CASE REPORT
GENERAL OTOLARYNGOLOGY, CASE REPORTS AND CLINICAL PEARLS
DOI: 10.5152/B-ENT.2021.21585

Diffuse large B-cell lymphoma of the pterygopalatine fossa with multiple cranial nerve palsies

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Cite this article as: Ida S, Matsuyama T, Ishizawa K, Nagashima K, Yoshida Y, Chikamatsu K. Diffuse large B-cell lymphoma of the pterygopalatine fossa with multiple cranial nerve palsies. B-ENT 2021; 17(3): 196-200.

ABSTRACT

We report a case of diffuse large B-cell lymphoma (DLBCL) of the pterygopalatine fossa (PPF) that developed with multiple cranial nerve palsies. A 70-year-old woman received steroid treatment for right facial palsy but was referred to our hospital because of additional diplopia and dysarthria. Neurological examination revealed multiple cranial nerve palsies associated with the right IV and XII and bilateral VII nerves. Computed tomography and magnetic resonance imaging showed lesions infiltrating Meckel's cavity and the cavernous sinus from the right PPF. Subsequently, right visual impairment and III and V1 cranial nerve palsies appeared; however, the right XII and left VII cranial nerve palsies improved spontaneously. A biopsy from the PPF was performed using an endoscopic transnasal approach, and the histological diagnosis was DLBCL. She was treated with chemotherapy. Although the PPF is an anatomically difficult site to access, biopsy using the endoscopic transnasal approach makes a minimally invasive diagnosis possible.

Keywords: diffuse large B-cell lymphoma, endoscopic sinus surgery, malignant lymphoma, non-hodgkin lymphoma, paranasal sinus diseases

Introduction

We report a case of diffuse large B-cell lymphoma (DLBCL) of the pterygopalatine fossa (PPF) with multiple cranial nerve palsies in a patient who was diagnosed based on a biopsy using the endoscopic transnasal approach.

Case presentation

A 70-year-old woman who developed right facial paralysis a month previously was treated with steroids as peripheral facial nerve paralysis at a municipal hospital. However, two weeks later, additional diplopia and dysarthria appeared. She was referred to the Department of Neurology at our hospital, and her neurological examination revealed multiple cranial nerve palsies associated with the right IV and XII and bilateral VII nerves. Computed tomography (CT) and magnetic resonance imaging (MRI) showed lesions infiltrating Meckel's cavity and the cavernous sinus from the right PPF and an expanded foramen rotundum. Contrast-enhanced effects were observed in the area along the skull base on both sides of the cavernous sinus and around the facial nerve, predominantly on the right side (Figures 1a and b). Fluorodeoxyglucose (FDG) positron emission tomography (PET) showed FDG accumulation only in the PPF lesions (Figure 1c). As a differential diagnosis, tumor, infectious diseases, and inflammatory lesions such as vasculitis and sarcoidosis were considered but could not be confirmed on hematological and cerebrospinal fluid examination. She was referred to our department with a request for a local biopsy. There was no tumor exposure in the nasal cavity, suggesting the necessity for a biopsy from the PPF lesion. Therefore, we planned a biopsy from the PPF using an endoscopic transnasal approach. In the preoperative examination, additional right visual impairment and III and V1 cranial nerve palsies were observed; however, the right XII and left VII cranial nerve palsies improved spontaneously.

Preoperative CT angiography showed the maxillary artery running through the PPF lesion in the arterial phase (Figure 2). Therefore, the surgery was performed with embolization by interventional radiology on standby. The right maxillary sinus was opened, and we reached the posterior wall, but there was a bone defect. Using a navigation system with CT scan fusion, we reached the PPF and collected fat and fibrous tissue in the PPF, paying attention to bleeding from the maxillary artery and

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Received: March 7, 2021 **Accepted:** September 14, 2021
Available online at www.b-ent.be

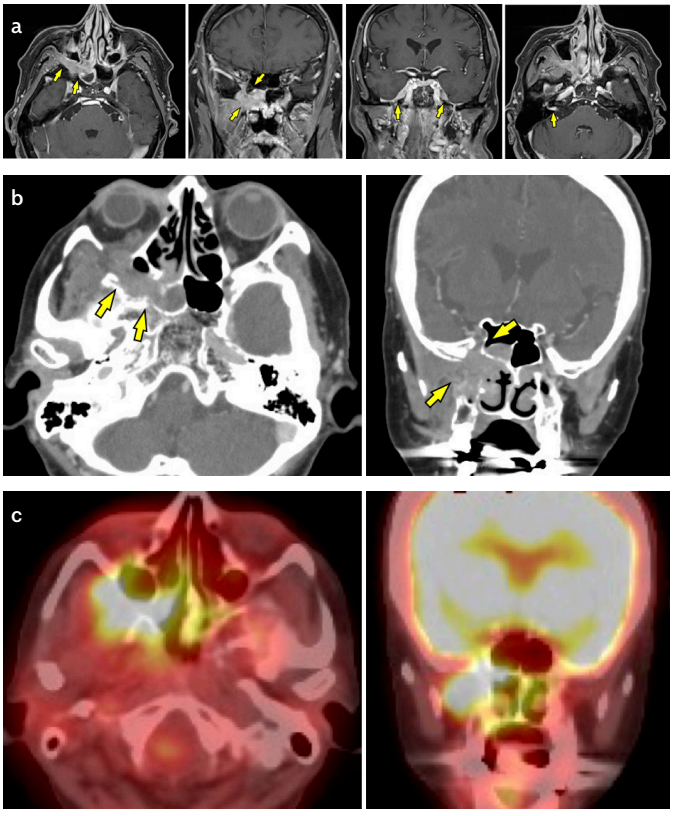

Figure 1. a-c. Contrast-enhanced MRI and CT showing lesions infiltrating Meckel's cavity and the cavernous sinus from the right PPF and an expanding foramen rotundum (arrow). Contrast-enhanced effects are observed in the area along the skull base on both sides of the cavernous sinus and around the facial nerve, predominantly on the right side (a, b). Bone destruction and osteosclerosis are observed in the surrounding bones, including the sphenoid bone. FDG-PET shows FDG accumulation consistent with the PPF lesions (SUVmax 8.2), but no other lesions (c).
MRI: magnetic resonance imaging, CT: computed tomography, PPF: pterygopalatine fossa, FDG: fluorodeoxyglucose, PET: positron emission tomography, SUVmax: maximum standardized uptake value

its branches (Figure 3). There were no obvious postoperative complications.

Histopathological examination revealed diffuse proliferation of large, atypical lymphocytes (Figure 4a). Immunostaining revealed cluster of differentiation 20 positivity (Figure 4b), and a pathological diagnosis of DLBCL was established.

She received rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisolone chemotherapy in the Department of Hematology, and FDG-PET after three courses of chemotherapy showed complete response. Symptoms of cranial nerve palsy in the right III and VII and left VII nerves tended to improve, but the other symptoms remained. A written informed consent was obtained from the patient for publication of this case report.

Main Points:

- Malignant lymphoma of the pterygopalatine fossa can cause multiple cranial nerve palsies, which is presumed to be owing to the anatomical features of the PPF.
- It was characteristic that multiple cranial nerve palsies occurred in heterochrony, and some neurological symptoms improved before treatment.
- Although the PPF is an anatomically difficult site to access, an endoscopic transnasal approach makes a minimally invasive diagnosis possible.

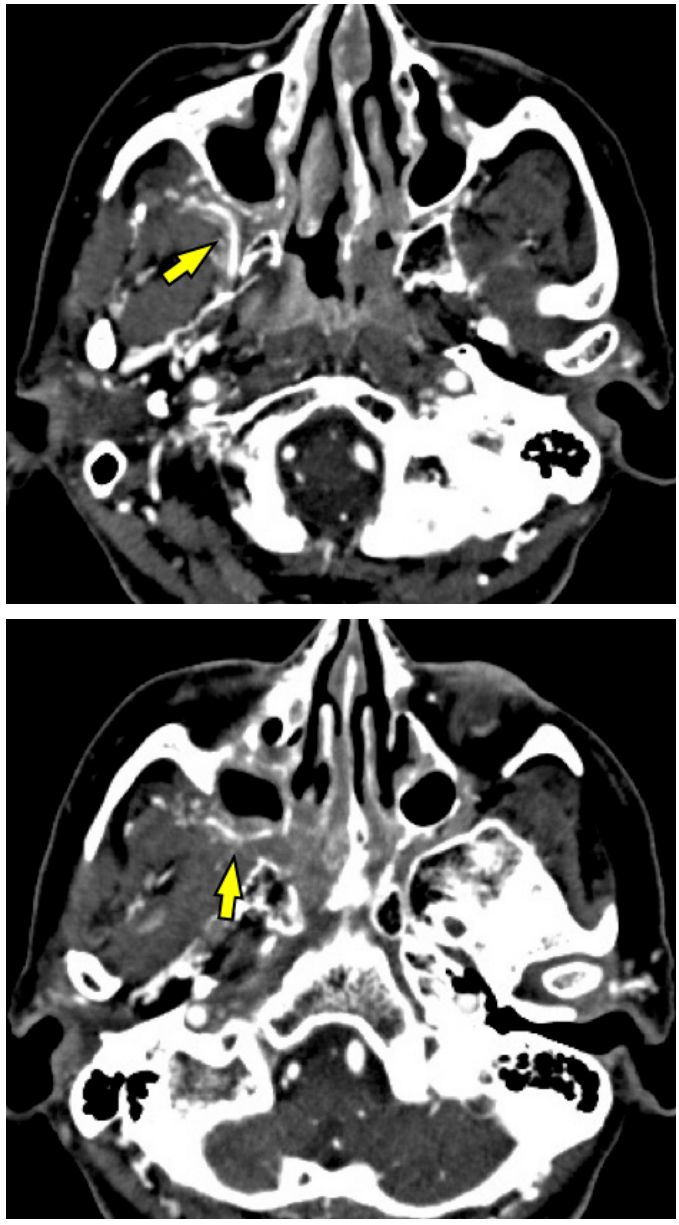

Figure 2. CT angiography showing the maxillary artery (arrow) running through the PPF lesion in the arterial phase.
CT: computed tomography, PPF: pterygopalatine fossa

Discussion

Malignant lymphoma is classified into nodal lymphoma, which develops in the lymph nodes and extranodal lymphoma, which develops in organs other than the lymph nodes. The most common sites for extranodal lymphoma in the head and neck are the orbit, sinonasal cavity, salivary glands, and thyroid gland (1); however, occurrence in the PPF is rare.

Till date, several cases of malignant lymphoma in and around the PPF have been reported (2-8). On the basis of these re-

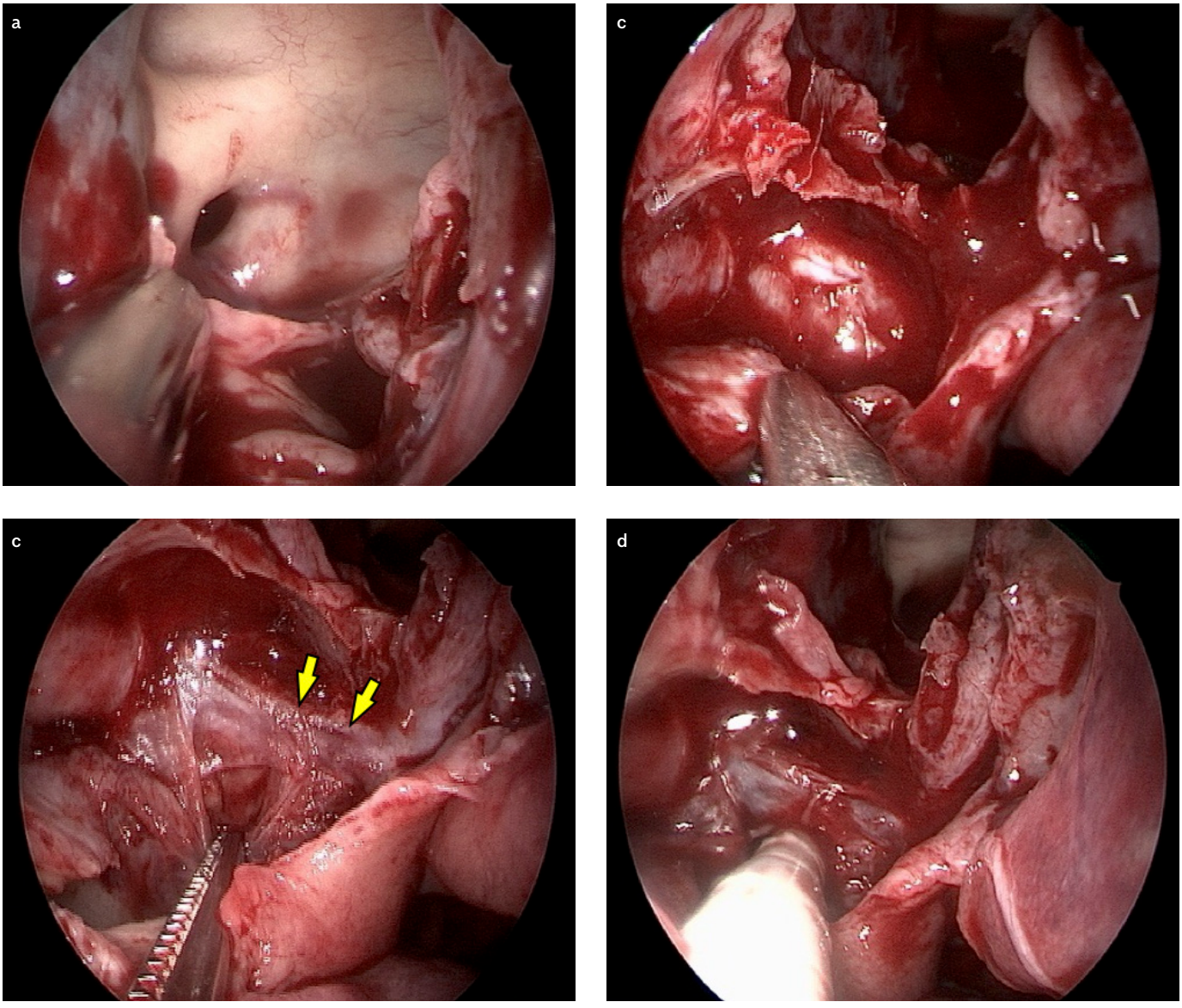

Figure 3. a-d. Endoscopic image during surgery. In the right maxillary sinus and sphenoid sinus, there is only a slight thickening of the mucosa and no tumors or fungal masses (a, b). We approached the PPF using a transmaxillary sinus approach. As no macroscopic tumor was observed, a biopsy was performed from the fat and fibrous tissue in the PPF (c, d), paying attention to bleeding from the maxillary artery and its branches (arrow).
PPF: perygopalatine fossa

ports, histologically, B-cell lymphoma containing DLBCL was the most common, accounting for five cases, with mucosa-associated lymphoid tissue lymphoma and natural killer/T-cell lymphoma accounting for one case each.

The most common reported symptom of malignant lymphoma in the PPF were cranial nerve palsies, with the most frequent being paralysis of the V nerve, followed by III and VI nerve palsies. Metachronous and multiple cranial nerve palsies are suggested as a characteristic clinical symptom of malignant lymphoma of the PPF, which is presumed to be owing to the anatomical features of the PPF. The PPF is a small fat-filled space between the posterior wall of the maxillary sinus and the pterygoid process of the sphenoid bone, and it is an important anatomic "crossroad" that relates to numerous intracranial and extracranial spaces through the foramen and fissures. In particular, the PPF communicates with the orbit through the inferior orbital fissure, with the middle cranial fossa through the foramen rotundum, and with the nasal cavity through the sphenopalatine foramen (9, 10). As a result of these anatomical features, tumors that develop in the PPF spread by infiltrating the surrounding space directly through the foramen and fissures or by perineural invasion along the trigeminal nerve, which can be expected to cause cranial nerve palsy. The most common result is paralysis of the V2 cranial nerve, which runs within the PPF, and infiltration of the trigeminal ganglion in Meckel's cavity can cause V1 and V3 cranial nerve palsies. In addition, orbital infiltration can cause cranial nerve palsy in II nerve, and cavernous sinus infiltration can cause III, IV, and VI nerve palsies. In addition, the pterygopalatine ganglion in the PPF and vidian nerve are connected to the VII nerve by the greater petrosal nerve and the XII nerve by the superior cervical ganglion, and invasion along the nerve is thought to cause these cranial nerve palsies.

In this patient, unexpectedly, some cranial nerve palsies improved spontaneously before chemotherapy for DLBCL. Ac-

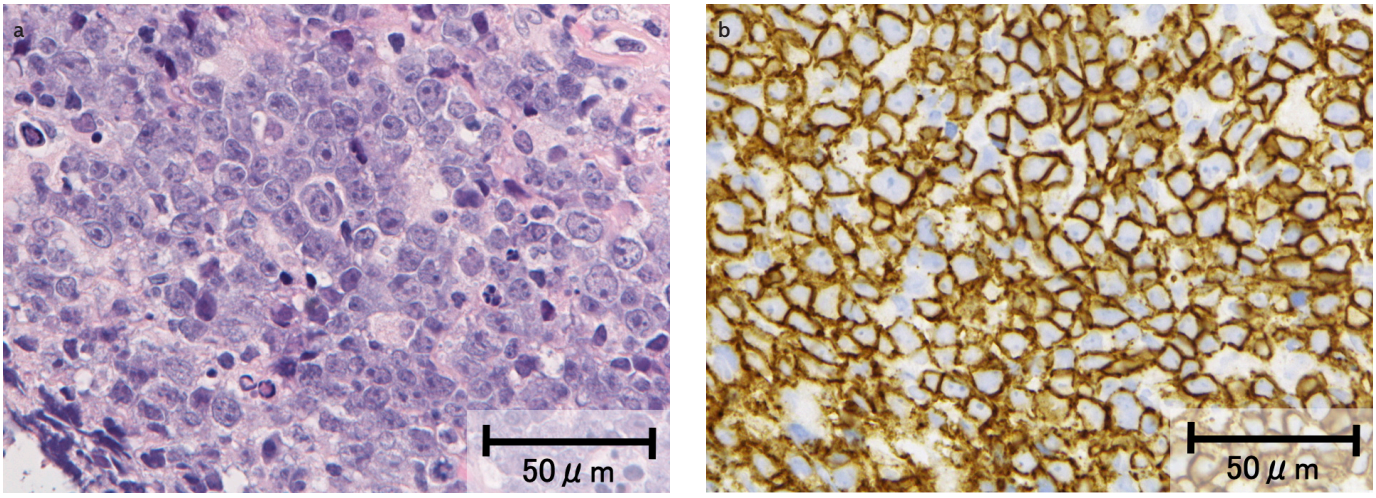

Figure 4. a, b. Hematoxylin and eosin staining showing diffuse proliferation of large atypical lymphocytes (original magnification ×400) (a). The tumor cells tested positive for CD20 (original magnification ×400) (b).
CD20: cluster of differentiation 20

cording to the report (11), spontaneous recovery of neurological symptoms of malignant lymphoma may be observed after the use of immunosuppressive drugs, surgery, and infection, and the host's immunological factors may be involved. In this patient as well, steroids were administered. The existence of a spontaneous recovery of neurological symptoms may be useful for the clinical diagnosis of malignant lymphoma.

A biopsy of the tumor is essential for the pathological diagnosis of malignant lymphoma. However, the PPF is difficult to approach because it is located deep in the face and has a complex array of blood vessels and neural structures (12). Regarding the method of biopsy for PPF lesions, external incisions and maxillofacial osteotomies are highly invasive, and these methods should be avoided as much as possible. Therefore, we performed a biopsy using the endoscopic transnasal approach as a minimally invasive method and succeeded in establishing a diagnosis. The most notable point of a biopsy using the endoscopic transnasal approach from the PPF is the risk of vascular complications, mainly related to damage to the maxillary artery. Active arterial bleeding can be difficult to control during endoscopic surgery. A preoperative evaluation with imaging studies is essential to understand the extension and relationship of the lesion with the surrounding neurovascular structures. It is also necessary that adequate technical equipment (angled endoscopes, a navigation system, and hemostatic tools such as vascular clips/coagulators with suction, etc.) is available (13). Embolization by interventional radiology and external carotid artery ligation should also be on standby in case of difficulty in bleeding cessation. Sufficient preparation and preoperative planning will make it possible to perform this surgery safely.

We reported a patient with DLBCL of the PPF. Malignant lymphoma of the PPF can cause multiple cranial nerve palsies, presumably owing to the anatomical features of PPF. It was characteristic that some neurological symptoms improved before treatment in this patient. Although PPF is an anatomically difficult site to access, biopsy via an endoscopic transnasal approach can ensure a minimally invasive diagnosis.

Informed Consent: Written informed consent was obtained from the patients who agreed to take part in the study.

Peer-review: Externally peer-reviewed.

Author Contributions: Consept – S.I., T.M., K.I., K.N., Y.Y., K.C.; Design – S.I.; Supervision – K.C.; Resources – S.I.; Materials – S.I.; Data Collection and/or Processing – S.I.; Analysis and/or Interpretation – S.I.; Literature Search – S.I.; Writing Manuscript – S.I.; Critical Review – S.I.

Conflict of Interest: The authors have no conflict of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

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