of the tumour cells was identified to CD20 (B lymphocyte marker) (figure 3b), CD30 (T lymphocyte and activated B lymphocyte marker), CD10 (germinal centre B cell marker) (figure 3c), and negativity for CKAE1/AE3 (epithelial cell marker), CD5 (T population marker), CD15 (Reed Sternberg cell marker), CD23 (B cell marker). Cellular proliferation index marked with KI 67 was close to 80% (figure 3d). The findings were compatible with diffuse large B cell lymphoma.

Posteriorly a positron-emission tomography (PET) was done, previous to the start of treatment (figure 4), where fluorodeoxyglucose acquisition by the mediastinal mass was observed. Ganglionar or extra-mediastinal viscera compromise was discarded, compatible with the primary diffuse large B cell lymphoma of the mediastinum.

In the CT and PET (figure 5) done after the treatment a partial response was shown given the decrease in the size of the mediastinal lesion and lower acquisition of the fluorodeoxyglucose when compared to the initial study.

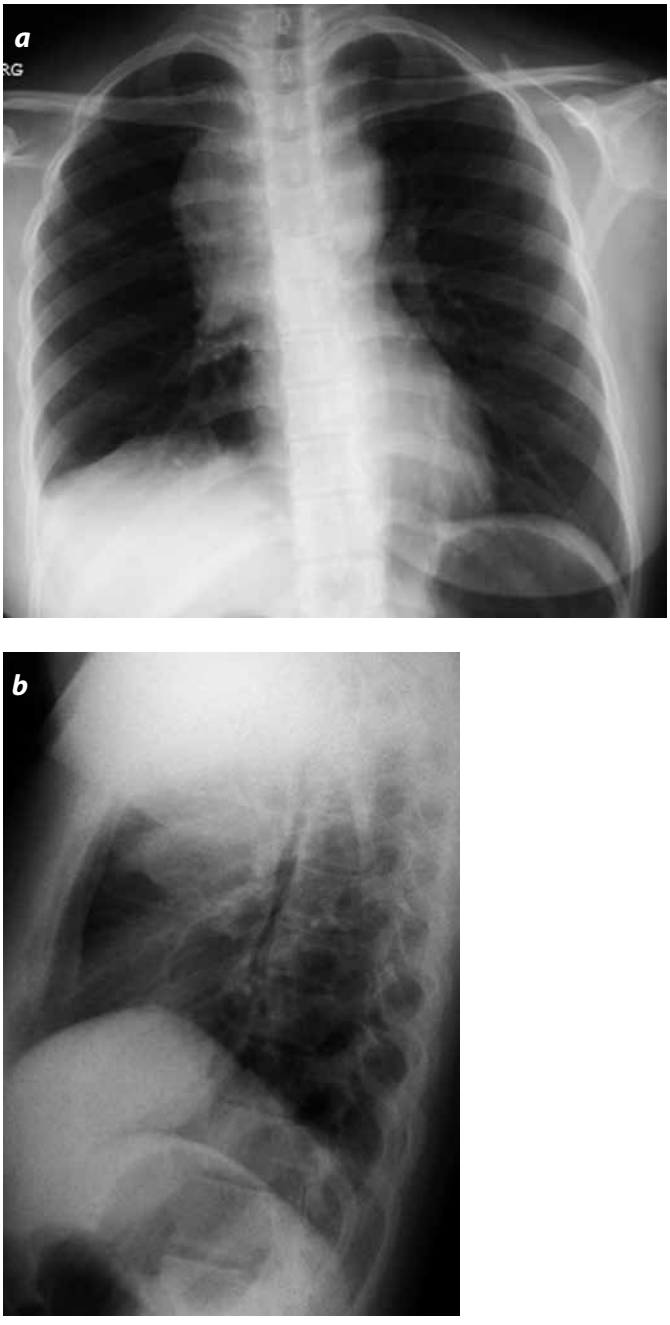

Figure 1. a and b). Radiography of the thorax, PA and lateral projection. Mediastinal engrossing due to lesion in the anterior mediastinum.

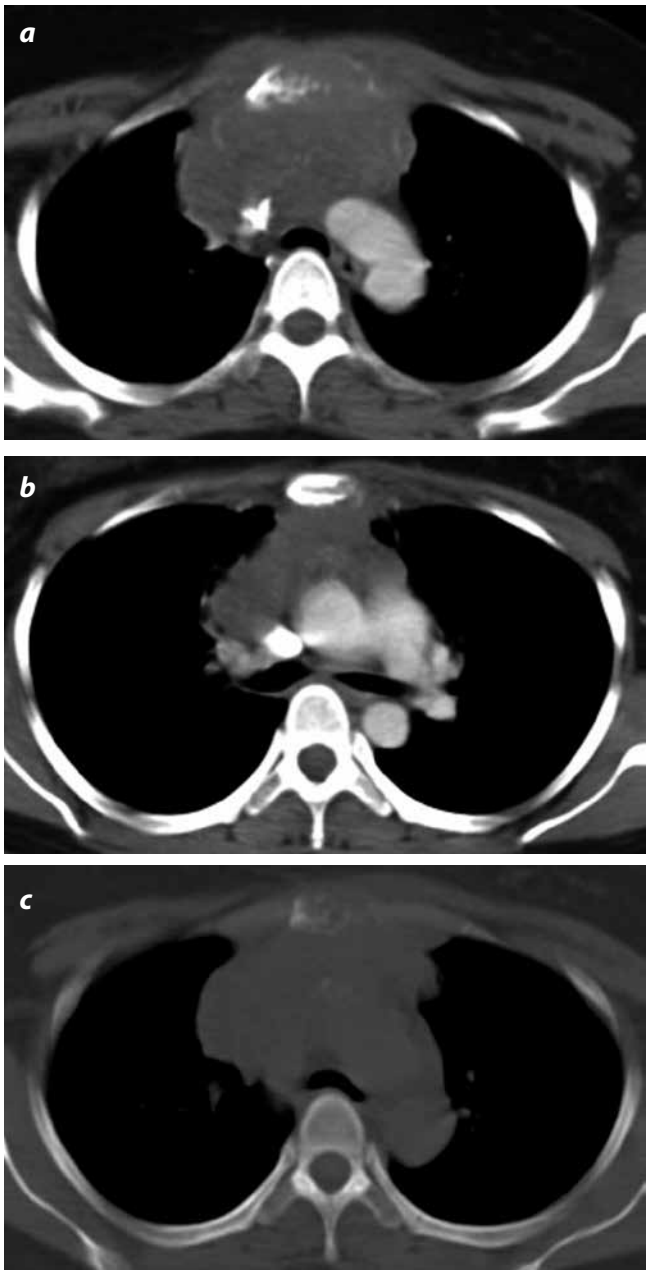

Figure 2. a and b). Thorax CT with endovenous contrast medium in window of soft tissue, c) bone. Lobuled contour mass with soft tissue density and scarce enhancement of the contrast medium, localized in the anterior mediastinum and producing compressive effect over the superior cava vein, decrease in the AP diameter of the trachea and infiltration to the sternum and the thoracic wall.

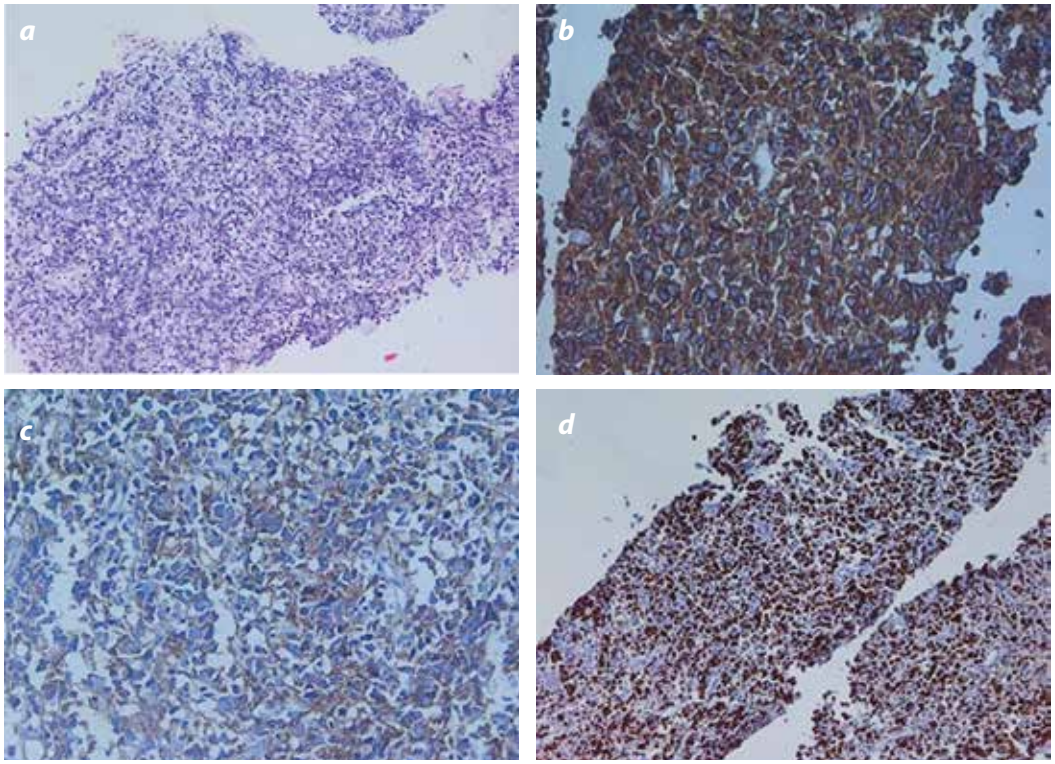

Figure 3. a). Eosine hematotoxiline coloration. b) Cellular immunoreactivity (membranous and cytoplasmatic) to CD20. c) Cellular immunoreactivity (membranous and cytoplasmatic) to CD10. d) Cellular proliferation index marked with KI67 (nuclear marker).

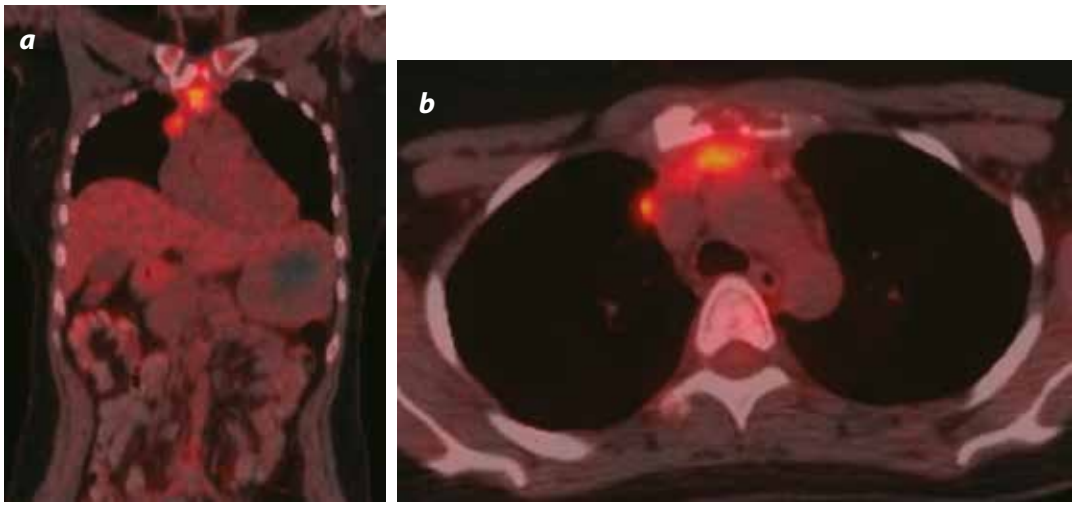

Figure 4. PET. a) Coronal reconstruction, b) axial section. Fluorodeoxyglucose acquisition by the mediastinal mass.

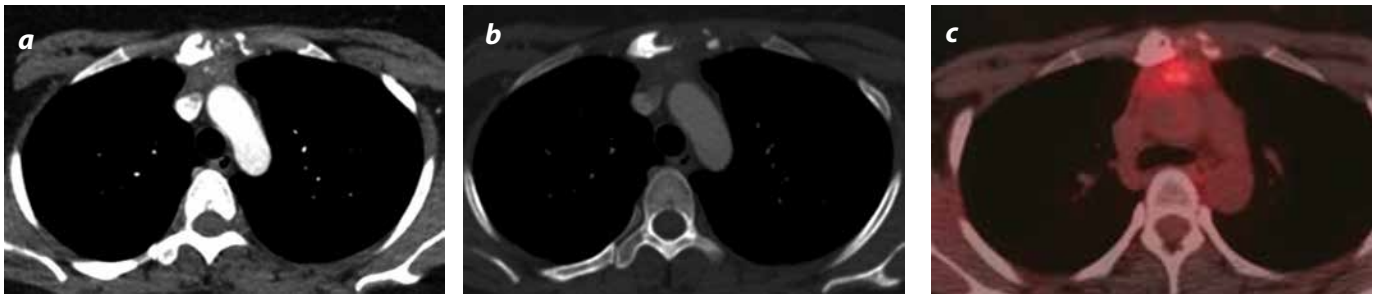

Figure 5. a) Contrasted CT of the thorax in soft tissue window, b) in bone window: decrease in size of the lesion compared to previous study. Invasion to the sternum and thoracic wall persists. c) PET, decrease in the acquisition of the fluorodeoxyglucose is identified.

Discussion

Tumours of the anterior mediastinum represent 50% of all mediastinal lesions; they include thymoma, teratoma, thyroid and lymphoma disease. Lymphoma represents 20% of all mediastinal neoplasias in adults and 50% in children (2).

Mediastinal infiltration due to lymphoma occurs as a systemic dissemination of the disease in the majority of patients, and in a less frequent form, as a primary tumour in upto 10% of the cases (3).

Among the group of primary mediastinal lymphomas a 15 to 25% are of the non-Hodgkin's type (NHL). Less than 3% of all NHL cases correspond to a rare subtype of lymphoma known as primary diffuse large B cell mediastinal lymphoma or thymic lymphoma (4).

The primary NHL of the mediastinum was described by Van Heerdemn and collaborators in 1970 (1); it corresponds to an aggressive subtype of lymphoma with a high dissemination tendency (5). The two main forms of mediastinal NHL are the T lymphoblastic lymphoma and diffuse large B cell lymphoma. The primary mediastinal diffuse large B cell lymphoma or thymic lymphoma is a neoplasm of aggressive behaviour whose origin are thymic B cells localized in the medulla of this organ. The age of diagnosis is between the third and fourth decade of life and there is predominance in the female sex (2,6). The clinical manifestations at the moment of appearance include coughing, thoracic pain and dyspnea. It is frequent the appearance of compressive symptoms when the airway and vascular structures are invaded (7).

In the evaluation by images, the thorax radiography in patients with a mediastinal mass due to lymphoma show paratracheal or prevascular lymphadenopathies in 76% of the cases and can be accompanied by pleural leakage (2,5).

This tumour is usually present in the CT as a large mediastinal mass, reaching in 75% of patients more than 10 cms in diameter. With frequency it infiltrates the lungs, the thoracic wall, the pleura and the pericardium; besides, a third of patients present pleural or pericardial leakage (7). Its borders can be smooth or lobuled and in half the cases its aspect is heterogeneous with low signal areas due to the presence of necrosis, haemorrhage or cystic degeneration. After contrast medium administration the enhancement is usually heterogeneous (2).

In the magnetic resonance (MR) evaluation, the thymic lymphomas have a low signal in sequences with T1 information, variable signal in sequences with T2 information and heterogeneous enhancement of the contrast medium (8). It is not possible to differentiate by images the thymic lymphoma from other primary thymus neoplasias; however, the presence of lymphatic ganglia of increased size and invasion of the thoracic wall are suggestive of lymphoma (9).

At the end of the therapy it is expected that the thymic lymphoma is of low signal in T1 and T2 due to the presence of residual fibrosis; however, in the recurrent lymphoma a high signal in T2 persists (10).

After chemotherapy, approximately in 10-25% of patients a rebound thymic hyperplasia is manifested. In occasions, this can be difficult to differentiate from the recurrent disease. A useful tool in the differentiation of these two entities is the valuation with sequences in phase and out of phase, since in the rebound thymic hyperplasia the intracellular fat infiltration makes the signal drop in the sequences that are out of phase, phenomena that does not happen in the recurrent lymphoma. This tool has a limited use in young patients where fatty infiltration has not happened. In them the restriction to valuation of infiltration with diffusion sequences and the map of the apparent diffusion coefficient (ADC) help detect the recurrent disease (10).

The staging of the diffuse large B cell lymphoma is the same as the one for other lymphomas (11) where the infiltrated ganglionic groups, its relation with the diaphragm, the extension to extralymphatic organs and patient symptoms are evaluated.

The PET with fluorodeoxyglucose is considered the most sensitive and specific technique for patients with lymphoma and is used for the pre-treatment evaluation, response during treatment and post-treatment re-staging, since the metabolic changes precede the morphological ones. This technique is based in identifying areas with increased metabolic activity that, when fusioned with the CT, allow to perform an adequate anatomical localization of the place with metabolic increase (10). The standardized uptake values (SUV) used to define the thymic compromise due to lymphoma differ between some authors: for Gawande and collaborators, values above 3.4 are a strong predictor of lymphoma (12); however, the absence of a unique value for the diagnosis of lymphoma and the superposition that occurs in occasions between the measured SUV for lymphoma and rebound thymic hyperplasia makes it necessary to evaluation through MR to differentiate if the SUV measurements are undetermined. Otherwise, control with PET is enough in the follow-up of these patients.

When the diffuse large B cell lymphoma recurs it does so in the thorax, generally in the first 2 years of follow-up, for which evaluation with contrasted thorax CT has also been proposed (2). Faced with the suspicion of recurrence a histological confirmation must be made. A 5-year survival rate free of recurrence of a 65% has been described (7).

The differential diagnosis must include the more frequent anterior mediastinal masses, among these other types of lymphoma and, specially, the NHL of lymphoblastic type.

The primary mediastinal diffuse large B cell lymphoma is a neoplasia of large to medium B cells. For the diagnosis of this entity it is required the evaluation of the morphological and immunophenotypic characteristics, by histology, immunohistochemistry or flow cytometry. Morphologically it is characterized by a patter of diffuse growth, although it has an ample cytomorphological range, the majority of these lesions have monomorphic characteristics (13).

Cells are characterized by a broad clear cytoplasm, ovoid and irregular nucleus and small nucleolus that, in occasions, can be absent. It is associated to mitotic activity and intermixed collagen fibres (7,13). The neoplasic cells express specific immunohistochemical markers for the B cell lineage, such as CD19, CD20, CD22 and CD79a. It has been detected up to a 69-80% reactivity for CD30, 20-25% for CD10 and 45-100% for BCL6, with variable reactivity in the different studies for CD15 and MUM1. The CD15 and CD21 markers are always negative (7,13,14).

Conclusions

The lymphoma is part of the neoplasias that most frequently compromise the anterior mediastinum, in the majority of cases being a Hodgkin lymphoma (50-70%). The primary mediastine diffuse large B cell lymphoma is a low frequency entity with an atypical behaviour

given the tendency for local invasion and secondary invasion to the pleura, the pericardium, the thoracic wall and lung.

Its characteristics by images are similar to that of other primary thymus neoplasias, for which the only way to differentiate it from these is through the histological evaluation.

Although the PET is the most recommended technique in the diagnosis, follow-up and post-treatment evaluation, there exist other imaging techniques that are also useful, mainly the MR that allows to differentiate the rebound thymic hyperplasia from the lymphoma.

The survival in these patients is lower when compared with other subtypes of lymphoma and its recurrence is present with higher frequency in the thorax, in the first two years of follow-up.

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