Sinonasal non-Hodgkin’s malignant lymphoma – review of a clinical case

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Abstract

Malignant lymphomas represent one of the most important problems of modern medicine, with a constant increase in the last decades, becoming the most frequent tumor among young people. Sinonasal localization is a particular site of malignant lymphomas, representing the second most frequent among ear, nose and throat (ENT) tumors. In this paper, authors present the clinical, diagnostic and therapeutic aspects of a malignant sinonasal lymphoma, which despite an aggressive histological subtype and important regional extension had a favorable clinical outcome. The patient presented to the ENT specialist with an important deformity of the nasal pyramid developed in the last two months. The anatomopathological exam and immunohistochemical analysis were conclusive for non-Hodgkin’s lymphoma. The therapeutic course was cytostatic chemotherapy (in spite of the surgical approach) with beneficial oncological outcomes, which determined complete remission of the tumor. Computed tomography (CT) scan revealed a nasoethmoidal tumor with destruction of the nasal pyramid.

Keywords: sinonasal tumor, non-Hodgkin’s lymphoma, multimodal therapy, extranodal lymphoma.

Introduction

Defined as tumors of the lymphatic tissues, malignant lymphomas are one of the current issues of modern medicine. Cancers of the head and neck represent 3% of all cancers, lymphomas occupying the second place among them in terms of frequency [1, 2]. They may develop in the lymph nodes located at the levels of the head and neck, or as extranodal tumors, registering the second frequency after primary gastrointestinal lymphomas. Lymphomas of the upper aerodigestive tract are classified into three major categories, depending on the frequency of the respective types: lymphomas of the oral cavity, pharynx and Waldeyer ring, lymphomas of the sinuses and nasal cavity, and lymphomas of the larynx and trachea. In this territory, the mucosa-associated lymphoid tissue (MALT) is very rich, and can represent a starting point for various lymphoproliferative processes. Non-Hodgkin’s lymphomas represent 60% of these, and consist from a histological point of view in B-cell, T-cell and natural killer (NK)-T cell lymphomas, the highest frequency being that of diffuse large B-cell lymphoma [3–6].

Sinonasal non-Hodgkin’s lymphomas generally have aggressive progression, prone to important local extension. Macroscopically, the lesion presents itself as a polypoid mass accompanied by necrosis and ulcers in the initial stages. The prognosis can be calculated according to the revised international prognostic index [7]. Staging is based on the Ann Arbor classification [8, 9].

Histological, clinical and evolutionary heterogeneity of malignant lymphomas raises particular problems from a therapeutic point of view, treatment of these malignancies having seen significant changes over time. The primary means of treatment of malignant lymphomas is cytostatic chemotherapy. In this particular case, with an important deformity of the nasal pyramid, we are faced to choose the proper therapy. The diagnosis of certainty is based on the anatomopathological exam and immunochemistry study. Treatment is controversial with regard to the best therapeutic procedures for the patient. In spite of the tumoral dimensions, the chemotherapy is effective, therefore the surgical treatment is unnecessary. The aim of surgical treatment is essentially a diagnostic one, both for lymph node and extranodal localizations.

Case presentation

We present the case of a 78-year-old female patient, who addressed in October 2014 to “Prof. Dr. Dorin Hociotă” Institute of Phonoaudiology and Functional ENT Surgery, Bucharest, Romania, for bilateral chronic nasal obstruction, posterior mucopurulent rhinorrhea, diplopia and important deformation of the nasal pyramid. Endonasal symptomatology appeared six months ago, but two months prior to
presentation the patient observed an ongoing growth of a tumor of the nasal pyramid. In all this period of time, the patient did not undertake any treatment.

Ear, nose and throat (ENT) clinical examination and endoscopic nasal examination with a rigid 00 endoscope highlighted a vegetant tumor involving the middle and upper turbinates of the left nasal fossa, hemorrhagic, friable on palpation, completely blocking the left middle meatus and the frontal sinus recess on the same side, extending into the contralateral nasal fossa via the superior portion of the nasal septum, deforming the nasal pyramid, and infiltrating the soft tissues at this level (Figure 1).

Clinical exam of the patient revealed a mass with an irregular shape on top of the nasal pyramid, with imprecise margins and inhomogeneous content. The tumoral mass (5/4/4 cm) had no skin involvement and was adherent to the ethmoidal structures. The endoscopic view exposed a red tumoral mass in both anterior ethmoidal sinuses without involving bilateral frontal recesses and destruction of the superior part of the anterior cartilage of the septum.

Sinonasal computed tomography (CT) examination revealed: thickening of the soft tissues at the level of the nasal pyramid and nasal mucosa, demineralization of the nasal bones. Mucosal thickening involved the nasal septum region, as well. The maxillary, frontal, sphenoid sinus bones presented unaffected bone walls, with a well-defined outline, normal thickness, no air content, no secretion retention, and no intrasinusal masses. There was slight thickening of the maxillary sinus mucosa (Figure 2).

The microscopic examination of the pieces stained with Hematoxylin–Eosin (HE) showed a pathological sample with the appearance of lymph node fragments with remodeled architecture due to malignant lymphoid proliferation, composed of medium sized cells with irregular, hypertrophic nuclei, coarse chromatin and 1–2 small basophilic nucleioli, with relatively abundant eosinophilic cytoplasm and numerous atypical mitoses (Figure 3).

For the positive and differential diagnosis of the tumor, there were performed various immunohistochemical investigations, using the following antibodies: anti-CD20 for highlighting B lymphocytes (clone L26, 1/50 dilution, Dako); anti-CD3 for highlighting T lymphocytes (clone F7.2.38, 1/50 dilution, Dako); anti-CD10 for differentiating from acute lymphoblast leukemia (clone 56C6, 1/100 dilution, Novocastra); anti-CD5 for highlighting T lymphocytes and some subsets of B lymphocytes (clone 4C7, 1/200 dilution, Novocastra); anti-CD23 for highlighting dendritic cells (clone 1B12, 1/100 dilution, Novocastra); anti-CD68 for highlighting macrophages (clone KP1, 1/100 dilution, Dako); anti-Ki67 for highlighting the capacity of tumor cell proliferation (clone MIB-1, 1/50 dilution, Dako); anti-CD79-alpha for highlighting B-lymphocytes and prolymphocytes (clone JCB117, 1/20 dilution, Dako).

The immunohistochemical examinations showed an intense reaction for the following immunomarkers: CD20 (Figure 4), CD79-alpha (Figure 5) and CD5, poorly positive for CD23 (Figure 6) and negative for CD23 and CD68 (Figure 7). The reaction to the anti-Ki67 antibody was intense, more than 30% of all the tumor cells being positive (Figure 8).

Based on these data, there was established the diagnosis of B-cell non-Hodgkin’s malignant small lymphocytic lymphoma.

Osteomedular biopsy was subsequently performed, revealing hypercellular bone marrow, with alternating areas with different cell density (between 40% and, in small areas, 80% cell components) due to malignant lymphoid infiltration (approximately 30–35%), with interstitial but especially focal pattern (small inter trabecular nodules, imprecisely delimited), with small lymphocytic type cells, presenting very rare proliferation centers; areas with preserved hematopoiesis with slightly diminished presence of all lineages: relatively frequent groups of normoblastic type erythroblasts; granulocytes to erythrocytes (G/E) ratio ~3/1 (normal), granulocytic maturation present; dispersed normal size megakaryocytes, with preserved lobulation. Immunohistochemical analysis showed that tumor proliferation consisted of small B cells, positive for CD20, with aberrant expression of CD5 (T marker, aberrantly positive in some B-cell lymphoproliferations) and of CD23 (dendritic marker, aberrantly positive in some B-cell lymphoproliferations). Tumor proliferation was negative for cyclin D1 (B mantle cell lymphoma marker). The conclusion was consistent with the histopathological appearance of bone marrow infiltration (approx. 30–35%) by B-cell non-Hodgkin’s malignant small lymphocytic lymphoma (B-SLL/B-CLL – B-cell small lymphocytic lymphoma/B-cell chronic lymphocytic leukemia).

Two months later biopsy of a skin tumor mass was performed, the histopathology exam confirming the previously established diagnosis.
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Figure 3 – Small B-cell lymphocytic lymphoma. Dense lymphoid proliferation composed of medium cells, with hypertrophic nuclei and abundant cytoplasm. There are frequent mitotic figures. Nuclei with euchromatin and small nucleoli (HE staining, ×200).

Figure 4 – Intense immunohistochemical reaction of the tumor cells to the anti-CD20 antibody (Anti-CD20 antibody immunostaining, ×200).

Figure 5 – Tumor cells with an intense reaction to the anti-CD79-alpha antibody (Anti-CD79-alpha antibody immunostaining, ×200).

Figure 6 – Rare T lymphocytes, CD3 positive, present among the tumor cells (Anti-CD3 antibody immunostaining, ×200).

Figure 7 – Tumor cells with a negative reaction to the anti-CD68 antibody (Anti-CD68 antibody immunostaining, ×200).

Figure 8 – Tumor cells with intense reaction to the anti-Ki67 antibody (Anti-Ki67 antibody immunostaining, ×200).

Following an oncology consult the patient underwent six cycles of CHOP cytostatic therapy – Cyclophosphamide, Doxorubicin, Vincristine, Prednisolone, and eight cycles of MabThera (Rituximab) therapy, the recommendation being that for two years she is to undergo one perfusion every two months.

Follow-up CT examination did not reveal the presence of supradiaphragmatic or subdiaphragmatic enlarged lymph...
nodes. The positron emission tomography (PET)/CT scan performed one month later confirmed the results of the previously performed CT scan, finding no new metabolic active lesions given the known oncological context. The patient was followed-up regularly in a local outpatient ENT Service.

**Discussion**

Lymphomas are cancers that start in the lymphoreticular system, and are classified into Hodgkin’s lymphomas (described by Dr. Thomas Hodgkin, in 1832) and non-Hodgkin’s lymphomas [10, 11]. The onset of malignant lymphoma outside a lymph node is more and more frequently reported, currently over 30% of malignant lymphomas being diagnosed as having originated outside the lymph nodes and presenting special pathological, clinical and therapeutic features.

The vast majority of extranodal lymphomas are non-Hodgkin’s lymphomas. Malignant lymphomas of the head and neck reported in the literature frequently include lymphomas within the ENT scope, with a significant share of nearly 10% of all malignant lymphomas. Although second in terms of frequency in the ENT field, malignant lymphomas with sinus onset are very rare [12]. They represent 2–5% of total primary extranodal lymphomas. The maxillary sinus is the one most commonly involved [1, 13].

B-type phenotype is more common in sinus localizations, while T-phenotype is more frequent at the level of the nasal cavity [14–16]. From a histological point of view, small B-cell lymphocytic lymphoma is an aggressive form of lymphoma, prone to important local extension, and often causing extended ulcerative lesions, destructive at loco-regional level [17–19].

In terms of diagnosis, these entities raise important issues with regard to distinguishing them from non-neoplastic diseases with destructive features or other neoplasms developing at this level, because of the association of neoplastic infiltrates with nonspecific inflammatory tissue. Multiple biopsy fragment sampling from the suspicious areas is therefore mandatory, and the size of these fragments must be sufficiently large. The resulting biological material allows detailed histological assessment of the tumor, establishing the degree of invasiveness, the expression of specific surface markers and molecular markers of a certain type of lymphoma. A special entity is Wegener’s granulomatosis, which can be confused with this type of lymphoma. In the case reported, symptomatology was nonspecific, the patient addressing the clinic after significant growth in size of the tumor, which determined the deformation of the nasal pyramid, the only previous complaint of the patient being chronic nasal obstruction. This also confirms data from the specialized literature according to which approximately one third of patients live for years without obvious symptoms.

Histological, clinical and evolutionary heterogeneity of malignant lymphomas poses particular problems from a therapeutic point of view, treatment of these malignancies seeing significant changes over time. The primary means of treatment of malignant lymphomas is cytostatic chemotherapy. Its use is supported by the fact that two thirds of cases of non-Hodgkin’s lymphomas are disseminated diseases, presenting in stages III–IV from the very moment of diagnosis. This was the case for our patient as well, who because of bone marrow and skin involvement was classified as stage IVEA according to the Ann Arbor staging system. Chemotherapy was administered as in most cases in the form of polychemotherapy, namely standard CHOP protocol, to which anti-CD20 chimeric monoclonal antibody Rituximab, or MabThera, was added. Chemotherapy should be administered in curative doses, an aspect that correlates with a high percentage of complete remissions, the rapidity of obtaining such remissions reflecting the chance of a prolonged survival [20].

The aim of surgical treatment was diagnostic, its accuracy depending on the quality of the tissue sampling and its quantity. In the case up for discussion, although involving an aggressive histological subtype, clinical outcome was favorable, spectacular, after just six sessions of polychemotherapy, with significant quasi-complete lysis of the tumor mass and remission of symptoms.

**Conclusions**

Various manners of onset of malignant lymphopathies of the cephalic end and the cervical segment lead to the fact that the ENT specialist is often the first physician who sees the lymphoma patient, and therefore a correct therapeutic management is important for obtaining a prolonged remission, equivalent to healing. For a favorable therapeutic result, a histopathological certainty diagnostic is necessary. According to the literature, chemotherapy is the treatment of choice to the detriment of surgical approach. Taking into account the quality of patient’s life and dimensions of the tumor mass, it could have been initiated the surgical treatment.

Conflict of interests

The authors declare that they have no conflict of interests.

**References**


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