LARGE-B-CELL NON-HODGKIN'S LYMPHOMA *versus* THYMOMA: THE IMPORTANCE OF DIAGNOSIS ACCURACY IN THE LIGHT OF A REPORT CASE

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Introduction

The mediastinum is an anatomical area with great tissue diversity and, therefore, mediastinal tumors represent a great variety of neoplasia, with different origins and predilections by different locations within this compartment. In the anterior mediastinum compartment, thymomas, teratomas, thyroid goiter and lymphomas predominate; in the middle mediastinum, congenital and pericardial cysts are more common, whereas neurogenic tumors are found almost exclusively in the posterior mediastinum[1].

There has been an important evolution in diagnosis of neoplasia in more recent years. The inclusion of clinical, immunological and genetic aspects associated with histological analysis allowed a better characterization of this group of diseases. However, cases remain difficult to classify due to the overlapping of histological, biological and clinical characteristics. Establishing a correct diagnosis has, obviously, clinical consequences, since the different therapeutic approach between different types of neoplasia is well known[2].

Based on the research of the authors, it is possible to show the importance of a correct and accurate investigation of the neoplasia in order to avoid iatrogenic damages by the mistaken establishment of ineffective, devastating and unnecessary therapies. Thus, the importance of reporting this report case is justified.

This work was carried out based on the analysis of the medical records of this case and the reports and results of the examinations annexed thereto, authorized by the Ethics and Research Committee of the University Center Assis Gurgacz Foundation, under opinion number 2.929.771.

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Case report

DAC, 31, female, sought care in a highly complex medical service in a city in the interior of the State of Paraná, in December 2016. She presented thoracic pain in the dorsal region, irradiated to the left upper limb a day ago, with worsens due to movement and palpation, refractory to NSAIDs and opioids. She denied other manifestations and comorbidities. She denied smoking and alcoholism, with no significant family history.

She was in good general condition, lucid and oriented in time and space, colored and eupneic. Although the pain was ventilatory-dependent, the vital signs were normal: she was afebrile, without cough or hemoptysis.

The physical examination allowed the identification of elongated nodules in the cervical region at level II, of approximately 2 centimeters and small nodules at level V.

It was evaluated by chest X-ray, echocardiogram and electrocardiogram, which were considered normal. Hemogram, TAP and KPTT without alterations, preserved renal and hepatic functions.

The patient was hospitalized, received analgesia and evaluated with chest tomography, which identified a mediastinal mass.

The mass was evaluated with aspiration puncture in January 2017. Microscopic analysis identified scarce material with minute foci of necrotic neoplasia. The patient was submitted to videothoracoscopy (February 2017) and the material collected and submitted to histopathological analysis showed an undifferentiated necrotic malignant neoplasm.

The immunohistochemical study showed positivity for CD45RB and for CD20 and negativity for pan-cytokeratin. The diagnosis was of a large-B-cell non-Hodgkin's lymphoma.

The bone marrow examination, performed in the same period, showed a discrete erythroid series maturation deficiency and absence of signs of neoplastic infiltration.

PET-CT showed an increased bilaterally uptake in small cervical lymph nodes, at level II (0.7 cm), in pericardial hypodense mass on the right side (6.7 cm), in the anterior mediastinal, pre-vascular, paratracheal and infracarinal lymph nodes. The findings were suggestive of active lymphoproliferative disease, with score 5 of Deauville 5-point scoring system. The disease was staged as IIB (Ann Arbor).

In April 2017, the patient started chemotherapy with R-CHOP regimen (Rituximab combined with CHOP regimen - Cyclophosphamide, Doxorubicin, Vincristine and Prednisone). Six cycles were scheduled and subsequent re-evaluation.

She evolved without significant complications and the treatment was completed in August 2017. The re-evaluation PET-CT revealed mediastinal mass with soft tissue density

near the right pericardium, measuring 5.0 cm on the largest transverse axis: compared to the previous PET-CT, there was a small volumetric and metabolic reduction of the right paracardiac mediastinal mass and no paratracheal and infracarinal cervical or mediastinal lymph nodes with significant metabolic activity were observed.

The patient underwent to a new biopsy of the mediastinal mass and, before its result, the table was considered (by PET-CT) as refractory to the treatment and 4 cycles of second line chemotherapy with R-ICE scheme (Rituximab, Ifosfamide, Carboplatin and Etoposide).

The result of the biopsy was xanthogranulomatosis with extensive areas of necrosis, old hemorrhage and grafting images suggestive of histoplasmosis. A new immunohistochemical study was then requested.

The reevaluation suggested the diagnosis of fibrosing granulomatous mediastinitis and xanthogranulomatous reaction to crystals of superadded cholesterol, possibly induced by histoplasmosis or tuberculosis, or inflammatory myofibroblastic pseudotumor or idiopathic sclerosing mediastinitis.

Treatment was suspended, and the patient performed a new PET-CT (November 2017), which evidenced a reduction in volume and uptake of mediastinal mass, hypercaptation in the chest wall and right breast, with signs of fracture or osteotomy in the sixth right costal arch. It was then decided to forward the material available for evaluation to a center of reference (December 2017).

The tests review revealed coagulative necrosis, with no expression of CD20 in the studied cells, with the conclusion that there was no morphological evidence of malignancy. The patient was, along with all available material, sent to another referral center (January 2018). The pathological review showed vascular congestion and extensive necrotic area, absence of granulomas, searches for B.A.A.R. and negative fungi with no data that could corroborate the diagnosis of Non-Hodgkin's Lymphoma, revealing the diagnosis of Thymoma from the beginning of spontaneous regression with traces of lesion in the mediastinum. The recommendation of this service was to follow up with PET-CT every three months and reoperate if there is growth.

Discussion

The mediastinum is an area that involves many organs and structures with great tissue diversity, which explains the diversity of conditions, from small cysts to neoplasia with different histogenesis and predilection for distinct areas within the mediastinum itself. This,

often associated with the reduced amount of material for analysis, often makes the definitive diagnosis of neoplasm a challenge[1,3].

The initial anatomopathological diagnosis of non-Hodgkin's lymphoma was made in a patient complaining only of pain, without other manifestations such as B-Lymphoma symptoms (loss of 10% of body weight in six months, night sweats and fever greater than 38ºC). These, however, are only observed in 40% of patients with non-Hodgkin's lymphoma, usually with disseminated disease[4].

Non-Hodgkin's lymphomas, in addition to B symptoms, can lead to weakness, fatigue, anorexia, cachexia, normocytic anemia, bone marrow infiltration, neutrophilia, eosinophilia, lymphopenia, increased lactic dehydrogenase, reduced platelet count in late phases, HSV and increased CRP, conditions not presented by the patient too[5,6].

The diagnosis of non-Hodgkin's lymphoma should be based on the results of anatomopathological reports, complemented with immunohistochemical study and possibly immunophenotyping, cytogenetic and molecular analysis, among others. The extent of the disease (staging) is made by radiographic examinations, possibly complemented by biopsy of suspicious sites[7].

The diagnosis of the patient, as well as its staging, was based on anatomopathological, immunohistochemical and oncological PET-CT studies. Immunophenotyping and cytogenetic/molecular study were not performed. Occasionally, these tests may be useful in confirmation, when the tests performed routinely are inconclusive[7].

Anatomopathological examination often does not differentiate lymphoma from thymoma, and it is necessary to complement it with an immunohistochemical study, since immunohistochemistry and immunophenotyping by flow cytometry complement the findings of the anatomopathological study[8,9].

The treatment of aggressive non-Hodgkin's lymphoma is performed for curative purposes, using multi-therapy protocols, possibly complemented by radiotherapy (in localized disease). The most frequently used protocol is the R-CHOP regimen, 6 to 8 cycles, at intervals every 3 weeks[6].

Recurrences are treated with "rescue" chemotherapy regimens and many patients are being referred for transplantation with peripheral blood stem cells. The R-ICE regimen is frequently employed, and transplantation is the form of curative treatment[6].

The patient of this case was clinically well, with no consistent symptoms of Lymphoma, and no changes were observed in laboratory tests. The results of the tests

performed, despite the dissociation with the clinical state, led to the diagnostic error and led to the use of an aggressive and unnecessary treatment.

Thymoma may mimic and be confused with various diseases - neoplastic or otherwise - that can be asymptomatic, make compressive manifestations and paraneoplastic diseases. Therefore, the differential diagnosis of a mediastinal mass should be adequately investigated, especially in young patients[10].

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