

# Primary nasal diffuse large B-cell lymphoma with synchronous pulmonary involvement

## A case report

Shuhong Hao, MD<sup>a</sup>, Yan Sun, PhD<sup>a</sup>, Chunmei Hu, PhD<sup>a</sup>, Yunhui Zhi, MD<sup>b</sup>, Han Xiao, MD<sup>a</sup>, Yarong Li, PhD<sup>a,\*</sup>

### Abstract

**Rationale:** Diffuse large B-cell lymphoma (DLBCL) is the most commonly occurring type of non-Hodgkin's lymphoma, which may be found at various extranodal sites. The nose is not a common site for DLBCL as compared with natural killer/T-cell lymphoma, and synchronous pulmonary involvement is even rarer. We report a case of primary nasal DLBCL who presented with a mass in the left lower lobe, mimicking primary lung carcinoma.

**Patient concerns:** A 62-year-old Chinese female visited the Ear-Nose-Throat Department of our hospital with nasal congestion and rhinorrhea for 2 months.

**Diagnosis:** Computed tomography scan revealed a mass with soft tissue density in the left vestibule and nasal cavity. Histopathological examination revealed a large number of lymphoma cells, and immunohistochemistry confirmed the diagnosis of DLBCL.

**Interventions:** The patient was treated with 6 cycles of R-CHOP (cyclophosphamide, adriamycin, vincristine, prednisone, and rituximab).

**Outcomes:** The treatment was well tolerated and led to complete remission for the patient. There was no sign of relapse over the 3-year close follow-up.

**Lessons:** DLBCL can be present at various extranodal sites and clinicians irrespective of their specialty must be vigilant for the synchronous mode of presentation of such lesions. Immunohistochemical techniques play a vital role in the diagnosis, because clinical characteristics may be misleading.

**Abbreviations:** CT = computed tomography, DLBCL = diffuse large B-cell lymphoma, IPI = international prognostic index, LDH = lactate dehydrogenase, NHL = non-Hodgkin's lymphoma, NK = natural killer, PPL = primary pulmonary lymphoma.

**Keywords:** diffuse large B-cell lymphoma, nasal cavity, pulmonary involvement

## 1. Introduction

Lymphoma is the generic term given to tumors of the lymphoid system, which can be classified into 2 types: Hodgkin's lymphoma and non-Hodgkin's lymphoma (NHL).<sup>[1]</sup>

Nearly 25% of NHL cases occur at extranodal sites, with the gastrointestinal tract, skin, and central nervous system being the

most commonly affected sites.<sup>[2]</sup> In the upper aerodigestive tract, the majority of cases occur in lymphatic sites along Waldeyer ring or extralymphatic sites in the nasal region.<sup>[3]</sup> Among them, lymphomas of the Waldeyer ring are usually the diffuse large B-cell variety,<sup>[4,5]</sup> whereas the natural killer (NK)/T-cell type is more commonly seen in nasal lymphomas.<sup>[6,7]</sup>

Diffuse large B-cell lymphoma (DLBCL) is the most commonly occurring type of NHL and accounts for approximately 30% of all malignant lymphomas.<sup>[8]</sup> DLBCL can be present at various extranodal sites, resulting in varied clinical and pathobiologic features.<sup>[9]</sup> Additionally, advanced DLBCL can spread to extranodal organs, particularly bone marrow, pleura, peritoneum, liver, and the central nervous system.<sup>[10]</sup> Sometimes it brings many difficulties to clinicians to distinguish between primary and secondary involvement. The lung could also be involved, but DLBCL with pulmonary involvement is extremely rare. Therefore, such a lesion occurring in the lungs could be easily missed in asymptomatic patients without respiratory symptoms. We describe a case of primary DLBCL of the nose with pulmonary involvement, which to our knowledge has not been reported so far.

## 2. Case presentation

The patient, a 62-year-old Chinese female, visited the Department of Ear-Nose-Throat of our hospital on June 5, 2015, with nasal congestion and rhinorrhea for 2 months, without any other complaints such as fever, weight loss, night sweats, dyspnea, or

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<sup>a</sup> Department of Hematology and Oncology, The Second Hospital of Jilin University, Changchun, Jilin, <sup>b</sup> Department of Ultrasound, Jining No.1 People's Hospital, Jining, Shandong, China.

\* Correspondence: Yarong Li, Department of Hematology and Oncology, The Second Hospital of Jilin University, Changchun, Jilin, China (e-mail: meiyoushenmeibuxing@126.com).

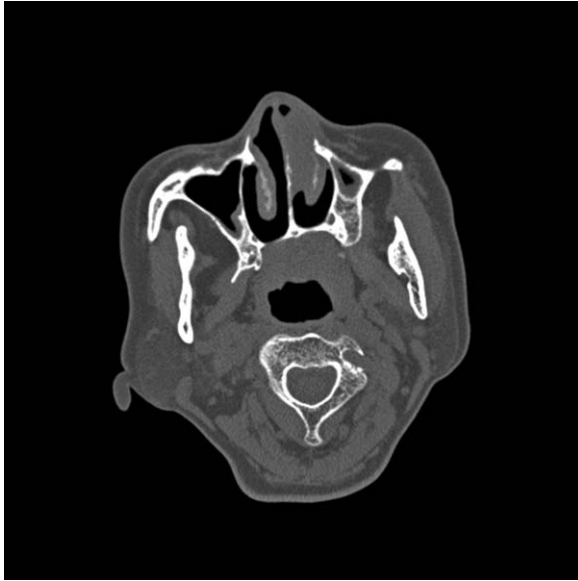
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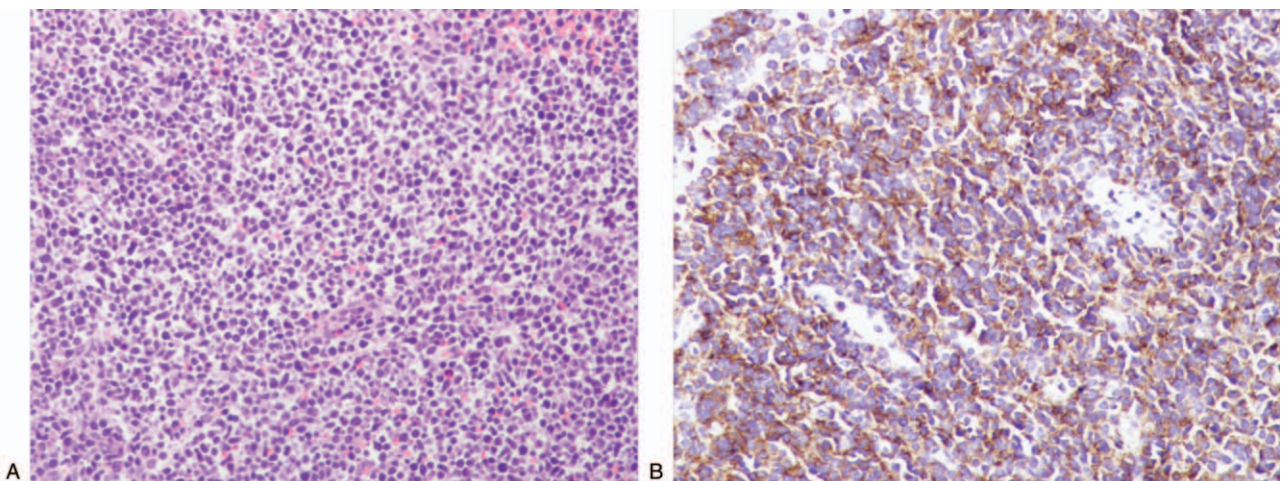
**Figure 1.** Nasal sinus CT scan revealed a mass with soft tissue density in the left vestibule and nasal cavity. CT = computed tomography.

cough. The patient had no previous medical history, smoking history, or history of cancer in the family. Physical examination revealed a bleeding mass in the left nasal cavity with swelling of the nasal root. Contrast-enhanced computed tomography (CT) scan of the nose and paranasal sinuses revealed a mass with soft tissue density in the left vestibule and nasal cavity (Fig. 1). Biopsy of the mass was performed which revealed a large number of lymphoma cells (Fig. 2A). On immunohistochemistry, the expression of BCL-2, CD79a, CD20, (Fig. 2B) and MUM1 was found to be elevated, but not of CK (AE1/AE3), CD56, EBER, CD5, CD3, CD2, TIA-1, BCL-6, and CD10. On Ki-67 staining, the proliferation fraction was found to be 90%. A diagnosis of “primary nasal DLBCL (nongerminal center origin)” was thereby made. Then, the patient was referred to the

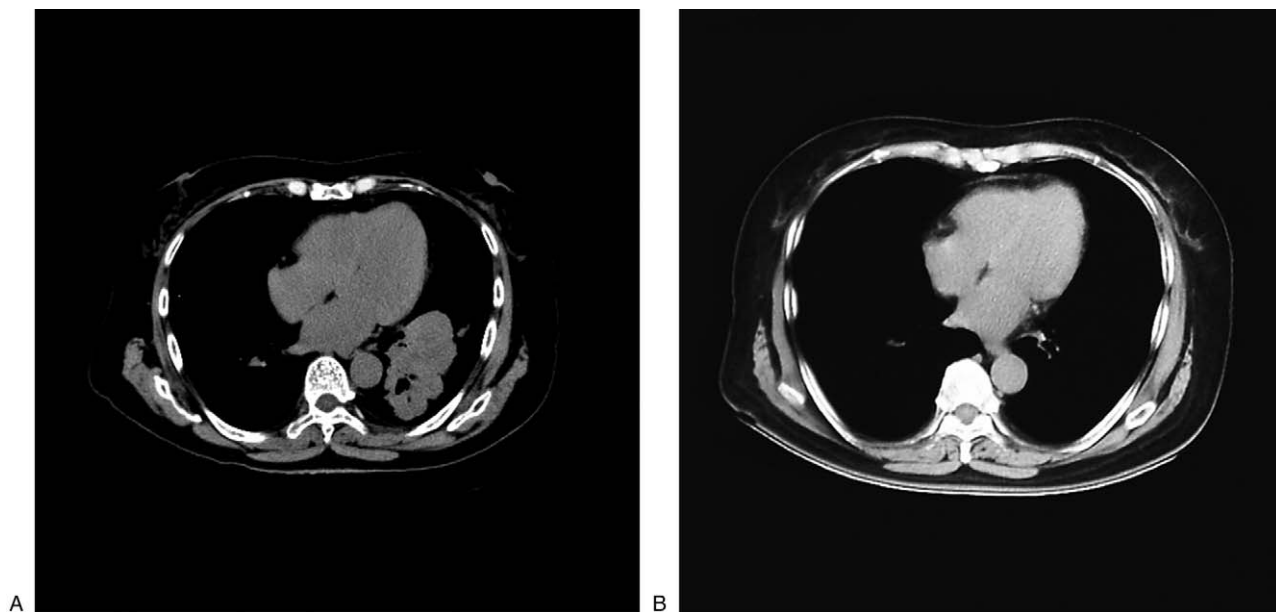
Department of Hematology and Oncology on June 11, 2015. Laboratory data, including tumor markers, peripheral blood count, serum chemistry, urinalysis, and hepatitis virus detection were all within normal limits, except for serum lactate dehydrogenase levels (LDH 296 U/L). Bone marrow biopsy was negative. Abdominal CT scan revealed splenomegaly without lymphadenopathy. Lung CT scan revealed a mass with irregular margins in the left lower lobe (size: 8.3 × 4.0 cm), which mimicked primary lung carcinoma without mediastinal lymphadenectasis or bilateral hydrothorax (Fig. 3A). Bronchoscopy revealed an endobronchial mass markedly narrowing the lumen and obstructing further entry. Biopsy indicated DLBCL, which was CD20 and CD79a positive on immunohistochemistry, with a proliferation fraction of 90% on Ki-67 staining, and no expression of CK (AE1/AE3), CD2, CD3, CD56, TIA-1, EBER, TTF-1, Syn, or CgA. Based on these findings, the patient was diagnosed with stage IIA “primary nasal DLBCL (nongerminal center origin),” according to the Ann Arbor classification<sup>[11]</sup> and international prognostic index (IPI) was 2. According to the IPI score, the patient was in the low-intermediate risk group with a relatively good prognosis.<sup>[12]</sup> R-CHOP (cyclophosphamide, adriamycin, vincristine, prednisone, and rituximab) was given for 6 cycles, which led to complete remission (Fig. 3B). She exhibited a desirable tolerance to this therapy without any negative side effects. There was no sign of relapse over the 3-year close follow-up. Written informed consent for publication of the case details was obtained from the patient and her son. The study was approved by the Ethics Committee of our hospital (No: 2018-169).

### 3. Discussion and conclusion

DLBCL is the most frequently reported NHL subtype.<sup>[8]</sup> Studies have found that approximately a third of the patients with DLBCL present with extranodal involvement. The most common extranodal involved site is gastrointestinal tract (34%), followed by head/neck (H&N; 14%) and skin/soft tissue (11%).<sup>[9]</sup> On the other hand, nasal lymphomas are mainly of a NK/T-cell origin.<sup>[6,7]</sup> Among the 33 cases of nasal lymphoma reported in Japan, 28 cases were the NK/T-cell subtype, and only 5 cases



**Figure 2.** (A) Histopathological examination revealed a large number of lymphoma cells. (H&E stain, ×200). (B) The expression of CD20 was found to be elevated. (CD20 immunostaining, ×200).



**Figure 3.** (A) Lung CT scan revealed a mass with irregular margin in the left lower lobar (size: 8.3 × 4.0 cm), which mimicked primary lung carcinoma. (B) Lung CT scan revealed that the mass disappeared after six cycles of chemotherapy. CT = computed tomography.

were the B-cell subtype.<sup>[13]</sup> Similarly, only 1 case out of 48 nasal lymphomas reported in China was B-cell lymphoma.<sup>[14]</sup>

In our case, 2 separate but simultaneously appearing lesions were found. One was located in the nasal cavity and the other was in the middle of the hilus pulmonis, which mimicked primary lung carcinoma. The lung lesion was incidentally detected on a thoracic CT scan carried out for routine hematology work up before the commencement of chemotherapy for the nasal lesion, which would have been missed otherwise. Thus, it is crucial to distinguish between primary nasal DLBCL with synchronous pulmonary involvement and primary lung cancer or primary pulmonary lymphoma (PPL). Primary lung cancer can be excluded with histopathology easily. PPL is extremely rare and is <1% of all lymphomas. The most common pathological type of PPL is mucosa-associated lymphoid tissue, accounting for approximately 70% to 90%.<sup>[15]</sup> PPL is defined as the clonal proliferation of the lymphoid tissue of the parenchyma or bronchi of 1 or both lungs, with no demonstrable involvement outside the lung up to 3 months after the primary diagnosis.<sup>[16]</sup> Our patient did not meet this definition. In addition, the main symptoms of the patient were nasal congestion, yellowish blood stained discharge, and the absence of respiratory symptoms such as fever, cough, chest pain, or dyspnea. Therefore, we diagnosed this case as primary nasal DLBCL with synchronous pulmonary involvement.

A population-based study showed that primary extranodal sites of involvement are associated with distinct outcomes in patients with DLBCL. Gastrointestinal, pulmonary, and liver/pancreas sites had a significant worse outcome, whereas H&N was associated with better survival.<sup>[9]</sup> Nasal DLBCL has been recognized as a distinct clinicopathologic subtype different from DLBCL of the lymph node or nasal NK/T-cell lymphoma. Nasal DLBCL usually presents in older male patients who have early-stage disease, rarity of B symptoms, good performance status, elevated LDH, and low IPI score.<sup>[17]</sup> Our patient met with most of these features.

The primary treatment for nasal DLBCL is chemotherapy, and CHOP is the standard treatment regimen.<sup>[18]</sup> Rituximab, a monoclonal anti-CD20 antibody, also improves outcomes by improving the remission rate, as well as the event-free and overall survival of patients with DLBCL,<sup>[18]</sup> especially in patients with tumors overexpressing the Bcl-2 protein.<sup>[19]</sup> Our patient was given six cycles of R-CHOP, and a good outcome was observed.

In conclusion, we describe for the first time a case of nasal DLBCL with synchronous pulmonary involvement. Clinicians irrespective of their specialty must be vigilant for the synchronous mode of presentation of such lesions. Immunohistochemical techniques play a vital role in the diagnosis, because clinical characteristics may be misleading. Chemotherapy with R-CHOP is highly effective, but longer follow-ups are needed and more cases need to be studied.

#### Author contributions

**Data curation:** Yan Sun, Yunhui Zhi.

**Investigation:** Chunmei Hu, Han Xiao.

**Supervision:** Yarong Li.

**Writing – original draft:** Shuhong Hao.

**Writing – review and editing:** Yarong Li.

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