Introduction

Ewing sarcoma (ES) is a tumor first described by James Ewing in 1921. Previously, it belongs to the spectrum of tumors known as the Ewing sarcoma family of tumors (ESFT), which also includes peripheral primitive neuroectodermal tumors, peripheral neuroepitheliomas, and Askin tumors which share similar biologic behavior and the same EWS/ETS oncogenic fusions. Recently, it is included to “undifferentiated small round cell sarcomas of bone and soft tissue tumors” in the 2020 WHO classification. It is the second most common tumor among adolescents and young adults that affects the bone or soft tissue, and it is more frequently found in males and Caucasians. It commonly occurs in the long bones of the extremities, pelvis, chest wall, and spine, and is known to be extremely rare when it occurs in the intracranial region. Similar to other head and neck tumors, there may be limitations to local management due to proximity to important surrounding tissues. However, whenever possible, wide local excision and combined modality therapy are recommended. We report a case of sino-nasal Ewing sarcoma who underwent endoscopic complete resection followed by adjuvant chemoradiation therapy.

Case report

A 21-year-old male patient with no significant past medical history presented to the ophthalmology department with one-week history of left exophthalmos, left periorbital swelling, and pain. A CT scan of the orbit revealed a soft tissue density measuring 4.5 x 3.0 cm that occupied the left eth-
moid and frontal sinuses and expanded inward towards the left medial orbit. The case was referred to the otorhinolaryngology department for further evaluation. Tenderness around the left orbit was noted on physical examination, but no significant findings were observed on nasal endoscopy examination. Contrast-enhanced MRI of the sinuses revealed an ethmoid sinus mass lesion that showed heterogeneous enhancement with expansion towards the lamina papyracea and floor of the frontal sinus. A tissue biopsy was performed by breaking through the ethmoid bulla and the lesion showed a small round cell tumor with areas of necrosis and bone invasion. Positron emission tomography (PET) scan showed increased FDG uptake in the same area, but there were no findings of cervical lymph node metastasis or distant metastasis. Additionally, bone marrow aspiration biopsy (BMAB) did not reveal any evidence of metastasis (Fig. 1).

The entire mass was resected piecemeal using a debrider and forceps under endoscopic guidance. According to the surgical findings, the epicenter of the tumor was located at the lamina papyracea and it extended from the medial to the lateral posterior ethmoid sinus. The tumor invaded the lacrimal bone anteriorly and extended superiorly up to the entrance of the frontal sinus. The lamina papyracea was drilled and no infiltration of the periorbita was observed, so the periorbita was preserved. The area around the frontal sinus ostium was also drilled. According to the initial report, olfactory neuroblastoma was suspected, but further immunohistochemical staining revealed diffuse positive results for CD99 and FLI-1, leading to the final diagnosis of Ewing sarcoma (Fig. 2). The tissue sample showed infiltration into

Fig. 1. Contrast enhanced T1-weighted (A) and T2-weighted PNS MRI (B) shows about 4.2x2.8cm sized mass-like lesion with mixed signal intensity, and PET-CT shows FDG uptake lesion in left ethmoid sinus. (C).

Fig. 2. H-E stain, x400 shows monotonous, round tumor cells with fine chromatin occasional nucleoli, and scant or clear cytoplasm (A) and bone destruction by tumor cells (B). (C) CD99 immunohistochemical stain, x400 shows characteristically strong, diffuse, and membranous expression. (D) FLI-1, x400, : Nuclear FLI-1 stain.
the agger nasi cell, superior turbinate, maxillary sinus muco-
sa, and the lamina papyracea, but there was no infiltration
into the sphenoid sinus.

After the surgery, radiation therapy of 5040cGy was per-
formed, and 11 cycles of Ifosfamide, Etoposide (IE) and
7 cycles of Vincristine, Actinomycin D, Cyclophosphamide
were administered. The patient has been under observation
without complication and recurrence for 5 years since the
end of treatment (Fig. 3).

**Discussion**

Ewing sarcoma is a highly aggressive round cell mesen-
chymal neoplasm which is included to “undifferentiated
small round cell sarcomas of bone and soft tissue tumors”
in the 2020 WHO classification on the basis of the gene
fusion type with round cell sarcomas with EWSR1-non-ETS
fusions, CIC-rearranged sarcoma, and sarcomas with BCOR
genetic alterations.²,⁵

It commonly affects children and young adults, with 80%
of cases occurs before the age of 20 years old and usually
involves the long bones of extremities, less commonly pel-
vis, ribs, skull, vertebra, scapula. About 12% of ES cases
are extraskeletal and head and neck ES is rare.⁶ The pre-
senting symptoms typically comprise a slow growing, firm
mass. It can accompany with local pain or tenderness and
swelling without erythema. Depending on the site of in-
vasion, it may be associated with loose teeth,⁷ otitis media,
or exophthalmos. Lymphatic spread to the cervical region
is uncommon. Initial evaluation should include CT and MRI
of the primary site, chest CT, and bone scan. Bone marrow
biopsy or screening MRI of the spine and pelvis should be
considered. ES tumors are mostly lytic-sclerotic and show
speculated periosteal reactions on plain films and CT scans.⁸

The small round blue cell tumor (SRBCT) to which Ewing
sarcoma belongs is characterized by small and round un-
differentiated cells with scant cytoplasm and numerous nu-
clei, which stain blue with H&E staining.⁹ Since SRBCTs
include not only Ewing's sarcoma but also rhabdomyosarco-
ma, olfactory neuroblastoma, lymphoma, mucosal melanoma,
squamous cell carcinoma, NUT carcinoma, sinonasal
undifferentiated carcinoma, neuroendocrine carcinoma, pi-
tuitary adenoma, mesenchymal chondrosarcoma, small cell
osteosarcoma, and plasmacytoma, it is important to differ-
entiate them.¹⁰ However, since SRBCTs have the character-
istics of undifferentiated and primitive cells, it is difficult
to distinguish them histologically. Therefore, it is best to make
a comprehensive judgment through immunohistochemical,
cytogenetic, and molecular genetic analysis. In particular,
Ewing's sarcoma among SRBCTs often shows positive re-
results for CD99 (MIC2) and FLI-1 protein.¹¹ Vimentin posi-
tivity is a sarcoma tumor marker that indicates a mesen-
chymal origin, while in the case of neuroblastoma, NSE,
neurofilament, CD56 (NCAM), synaptophysin, and chro-
mogranin are often positive.¹² In this case, although olfac-
tory neuroblastoma was misdiagnosed in the initial tissue
examination, further testing revealed positive results for vi-
mentin, CD99, FLI-1 and negative results for S-100, syn-
aptoxyphsin, and chromogranin, leading to a final diagnosis
of Ewing sarcoma.

Sinonasal ES is an exceptionally rare malignancy with
no clearly defined treatment paradigm. While combination
chemotherapy is consistently utilized, there remains a paucity of literature discussing the utility of surgery and/or radiation therapy to aide in locoregional control.\textsuperscript{13} Surgical vs radiation treatment for ES has been debated over the years. The prognosis of ES varies depending on the size of the lesion, presence of metastasis, response to treatment, histological characteristics, age, and molecular genetic features. Although ESs with metastasis at the time of diagnosis are relatively rare, accounting for less than 25%, the high recurrence rate of 80-90% with local therapy alone suggests that the disease should be considered systemic. Therefore, for localized lesions, it is recommended to undergo multi-agent chemotherapy in addition to local therapy. Various studies have been conducted on anticancer treatment, and in the Intergroup Ewing Sarcoma Study (IEWS)-III, the use of vincristine, doxorubicin, cyclophosphamide, and dactinomycin (VDCA) along with ifosfamide and etoposide (I/E) resulted in higher 5-year survival rates of 69% and 54%, respectively, compared to using VDCA alone.\textsuperscript{14} Considering the patient's young age and endoscopic piecemeal resection, additional chemotherapy was administered based on the results of the IESS-III study.

In summary, for the treatment of sinonasal ES, surgery is the preferred treatment modality for locoregional control if a safe operation is attainable with negative margins. Neoadjuvant chemotherapy and/or radiotherapy is a reasonable strategy depending on tumor location. If negative surgical margins cannot be achieved, radiotherapy is likely required for local control. Chemotherapy is a mainstay of treatment in all cases and the addition of biological agents may be a promising strategy to improve outcomes.\textsuperscript{15}

Here, we demonstrate a rare case of Ewing sarcoma that originated from the paranasal sinus. Although initially suspected as olfactory neuroblastoma, subsequently, it was accurately diagnosed as Ewing sarcoma using appropriate immunohistochemistry studies. We would like to emphasize the possibility that these tumors may originate from the head and neck area, and hence, it is important to use appropriate techniques for accurate diagnosis and treatment.

\textbf{References}