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## Head and Neck

# Primary diffuse large B-cell lymphoma of the frontal sinus: A case report and literature review

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### ABSTRACT

Diffuse large B-cell lymphoma arising as a primary tumor in the frontal sinus is very rare. Moreover, it is often difficult to diagnose frontal sinus lesions. A 67-year-old Japanese man initially presented with diplopia and a swollen left upper eyelid. Diffusion-weighted magnetic resonance imaging suggested a malignant lymphoma of the frontal sinus, and subsequent extensive examination revealed diffuse large B-cell lymphoma of the frontal sinus with left orbital invasion. Six courses of combined immunodirected chemotherapy were administered. The patient is tumor-free owing to the accurate diagnosis of lymphoma at an early stage.

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## Introduction

Primary lymphoma of the paranasal sinuses is rarely extranodal; most cases primarily occur in the maxillary sinuses, followed by the ethmoid sinuses and the nasal cavity [1]. Primary involvement of the frontal sinus is very rare, representing only 0.17%–1.63% of all lymphoma types [2]. It is common for neoplasms of the frontal sinus to present with signs and symptoms

that overlap with those observed in benign tumors and inflammatory diseases, such as osteomyelitis and mucocele, thereby leading to a protracted time course between the onset of the disease and its diagnosis [3]. However, early diagnosis and treatment are essential for improving treatment outcomes in patients with malignant tumors, particularly those tumors that are difficult to differentiate from benign tumors and non-neoplastic infectious diseases. It is impossible to extensively visualize the frontal sinus through physical

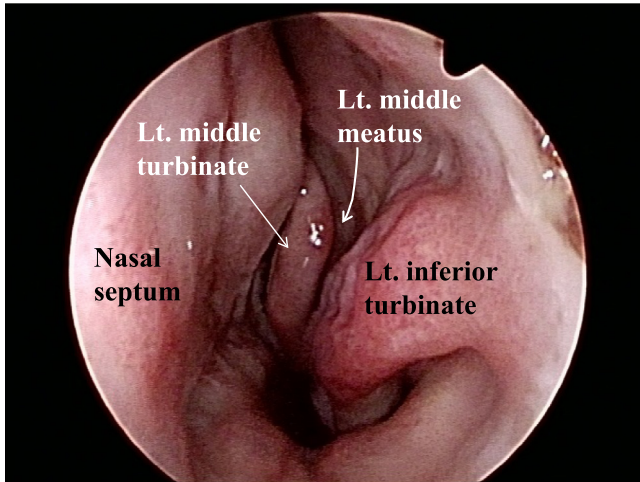
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**Fig. 1 – Endonasal endoscopy findings. The endoscopic view showed no nasal discharge or tumoral mass.**

examination alone; therefore, computed tomography (CT) and magnetic resonance imaging (MRI) are useful ancillary diagnostic methods.

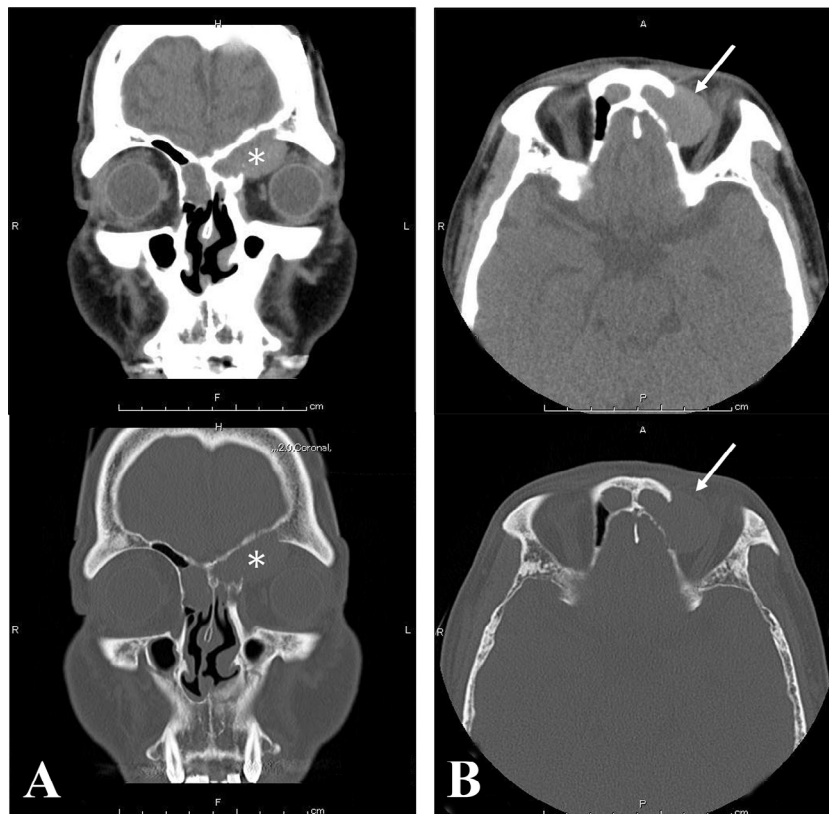
Diffusion-weighted imaging (DWI) is a more recently introduced imaging modality that provides morphologic and functional information. It is used to evaluate tumor histology and cancer grading in several anatomic regions including the

brain and breast [4,5]. Several studies have revealed that the apparent diffusion coefficient (ADC) obtained from DWI is useful for the characterization of head and neck lesions, and is especially helpful in differentiating squamous cell carcinoma from malignant lymphoma [6]. In this report, we present a patient with diffuse large B-cell lymphoma (DLBCL) located in the frontal sinus with left orbital invasion, for whom DWI proved to be a useful ancillary diagnostic method for preventing unwarranted surgery that would have required general anesthesia.

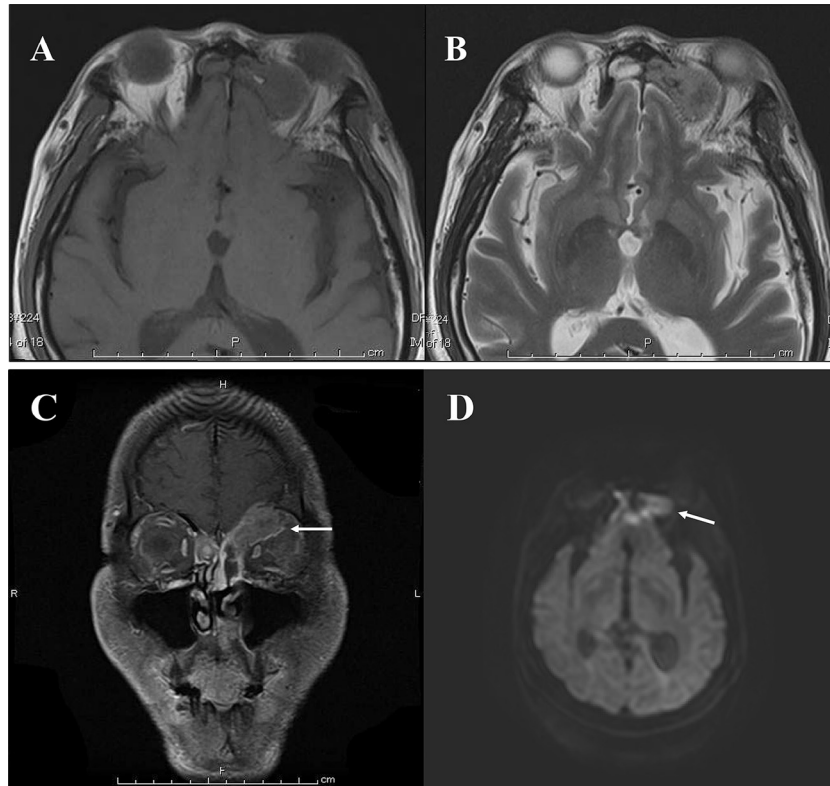
### Case report

A 67-year-old Japanese man who presented with diplopia and left upper eyelid swelling over a 2-week period was referred to our hospital. He had a history of bladder cancer but not of chronic rhinosinusitis. Ocular examinations revealed normal visual acuity and intraocular pressure. The endoscopic view showed no nasal discharge or tumoral mass in the left nasal cavity (Fig. 1). Serologic analysis revealed normal soluble interleukin-2 receptor and lactate dehydrogenase levels.

CT scans of the patient's paranasal sinuses revealed opacification of the left anterior ethmoidal sinus and right frontal sinus, as well as a soft tissue mass in the left frontal sinus with left orbital invasion from the anterior roof of the orbit (Fig. 2). T1- and T2-weighted MRI scans revealed a low-density mass (Fig. 3A and 3B); whereas, gadolinium-enhanced T1-weighted



**Fig. 2 – CT scan of the patient's tumor. (A) A coronal CT image revealed an expansive frontal mass (asterisk) in the patient's left frontal sinus with orbital invasion. (B) An axial CT image showing invasion of the mass into the left orbit (arrow). CT, computed tomography.**

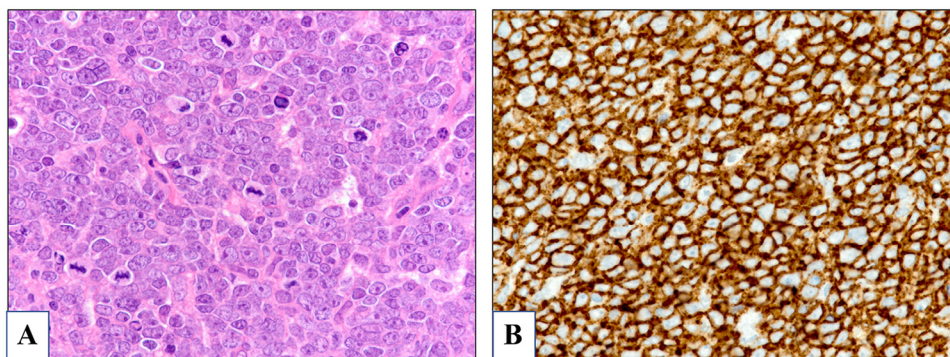


**Fig. 3** – MRI scan of the patient’s tumor. (A) Axial T1-weighted MRI scan revealed that the lesion in the left frontal sinus had a characteristic low density. (B) Axial T2-weighted MRI scan revealed that the lesion in the left frontal sinus had a relatively low density that reflected a neoplasm rather than inflammatory disease. (C) A coronal gadolinium-enhanced T1-weighted MRI scan of the patient’s paranasal cavities showed a moderately enhanced lesion (arrow) in the left frontal sinus. (D) Axial diffusion-weighted image with a b factor of 700 s/mm<sup>2</sup> shows a lesion (arrow) with moderately high signal intensity. MRI, magnetic resonance imaging.

MRI scan of the sinus showed a mildly and uniformly enhanced mass in the left frontal sinus with invasion of the superior oblique muscle. There was no evidence of invasion into the frontal lobe (Fig. 3C). DWI of the frontal sinus lesion demonstrated mild-to-high signal intensity with ADC values of  $0.58 \times 10^{-3}$  mm<sup>2</sup>/s (Fig. 3D). We speculated that our patient

had non-Hodgkin lymphoma (NHL) of the frontal sinus as ADC values of NHL are reported to be small.

The patient then underwent a biopsy through endonasal endoscopy under local anesthesia to obtain a sample for a pathologic diagnosis. Histopathologic analysis with hematoxylin and eosin staining revealed nodular infiltration of atypical



**Fig. 4** – Histopathologic features of the patient’s tumor. (A) In most lesions, the neoplastic cells exhibited uniformly large and round nuclei with little cytoplasm and dispersed coarse-to-fine nuclear chromatin and inconspicuous nucleoli, as observed using hematoxylin and eosin staining ( $\times 400$ ). (B) Immunohistochemical staining revealed that the tumor was positive for CD20 ( $\times 400$ ).

and large-sized lymphocytes (Fig. 4A). Immunohistochemical staining revealed that the neoplastic cells were positive for CD20, CD79a, bcl-2, bcl-6, and MUM-1 but negative for CD3, CD5, CD10, and cyclin D1. The Ki-67 labeling index was 80% (Fig. 4B). Hence, the patient was ultimately diagnosed with nongermlinal center B-cell type DLBCL of the frontal sinus [7].

The patient was referred to the hematology department of our hospital for tumor staging and chemotherapy. An 18F-fluorodeoxyglucose positron emission tomography CT (PET-CT) scan revealed localized abnormal 18F-fluorodeoxyglucose accumulation in the left frontal sinus and the neck lymph nodes bilaterally, with maximum standard uptake values of 19.8 and 3.88–5.56, respectively. Bone marrow aspiration and biopsy revealed no infiltration. The tumor was diagnosed as stage II DLBCL according to the Ann Arbor classification [8]; the prognostic index score of the patient is 2 according to the International Prognosis Index [9].

Chemotherapy and immunotherapy were initiated using rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (ie, the R-CHOP regimen) at the standard dose for the patient's weight. Six courses of combined immunodirected chemotherapy were administered. An 18F-fluorodeoxyglucose PET-CT scan after 12 months showed no evidence of recurrence. The patient provided written informed consent for this case report.

## Discussion

Primary malignancies originating in the frontal sinus are rare. Bhojwani et al. reported that the incidence of frontal sinus malignancies in their study was 0.011 per 100,000 individuals during a 12-year period, with squamous cell carcinoma as the most common histologic etiology, followed by NHL [10].

NHL located in the frontal sinus is also rare; only 16 cases have been reported in the existing literature to date [11,12]. Characteristic early-stage symptoms for malignancies of the frontal sinus are not well described; common symptoms only occur owing to the effect of the tumor mass [3]. Therefore, it remains challenging to detect NHL of the frontal sinus at an early stage. CT is commonly used for examining sites affected by paranasal diseases and morphologic changes. However, it is difficult to distinguish malignant tumors from benign lesions based on morphologic changes alone. DWI provides both morphologic and functional information, as this technique evaluates the diffusion motion of water protons in tissues, hence allowing the quantification of the random motion of water molecules via ADC measurements in tissues. DWI has been used to evaluate the histology and grade of tumors arising in several anatomic regions including the brain and breast [4,5], and it has also been used for detecting and staging malignant lymphomas [13]. Previous studies have shown that DWI is useful for characterizing head and neck lesions, as the mean ADC value of malignant lymphoma ( $0.66 \pm 0.17 \times 10^{-3} \text{ mm}^2/\text{s}$ ) is considerably smaller than those of carcinomas ( $1.13 \pm 0.43 \times 10^{-3} \text{ mm}^2/\text{s}$ ), benign solid tumors ( $1.56 \pm 0.51 \times 10^{-3} \text{ mm}^2/\text{s}$ ), and benign cystic lesions ( $2.95 \pm 0.62 \times 10^{-3} \text{ mm}^2/\text{s}$ ) [6,14].

We confirmed that the ADC value of the NHL located in the frontal sinus is small, which was consistent with those in NHLs

located at other sites. We were therefore able to correctly diagnose the patient with malignant lymphoma using minimally invasive procedures, and to commence prompt treatment before any surgery became necessary. Although it is often difficult to distinguish malignant tumors from frontal sinus lesions, determining the ADC value is useful for the evaluation of frontal sinus lesions before deciding the treatment; this finding ought to be useful to clinicians.

## Conclusion

DWI was valuable for narrowing the differential diagnosis, staging, biopsy planning, and follow-up of our patient. It is important for clinicians to scrutinize the pathology of lesions to avoid unnecessary surgeries, and DWI can be very useful in this regard.

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