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PRIMARY PULMONARY SMALL B-CELL NON-HODGKIN LYMPHOMA -CASE PRESENTATION-

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ABSTRACT

Primary pulmonary non-Hodgkin lymphoma is a rare entity, accounting for 3-4% of extranodal non-Hodgkin lymphomas. Indolent primary pulmonary non-Hodgkin lymphomas are the most frequent types, with the MALT subtype representing majority of cases. Other indolent subtypes of B-cell primary pulmonary lymphomas are rare. We present the case of a 56-year-old patient, non-smoker, who presents for pain in the right hemithorax, worsened by deep inhales. Pulmonary X-ray showed a right paramediastinal superior and medial lobe homogenous opacity with faded contour. Thoracic computed tomography scan described a dense right superior mediastino-pulmonary tumoral mass, the absence of hilar or mediastinal adenopathies. In this context, an ultrasound-guided transbronchial needle aspiration was performed. Histopathology and immunohistochemistry confirmed the diagnosis of primary pulmonary small B-cell non-Hodgkin lymphoma. After 6 chemotherapy cycles, from a clinical and imagistic (thoracic CT scan) point of view, the response was favourable. Positron emission tomography (PET/CT) aspect indicated a complete metabolic response to treatment.

Keywords: lung, non-Hodgkin lymphoma, small B-cell lymphoma

Introduction

Non-Hodgkin lymphomas (NHL) are heterogenous group of malignant monoclonal cell proliferations originating in the lymphoid tissue (B or T/NK cells) (1,2). Heterogeneity pertains to clinical presentation, histology, immunohistochemistry, evolution, and prognosis. There are two major groups of NHL with differing clinical and prognosis particularities: indolent and aggressive lymphomas (3).

Clinical onset in NHL can be nodal or extranodal. Extranodal subtypes can be either primary or secondary.

Small B-cell lymphocytic lymphoma is an indolent NHL. This term is used when there is nodal or extranodal involvement without leukemic transformation (4).

We present the case of a primary pulmonary small B-cell lymphocytic lymphoma.

Case presentation

This study was performed after approval of local hospital committees and with the written consent of the patient.

A 56-year-old patient, non-smoker, was admitted to the Haematology Department of the County Emergency Clinical Hospital Constanta in January of 2019, for pain of the right hemithorax,

worsened by deep inhale.

From the patient´s medical history, we noted that in 2015 she was admitted in a Pneumology Service for similar symptoms. Chest X-ray performed at that time showed a lung consolidation in the right superior lobe. Therapeutic trial (antibiotics and symptomatic treatment) was negative. The patient underwent a thoracic CT-scan which revealed a nodular lesion in the right upper lobe, adjacent to the mediastinal pleura, without mediastinal adenopathies. A broncho-alveolar lavage was uncharacteristic, while bronchoscopy was inconclusive. Thus, a PET-CT scan was recommended, which revealed a pulmonary mass with high metabolic activity (SUV 6.9 ng/ml). Afterwards, the patient was lost from follow-up.

Upon current admission to the Haematology Department, the patient was in an overall good state (ECOG=0) with pain in the right hemithorax, BMI=28.12.

Physical examination revealed diminished respiratory movements of the right hemithorax (on account of the pain). The rest of the physical examination was unremarkable.

In what regards laboratory testing, a complete blood count showed lymphopenia (670/mmc), normal renal and hepatic function, negative viral markers, normal pulmonary tumoral markers, LDH=186 U/L, beta-2 microglobulin=1.69 g/dL. Spirometry and bronchial aspirate were unremarkable. Left ventricular ejection fraction (LVEF) was 65%.

Chest X-Ray showed a right paramediastinal homogenous opacity at the level of the superior and middle lobe, with a faded contour.

Thoracic CT scan described a dense superior right mediastino-pulmonary mass and the absence of hilar or mediastinal adenopathies (Figure 1).

Abdominal and pelvis CT scan with contrast substance were normal.

In this context, an ultrasound-guided transbronchial needle aspiration was performed (EBUS-TBNA).

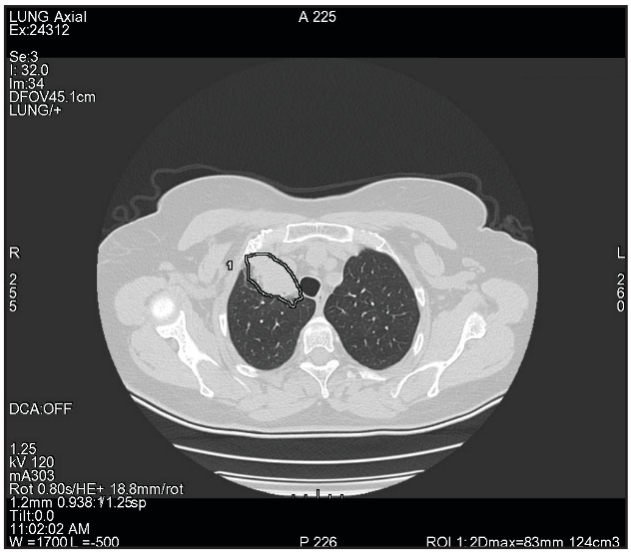

Figure 1. Thoracic CT scan before treatment

Histopathologic examination described fibrin and hematin fragments including fragments of bronchial epithelium and small, monotonous lymphoid aggregates (Figure 2).

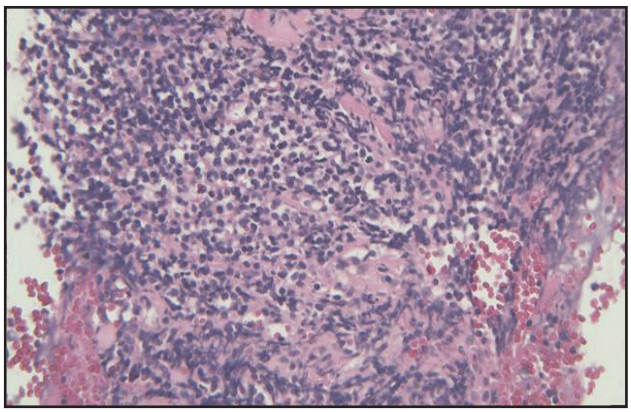

Figure 2. Malignant lymphoid proliferation with small, monomorphous lymphocytes, with hyperchromic nuclei, with irregular contour, reduced cytoplasm, arranged as aggregates

At this moment, the issue of a differential diagnosis between a lymphoma and a small-cell lung carcinoma was raised. Immunohistochemistry was performed for the following markers: CD 20, CD 23, CD 3, CD 10, ki67, BCL 6, CK 19, p53. The examination was positive for CD20 (Figure 3), and CD23 in proliferated B cells positive for CD3 in reactive T lymphocytes, Ki67 15% (Figure 4), negative for CD10, BCL 6 and CK 19 in proliferated B cells (Figure 5). Immunohistochemistry detected a ”wild-type” p53 mutation pattern, with isolated positive nuclear expression in some

tumoral lymphocytes (Figure 6). The results were confirmed through Fluorescence In Situ Hybridization (FISH).

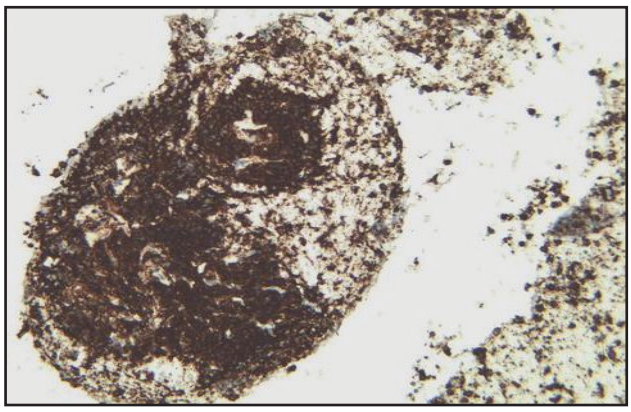

Figure 3. Intensely positive membrane CD 20

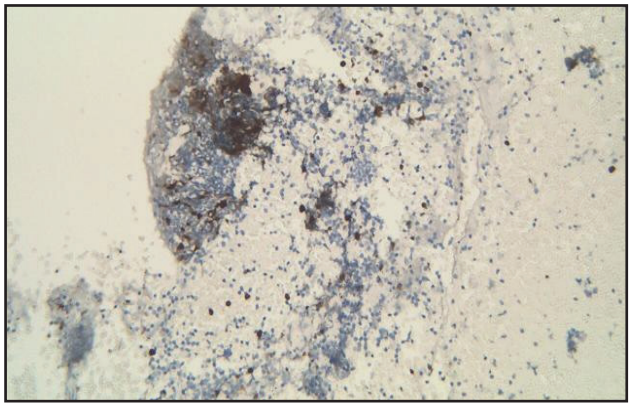

Figure 4. Immunohistochemistry expression of Ki67 is observed in 15% of tumoral cells nuclei

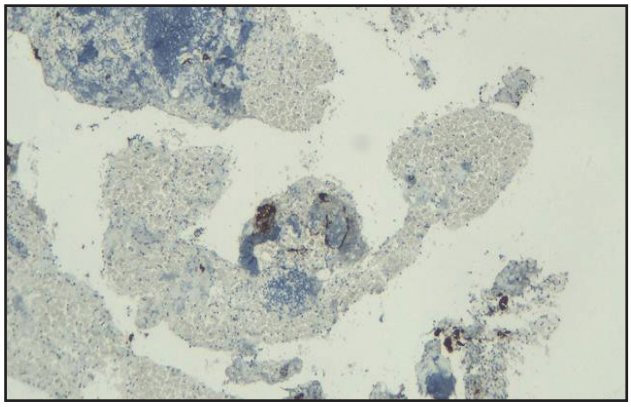

Figure 5. Immunohistochemistry expression of CK19 is negative in tumoral lymphocytes and positive in the membrane of isolated epithelial cells (pneumocytes)

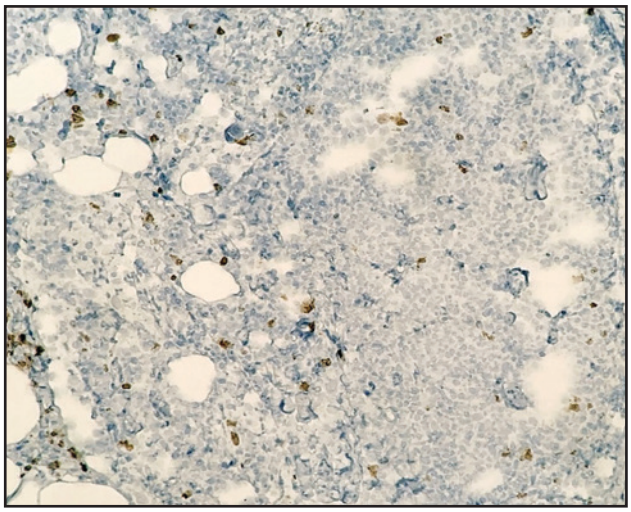

Figure 6. Nuclear immunohistochemistry expression of "wild-type" p53 in tumoral lymphocytes

Standard staining microscopic aspect and immunohistochemistry phenotype of tumoral proliferation were highly suggestive for the diagnosis of small B-cell primary pulmonary lymphoma with a p53 "wild-type" expression and excluded the presence of cells related to a small-cell lung carcinoma.

Bone marrow aspirate was unremarkable.

After signing the informed consent and evaluation the frailty score of the patient, treatment according to protocol with R-CHOP was initiated (Rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone).

After 6 chemotherapy cycles, both from clinical and imagistic (thoracic CT scan) point of view, the response was favourable (Figure 7 a, b).

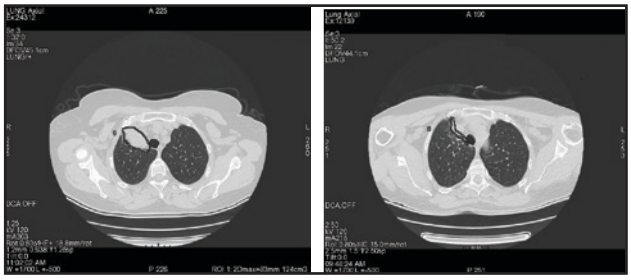

Figure 7a, b. Thoracic CT scan before and after treatment

PET/CT aspect indicated a complete metabolic response to treatment.

After 12 months, the patient is in complete remission.

Discussions

In the case presented herein, the first challenge was represented by differentiating between a primary pulmonary NHL and a small lung cell carcinoma.

Primary pulmonary lymphoma is a rare clinical entity, with non-specific symptoms or radiographic findings, representing less than 1% of NHL, 3-4% of extranodal NHL and <1% of primary pulmonary malignancies (5, 6).

Amongst low malignancy primary pulmonary lymphomas, MALT lymphoma represents 70-90% of cases and the rest of 10% are other entities, which, according to the WHO classification, comprise follicular lymphoma, mantle cell lymphoma, and lymphocytic lymphoma/chronic lymphatic leukaemia. A „pure" lymphocytic lymphoma, without leukemic transformation, is found in less than 10% of NHL cases (7, 8).

Small lung cell carcinoma usually appears in smokers and is the most aggressive type of pulmonary cancer. It metastasises early in the mediastinal lymph nodes, liver, suprarenal glands and cerebrum.

In this case, 3 years passed between the time of the first PET/CT, which showed the presence of a pulmonary mass with high metabolic activity, and the current admission. During this whole period, the patient was asymptomatic.

In primary pulmonary small B-cell NHL, clinical presentation is often non-specific and symptoms can be absent for a long period of time (like in our case) or can manifest with cough, thoracic pain, moderate dyspnoea, and, rarely, haemoptysis. Upon auscultation, pulmonary rales can be heard in less than 20% of cases and imaging tends to be non-specific, meaning that histological examination is mandatory for the positive diagnosis (9, 10, 11).

From an immunohistochemistry point of view, tumoral cells express specific markers for small B-cell non-Hodgkin lymphoma, but with a "wild-type" p53 mutation pattern. Sometimes, negative immunohistochemistry expression of p53 can be caused by the complete deletion of the p53 gene, which leads to a halt in the synthesis of the p53 protein, but this is a rare occurrence. An insertion which introduces a stop codon can lead to the synthesis of a sufficient amount of p53 protein, enough for it to be detected (12).

In the case presented, the small-B cell primary pulmonary non-Hodgkin lymphoma with "wild-type"/normal p53 expression confirms the low malignancy grade of the lymphoid proliferation, which was also in accordance to the patient s evolution.

In what regards treatment, this includes the „wait and watch" approach, surgical intervention for localized masses, chemotherapy, radiotherapy. Currently, there are no guidelines that have convened on a therapeutic approach. In our case, the therapeutic choice consisted of chemotherapy associated with the monoclonal antibody Rituximab, as surgical intervention was not feasible.

Conclusions

Non-specific clinical manifestation and indolent evolution of certain types of lymphoma often lead to a delayed diagnosis or misdiagnosis in many cases. Indolent lymphoma should be taken into account into the differential diagnosis of pulmonary masses, particularly for patients without risk factors for lung cancer or lung metastases. Although patient survival is good, further clinical experience and long-term follow-up are needed to identify prognostic factors.

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Conflict of interests

The authors declare that they have no conflict of interests. Authors have contributed equally.

Disclaimers: The views presented in the submitted article are that of the authors and not an official position of the institution or funder.

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