

Aleksandra E. Danieluk¹, Joanna H. Mańdziuk¹, Marek Z. Wojtukiewicz^{2, 3}, Ewa Sierko^{2, 3}

¹Students' Scientific Association affiliated with the Department of Oncology, Medical University of Białystok

²Department of Oncology, Medical University of Białystok

³Comprehensive Cancer Center in Białystok

A rare case of an extranodal head and neck lymphoma primarily diagnosed as sarcoma

Address for correspondence:

Dr hab. n. med. Ewa Sierko
 Klinika Onkologii
 Uniwersytet Medyczny w Białymstoku
 Białostockie Centrum Onkologii
 ul. Ogrodowa 12, 15-027 Białystok
 Phone: +48 85 664 68 27
 e-mail: ewa.sierko@iq.pl

Oncology in Clinical Practice
 2017, Vol. 13, No. 2, 67-70
 DOI: 10.5603/OCP.2017.0011
 Copyright © 2017 Via Medica
 ISSN 2450-1654

ABSTRACT

Diffuse large B-cell lymphomas-not otherwise specified (DLBCL-NOS) are a common lymphoid malignancy, being the most common form of non-Hodgkin lymphoma (NHL). Typically, DLBCL-NOS arises in lymph nodes, however primarily extranodal involvement is possible, and it can present itself in various clinical and morphological types, posing a diagnostic challenge. In some cases, extranodal lymphomas may mimic non-lymphoid tumours, among them sarcomas. Treatment of DLBCL may involve chemotherapy, immunotherapy, radiotherapy and autologous stem cell transplant, while in the care of sarcomas surgery is an important modality of treatment.

A-36-year-old male patient presented with a tumour of the left angle of the mandible which appeared a few days after a tooth extraction. It was first diagnosed as inflammation and treated with antibiotics. Afterwards, a biopsy indicated liposarcoma. A repeated biopsy and histopathological examination at an oncology centre revealed extranodal diffuse large B-cell lymphoma-not otherwise specified (DLBCL-NOS). The patient was successfully treated with chemotherapy with rituximab and radiotherapy. Complete remission was achieved and the patient remains DLBCL-NOS free for over six years.

It is vital for extranodal lymphomas to be thoroughly differentiated from other malignancies by experienced oncology centres, since a false diagnosis may lead to a dramatic mistreatment.

Key words: lymphoma, non-Hodgkin, extranodal, mandible, diagnostic errors

Oncol Clin Pract 2017; 13, 2: 67-70

Introduction

Diffuse large B-cell lymphomas (DLBCL) are a common lymphoid malignancy, accounting for approximately 37% of B-cell tumours worldwide [1]. Among those, malignancies that belong to the group of DLBCL-not otherwise specified (NOS), are a frequent finding, being the most typical form of non-Hodgkin lymphoma (NHL) [1]. In extranodal NHL, head and neck is the second most frequent site involved [2], accounting for 4-15% of all NHL patients [3]. However, NHL may mimic non-lymphoid tumours, among them sarcomas [4, 5]. Treatment of DLBCL may involve chemotherapy, immunotherapy, radiotherapy and autologous stem cell transplantation [1], while in the case

of sarcomas — surgery is the most important modality of treatment. It is vital to thoroughly differentiate the two types of neoplasms, since confusing them may lead to a dramatic mistreatment.

In this article a rare case of a patient with a DLBCL-NOS which in the diagnostic process was primarily confused with liposarcoma is presented.

Case report

A-36-year-old male patient was admitted to the non-oncologic department with a fast growing tumour of the left angle of the mandible which appeared a few days after a tooth extraction. Clinical examination

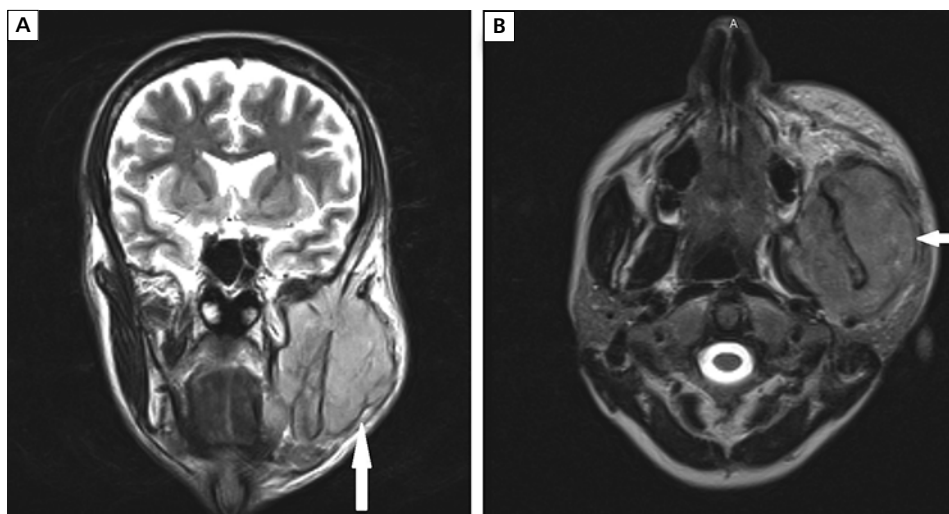


Figure 1. Frontal (A) and axial (B) head and neck magnetic resonance imaging scan before treatment. Tumour of the left ramus of the mandible (arrows). The tumour infiltrated infratemporal and pterygopalatine fossae, deforming the pharynx and the left parapharyngeal space

revealed extension of the tumour to the oral cavity. A contrast head and neck computed tomography (CT) examination showed a tumour of the left ramus of mandible (66 × 67 mm) infiltrating infratemporal and pterygopalatine fossae, deforming the pharynx and the left parapharyngeal space with enlargement of the left mandibular (16 mm) and the perivascular lymph nodes (Fig. 1). The radiologist couldn't differentiate between inflammation versus a neoplastic tumour.

The microbiological examination of the culture from dental alveolus revealed presence of *Streptococcus viridans* and other bacteria from *Streptococcus* species. During the next two weeks the patient was treated with antibiotics and analgetics.

Histopathological examination of the excised specimen revealed chronic inflammation, while a fine needle aspiration biopsy of enlarged lymph node identified neoplastic cells, probably malignant, non-epithelial. The presence of rhabdomyosarcoma could not be excluded and pathology report stated that another histopathological examination should be performed to achieve the final diagnosis. Excisional biopsy from the tumour was thus repeated and histopathological examination of another specimen revealed pleomorphic liposarcoma, Ki 67 (+), SMA (+), HMF (+), desmin (-), S100(-), CD 34 (+), EMA (-), vimentin (+) and pan-cytokeratin (-). Abdomen ultrasound examination showed a slightly enlarged spleen (128 × 59 mm), chest X-ray was normal. Head and neck CT showed fast progression of the disease: a large tumour infiltrating both pterygoid muscles, pterygoid process of sphenoid bone, parotid gland and the floor of oral cavity with enlarged left submandibular and superior deep cervical lymph nodes on the left side. Left cervical vessels were incorporated in the tumour

mass. Because of the unreliable pathological diagnosis (performed at an unexperienced pathology centre), another histopathological and immunohistochemical examination was performed, which unexpectedly revealed extranodal diffuse large B-cell lymphoma — not otherwise specified (DLBCL-NOS), CD 20 (+), CD 30 (+), Ki67 (+++), CD3 (-), S100 (-), desmin (-). The diagnosis was confirmed by pathologist in another Oncology Centre.

On admission to the oncology centre the tumour was hard in palpation, about 15 cm in size, enlarging towards the ear, narrowing external acoustic meatus, and towards the left eye to the zygomatic bone, involving the whole left side of mandible. Infiltration of the cheek and partial trismus in the oral cavity was seen. Laboratory tests revealed highly elevated LDH blood level.

A chest and abdomen CT showed two nodules (both 15 × 12 mm) located between the spleen, left suprarenal gland and diaphragm as well as two nodules (diameter: 7 and 8 mm) in the adipose tissue in the abdomen wall, in the left epigastric region between rib and parietal peritoneum. Spleen was enlarged (124 × 57 × 134 mm) as well. No infiltration of the bone marrow by lymphoma was found in myelography. In bone marrow biopsy, increased normoblastic erythropoiesis was noted. The count of the white blood cell group was relatively decreased. The disease was staged as CS-IIISA. The IPI score was 2.

The patient underwent chemotherapy comprising of intravenous doxorubicin (50 mg/m²), cyclophosphamide (750 mg/m²), vincristine (1.4 mg/m²) on the day 1 followed by intraspinal methotrexate (10–15 mg/m², maximal dose 15 mg) on the day 2, which was combined with rituximab (556 mg/m²). In total, the patient received 8 courses of

chemotherapy administered every 21 days in the period of four and half months. The treatment was well-tolerated. Only G3 polyneuropathy after the 7th course was experienced by the patient which resulted in replacement of vincristine by vinblastine in the last course. The complete radiologic remission of the disease was achieved.

Subsequently the patient underwent megavoltage photon beam radiation therapy to the area of the head and neck tumour bed (to the total dose of 40 Gy delivered in 20 fractions). The radiotherapy was given due to the fact that only partial remission after sixth course of chemotherapy was achieved and because of the large initial size of the tumour mass and its aggressive growth. Three months after radiation cessation CT scans of the neck, chest and abdomen were normal. Two months later positron emission tomography — computed tomography (PET-CT) showed no signs of metabolically active disease and complete metabolic response to the combined treatment.

In the fifth year after the treatment abdomen CT showed a few hypodense areas in the liver (the largest was 14 mm, located in the 6th segment) and two in the spleen (8 and 9 mm) as well as enlarged portocaval and hepatic hilum lymph nodes. As the result was inconclusive, PET-CT was recommended. It suggested the relapse of lymphoma in the liver, spleen as well as axillary and abdomen lymph nodes. The patient underwent lymph nodes excision and pathologic examination revealed inflammation. PET-CT performed four months later showed regression of the metabolic changes in the organs. One and half year later the abdomen CT revealed enlargement of portocaval and hepatic hilum lymph nodes (up to 20 mm), a hypodense area of 14 mm in the liver and two hypodense areas in the spleen. PET-CT revealed metabolically active process in the liver and in the above mentioned lymph nodes suggesting malignancy. Laparotomy was performed with excision of aortocaval lymph node (2.9 × 1.6 cm) as well as a 1.5 cm of diameter lymph node from hepatoduodenal ligament. Again, inflammatory process was diagnosed without a relapse of the neoplastic disease. To date, for over six years the patient is DLBCL-NOS free.

Discussion

NHL is a heterogeneous group of malignancies. The most typical primary presentation is nodal involvement, however primary extranodal involvement is present in a wide group of patients, accounting for approximately 40% of cases [6]. Lymphoma accounts for 2.5% of all head and neck malignancies [7] with NHL representing less than 1% of this region's malignant tumours [8]. The most commonly involved areas in the head and neck NHL include the Waldeyer's ring,

oral cavity, thyroid gland, skin, paranasal sinuses, nasal cavity, and larynx [9, 10]. Bone localization of NHL is a rare finding. A retrospective review revealed that 16 patients out of 381 cases of head and neck NHL presented with jaw bone involvement with most common site being the mandible [11]. The incidence of oral manifestation of NHL is approximately 2% of all extranodal lymphomas [12].

There are several subtypes and entities of DLBCL with predominant extranodal presentation [1]. The heterogeneity of clinical presentation of extranodal lymphoma may be the cause of the diagnostic challenges. In some cases, lymphomas may easily be confused with other diseases. For example, oral lymphomas may primarily mimic benign conditions [12]. Lymphomas may also present common features with other neoplastic lesions, such as sarcomas [13, 14] both in clinical, radiological and pathological presentation [13]. There are studies suggesting that clinical features pointing to a lymphoma rather than a sarcoma involve increased tenderness, lymphadenopathy and elevated serum LDH levels [13]. Radiologically, confluent adenopathy is a feature associated with lymphomas whereas is a rare finding in sarcomas [13]. Nevertheless, a histopathological analysis is vital in obtaining a final diagnosis of these malignancies [13].

In the case described above the patient was primarily diagnosed with sarcoma because of the suggestion of sarcoma cell presence in the fine needle aspiration biopsy (FNAB) result. However, FNAB has limitations concerning the accuracy of the histologic grading and stating the subtype of sarcoma. It can also pose difficulties in distinguishing between low-grade sarcomas and benign or borderline cellular lesions [15]. Core needle biopsy (CNB) or excisional biopsy should be considered as the method of choice to obtain an accurate diagnosis due to its reliability in differentiating benign and malignant soft tissue tumours as well as identifying other tumours imitating sarcoma [16]. The CNB has also a higher diagnostic value than FNAB in terms of establishing the histologic type and grade and achieving a specific diagnosis [17]. According to some studies the CNB is also useful tool for diagnosis of lymphoma and should be recommended as a first-line investigation over excisional biopsy in diagnostic process because it provides faster and more cost-effective diagnosis with histological accuracy equal to open biopsy [18].

In staging of lymphomas, CT is used as a standard imaging method [19, 20]. It is useful in diagnosing lesions in the lymph nodes and the lung tissue [20] as well as in the mediastinum [21] and the abdomen [22]. In the described patient's case, only a chest X-ray was performed shortly after the first suspicion of a neoplastic malignancy appeared. It showed no signs of the disease. A chest CT performed a month later at an oncology

centre, revealed two lesions, possibly enlarged lymph nodes. However, PET-CT is currently considered the most sensitive and specific imaging modality [21] and it may prove to be a cost-effective staging method in the future [23]. It is used in the initial evaluation of the patients, in the assessment of the treatment efficacy, and also in patients with suspected recurrence [24]. However, false-positive results are possible in PET scans, caused by inflammation, infection or granulomatous disease [25]. In the case described above, lymphoma recurrence was suspected twice due to positive PET-CT results. However, an excision and pathologic examination of the metabolically active lymph nodes revealed inflammatory changes both times. The patient is alive for 6 years after the antineoplastic treatment.

Conclusion

The case presented above shows how many diagnostic problems can be caused by extranodal lymphoma occurrence. It is vital to perform the differentiating diagnostic process in experienced oncology centres to obtain proper diagnosis and offer optimal treatment.

Authorship

Ewa Sierko and Marek Wojtukiewicz supervised and coordinated the study, assisted with analyses and revised the manuscript. Aleksandra Danieluk and Joanna Mańdziuk carried out the acquisition of data, literature review and prepared the drafts of the manuscript. All authors read and approved the final manuscript.

References

- Martelli M, Ferreri AJM, Agostinelli C, et al. Diffuse large B-cell lymphoma. *Crit Rev Oncol Hematol*. 2013; 87(2): 146–171, doi: [10.1016/j.critrevonc.2012.12.009](https://doi.org/10.1016/j.critrevonc.2012.12.009), indexed in Pubmed: [23375551](https://pubmed.ncbi.nlm.nih.gov/23375551/).
- Tülin Kayhan F, Ozkul N. Case report: extranodal non-Hodgkin's lymphoma of the parapharyngeal space. *Auris Nasus Larynx*. 1999; 26(2): 201–205, indexed in Pubmed: [10214901](https://pubmed.ncbi.nlm.nih.gov/10214901/).
- Chi HS, Lee KW, Chiang FY, et al. Head and neck extranodal lymphoma in a single institute: a 17-year retrospective analysis. *Kaohsiung J Med Sci*. 2012; 28(8): 435–441, doi: [10.1016/j.kjms.2012.02.014](https://doi.org/10.1016/j.kjms.2012.02.014), indexed in Pubmed: [22892165](https://pubmed.ncbi.nlm.nih.gov/22892165/).
- Hudacko R, Rapkiewicz A, Berman RS, et al. ALK-negative anaplastic large cell lymphoma mimicking a soft tissue sarcoma. *J Cytol*. 2011; 28(4): 230–233, doi: [10.4103/0970-9371.86362](https://doi.org/10.4103/0970-9371.86362), indexed in Pubmed: [22090705](https://pubmed.ncbi.nlm.nih.gov/22090705/).
- Jairajpuri ZS, Rana S, Khetrpal S, et al. Extranodal anaplastic large cell lymphoma mimicking sarcoma: A report of an interesting case. *Int J Appl Basic Med Res*. 2014; 4(Suppl 1): S50–S52, doi: [10.4103/2229-516X.140741](https://doi.org/10.4103/2229-516X.140741), indexed in Pubmed: [25298944](https://pubmed.ncbi.nlm.nih.gov/25298944/).
- Kini R, Saha A, Naik V. Diffuse large B-cell lymphoma of mandible: a case report. *Med Oral Patol Oral Cir Bucal*. 2009; 14(9): e421–e424, indexed in Pubmed: [19718002](https://pubmed.ncbi.nlm.nih.gov/19718002/).
- Vaid S, Jadhav J, Chandorkar A, et al. Bilateral Non-Hodgkin's Lymphoma of the Temporal Bone: A Rare and Unusual Presentation. *Case Rep Otolaryngol*. 2016; 2016: 2641876, doi: [10.1155/2016/2641876](https://doi.org/10.1155/2016/2641876), indexed in Pubmed: [28116198](https://pubmed.ncbi.nlm.nih.gov/28116198/).
- Doumas S, Sakkas L, Panayiotidis P, et al. Favorable outcome in non-Hodgkin lymphoma of the maxillary sinus treated with R-CHOP. *Arch Med Sci*. 2014; 10(2): 406–409, doi: [10.5114/aoms.2013.34986](https://doi.org/10.5114/aoms.2013.34986), indexed in Pubmed: [24904680](https://pubmed.ncbi.nlm.nih.gov/24904680/).
- Shima N, Kobashi Y, Tsutsui K, et al. Extranodal non-Hodgkin's lymphoma of the head and neck. A clinicopathologic study in the Kyoto-Nara area of Japan. *Cancer*. 1990; 66(6): 1190–1197, indexed in Pubmed: [2205355](https://pubmed.ncbi.nlm.nih.gov/2205355/).
- Dixit S, Upadhyaya C, Humagain M, et al. Clinico-histopathological Survey of Head and Neck Cancer at Tertiary Health Care Centre - Dhulikhel Hospital. *Kathmandu Univ Med J (KUMJ)*. 2016; 14(54): 167–171, indexed in Pubmed: [28166075](https://pubmed.ncbi.nlm.nih.gov/28166075/).
- Bugshan A, Kassolis J, Basile J. Primary Diffuse Large B-Cell Lymphoma of the Mandible: Case Report and Review of the Literature. *Case Rep Oncol*. 2015; 8(3): 451–455, doi: [10.1159/000441469](https://doi.org/10.1159/000441469), indexed in Pubmed: [26600778](https://pubmed.ncbi.nlm.nih.gov/26600778/).
- Shah GH, Panwar SK, Chaturvedi PP, et al. Isolated primary extranodal lymphoma of the oral cavity: A series of 15 cases and review of literature from a tertiary care cancer centre in India. *Indian J Med Paediatr Oncol*. 2011; 32(2): 76–81, doi: [10.4103/0971-5851.89776](https://doi.org/10.4103/0971-5851.89776), indexed in Pubmed: [22174494](https://pubmed.ncbi.nlm.nih.gov/22174494/).
- O'Neill JK, Devaraj V, Silver DAT, et al. Extranodal lymphomas presenting as soft tissue sarcomas to a sarcoma service over a two-year period. *J Plast Reconstr Aesthet Surg*. 2007; 60(6): 646–654, doi: [10.1016/j.bjps.2006.03.040](https://doi.org/10.1016/j.bjps.2006.03.040), indexed in Pubmed: [17485053](https://pubmed.ncbi.nlm.nih.gov/17485053/).
- Katsura M, Nishina H, Shigemori Y, et al. Extranodal lymphoma originating in the gluteal muscle with adjacent bone involvement and mimicking a soft tissue sarcoma. *Int J Surg Case Rep*. 2015; 7C: 161–164, doi: [10.1016/j.ijscr.2015.01.024](https://doi.org/10.1016/j.ijscr.2015.01.024), indexed in Pubmed: [25618843](https://pubmed.ncbi.nlm.nih.gov/25618843/).
- Singh HK, Kilpatrick SE, Silverman JF. Fine needle aspiration biopsy of soft tissue sarcomas: utility and diagnostic challenges. *Adv Anat Pathol*. 2004; 11(1): 24–37, indexed in Pubmed: [14676638](https://pubmed.ncbi.nlm.nih.gov/14676638/).
- Strauss DC, Qureshi YA, Hayes AJ, et al. The role of core needle biopsy in the diagnosis of suspected soft tissue tumours. *J Surg Oncol*. 2010; 102(5): 523–529, doi: [10.1002/jso.21600](https://doi.org/10.1002/jso.21600), indexed in Pubmed: [20872955](https://pubmed.ncbi.nlm.nih.gov/20872955/).
- Yang YJ, Damron TA. Comparison of needle core biopsy and fine-needle aspiration for diagnostic accuracy in musculoskeletal lesions. *Arch Pathol Lab Med*. 2004; 128(7): 759–764, doi: [10.1043/1543-2165\(2004\)128<759:CON-CBA>2.0.CO;2](https://doi.org/10.1043/1543-2165(2004)128<759:CON-CBA>2.0.CO;2), indexed in Pubmed: [15214827](https://pubmed.ncbi.nlm.nih.gov/15214827/).
- Allin D, David S, Jacob A, et al. Use of core biopsy in diagnosing cervical lymphadenopathy: a viable alternative to surgical excisional biopsy of lymph nodes? *Ann R Coll Surg Engl*. 2017; 99(3): 242–244, doi: [10.1308/rcsann.2016.0353](https://doi.org/10.1308/rcsann.2016.0353), indexed in Pubmed: [27917669](https://pubmed.ncbi.nlm.nih.gov/27917669/).
- Gossmann A, Eich HT, Engert A, et al. CT and MR imaging in Hodgkin's disease — present and future. *Eur J Haematol Suppl*. 2005(66): 83–89, indexed in Pubmed: [16007874](https://pubmed.ncbi.nlm.nih.gov/16007874/).
- Werewka-Maczuga A, Chrzan R, Urbanik A, et al. [Optimalisation of lymph node assessment in patients undergoing therapy for lymphoma using a multi-row CT]. *Przegl Lek*. 2010; 67(4): 256–261, indexed in Pubmed: [20687356](https://pubmed.ncbi.nlm.nih.gov/20687356/).
- Priola AM, Galetto G, Priola SM. Diagnostic and functional imaging of thymic and mediastinal involvement in lymphoproliferative disorders. *Clin Imaging*. 2014; 38(6): 771–784, doi: [10.1016/j.clinimag.2014.05.012](https://doi.org/10.1016/j.clinimag.2014.05.012), indexed in Pubmed: [24997534](https://pubmed.ncbi.nlm.nih.gov/24997534/).
- Yu RS, Zhang WM, Liu YQ. CT diagnosis of 52 patients with lymphoma in abdominal lymph nodes. *World J Gastroenterol*. 2006; 12(48): 7869–7873, indexed in Pubmed: [17203536](https://pubmed.ncbi.nlm.nih.gov/17203536/).
- Cerci JJ, Trindade E, Buccheri V, et al. Consistency of FDG-PET accuracy and cost-effectiveness in initial staging of patients with Hodgkin lymphoma across jurisdictions. *Clin Lymphoma Myeloma Leuk*. 2011; 11(4): 314–320, doi: [10.1016/j.clml.2011.06.006](https://doi.org/10.1016/j.clml.2011.06.006), indexed in Pubmed: [21816369](https://pubmed.ncbi.nlm.nih.gov/21816369/).
- You JJ, Cline KJ, Gu CS, et al. (18)F-fluorodeoxyglucose positron-emission tomography-computed tomography to diagnose recurrent cancer. *Br J Cancer*. 2015; 112(11): 1737–1743, doi: [10.1038/bjc.2015.151](https://doi.org/10.1038/bjc.2015.151), indexed in Pubmed: [25942398](https://pubmed.ncbi.nlm.nih.gov/25942398/).
- Seam P, Juweid ME, Cheson BD. The role of FDG-PET scans in patients with lymphoma. *Blood*. 2007; 110(10): 3507–3516, doi: [10.1182/blood-2007-06-097238](https://doi.org/10.1182/blood-2007-06-097238), indexed in Pubmed: [17709603](https://pubmed.ncbi.nlm.nih.gov/17709603/).