



안구 돌출을 주소로 내원한 21세 남환에서 사골동 유잉 육종 1예

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An Ethmoid Sinus Ewing Sarcoma with Exophthalmos in A 21-Year-Old Male

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= Abstract =

Ewing sarcoma is a rare tumor in head and neck area. We demonstrate a rare case of sinonasal Ewing sarcoma initially suspected as olfactory neuroblastoma. After the surgery and immunohistochemical studies, it was accurately diagnosed as Ewing sarcoma. We would like to emphasize the possibility that Ewing sarcoma may originate from the head and neck area, and hence, it is important to use appropriate techniques for accurate diagnosis and treatment.

Key Words : Ewing sarcoma · Exophthalmos · Tumor

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.¹⁾ Recently, it is included to “undifferentiated small round cell sarcomas of bone and soft tissue tumors” in the 2020 WHO classification.²⁾ 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.³⁾ 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.⁴⁾ We report a case of sinonasal 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-

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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 periorbital was observed, so the periorbital 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).

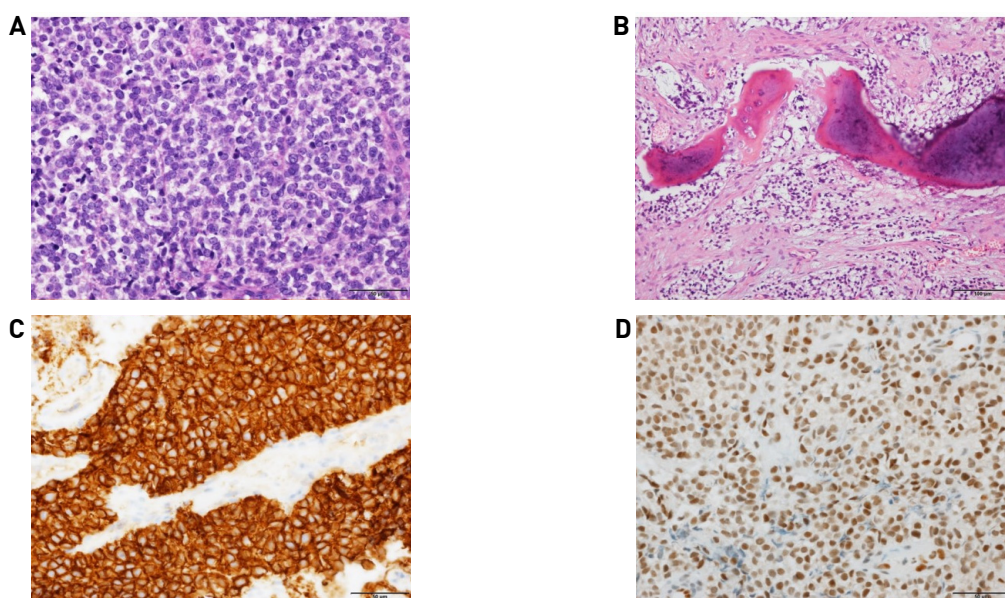


Fig. 2. H-E stain, x400 shows monotonous, round tumor cells with fine chromatin occasional nucleoli, and scant or clear cytoplasm (A) and bone destruction by tumor cells (B). (C) CD99 immunohistochemical stain, x400 shows characteristically strong, diffuse, and membranous expression. (D) FLI-1, x400, : Nuclear FLI-1 stain.

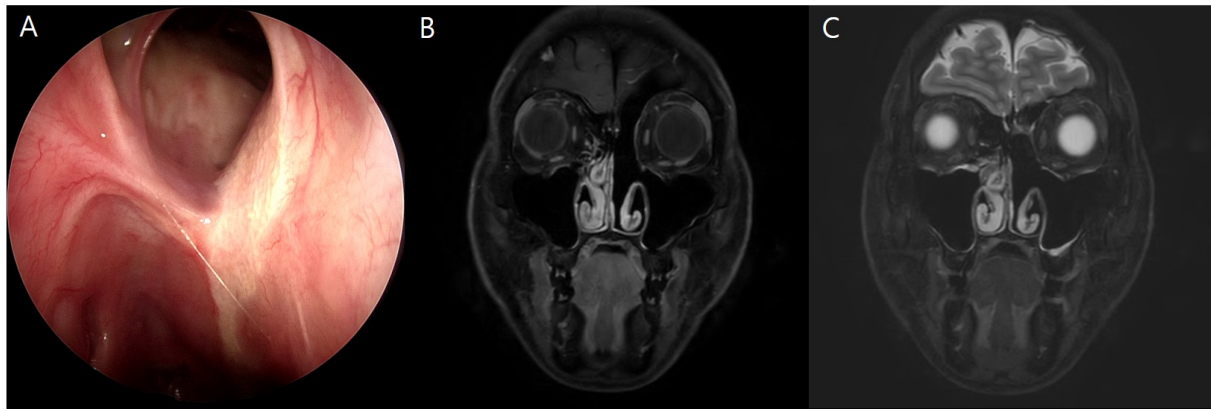


Fig. 3. Postoperative 5years, there is no recurred lesion on endoscopic examination (A), in contrast enhanced T1-weighted (B) and T2-weighted PNS MRI (C).

the agger nasi cell, superior turbinate, maxillary sinus mucosa, and the lamina papyracea, but there was no infiltration into the sphenoid sinus.

After the surgery, radiation therapy of 5040cGy was performed, 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 mesenchymal 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 pelvis, ribs, skull, vertebra, scapula. About 12% of ES cases are extraskelatal and head and neck ES is rare.⁶⁾ The presenting 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 invasion, 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 undifferentiated cells with scant cytoplasm and numerous nuclei, which stain blue with H&E staining.⁹⁾ Since SRBCTs include not only Ewing's sarcoma but also rhabdomyosarcoma, olfactory neuroblastoma, lymphoma, mucosal melanoma, squamous cell carcinoma, NUT carcinoma, sinonasal undifferentiated carcinoma, neuroendocrine carcinoma, pituitary adenoma, mesenchymal chondrosarcoma, small cell osteosarcoma, and plasmacytoma, it is important to differentiate them.¹⁰⁾ However, since SRBCTs have the characteristics 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 results for CD99 (MIC2) and FLI-1 protein.¹¹⁾ Vimentin positivity is a sarcoma tumor marker that indicates a mesenchymal origin, while in the case of neuroblastoma, NSE, neurofilament, CD56 (NCAM), synaptophysin, and chromogranin are often positive.¹²⁾ In this case, although olfactory neuroblastoma was misdiagnosed in the initial tissue examination, further testing revealed positive results for vimentin, CD99, FLI-1 and negative results for S-100, synaptophysin, 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.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 (IESS)-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.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.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.

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