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Case report

Sinonasal adamantinoma-like Ewing sarcoma: A case report

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ABSTRACT

We describe the case of a sinonasal adamantinoma-like Ewing sarcoma in a 41-year-old male. Histologically, the tumor exhibited distinctive areas of nested growth pattern with prominent stromal fibrosis and metaplastic bone formation. The tumor cells were small and uniform with minimal amount of pale eosinophilic to clear cytoplasm and round or oval nuclei with finely dispersed chromatin and small nucleoli. Approximately 20% of the tumor parenchyma comprised of small clusters of basaloid cells within an osteofibrous background resembling adamantinoma. The tumor showed strong expression of keratins, p63, CD99 and Fli-1, and *EWSR1* rearrangement. The diagnosis of sinonasal Ewing family tumors is particularly problematic owing to the large number of potential mimics. For any poorly differentiated or undifferentiated head and neck tumor, cellular monotony and CD99 immunoreactivity should prompt consideration for molecular studies that include analysis of both *EWSR1* and *FLI1*, even in the presence of strong cytokeratin expression or focal keratinization.

1. Introduction

The Ewing sarcoma family of tumors (EFT) is a group of malignant small round blue cell tumors (SRBCT) that arise in bone or soft tissue and primarily affects the pediatric and young adult population [1–3]. The pathological diagnosis of EFT is based on the finding of a SRBCT that stains for CD99 and expresses one of several reciprocal translocations, most commonly t(11;22)(q24;q12) between the amino terminus of the *EWSR1* gene and the carboxy terminus of the *FLI1* gene found in 85–90% of cases [1–3]. An emergent consensus favors it to be mesodermally derived [4]. Rare cases of adamantinoma-like Ewing sarcoma, a SRBCT resembling Ewing sarcoma but showing overt epithelial differentiation, resembling a carcinoma and yet harboring the characteristic molecular alterations of EFT have been reported [1–3,5–10]. Precise tumor classification is crucial for establishing prognosis and in guiding appropriate therapeutic strategies. Judging by the published literature, EFT involving the head and neck are extremely rare [1,2,5,6,8].

We present a diagnostically challenging case of adamantinoma-like Ewing sarcoma arising in the nasal cavity of a 41-year-old male.

2. Clinical history

A 41-year-old man presented with left orbital pain and swelling. A computed tomography (CT) scan of the head was performed, demonstrating a large heterogenous enhancing mass centered in the left nasal cavity extending into the left maxillary sinus and left orbit with marked anterior displacement of the globe (Fig. 1A and B). There was destruction of the lamina papyracea, medial orbital wall, anterior wall of the left sphenoid sinus, and medial wall of the left maxillary sinus. The mass measured approximately 5.2 × 4.8 × 4.2 cm in size and contained multiple small cystic components, bony fragments and calcifications, suggestive of chondroid matrix. The differential consideration included sinonasal chondrosarcoma, sinonasal adenocarcinoma, sinonasal squamous cell carcinoma, and invasive fungal sinusitis. Tissue sampling was recommended.

The patient is still alive 2 months after surgery.

3. Material and method

Representative tissue sections from the sinonasal mass were fixed in 10% buffered formalin and embedded in paraffin. Representative tissue blocks were submitted for frozen section and permanent sections. For routine microscopy, 4-μm-thick sections were stained with H&E. Immunohistochemical staining was performed using an automated immunostainer (Leica Bond-III, Leica

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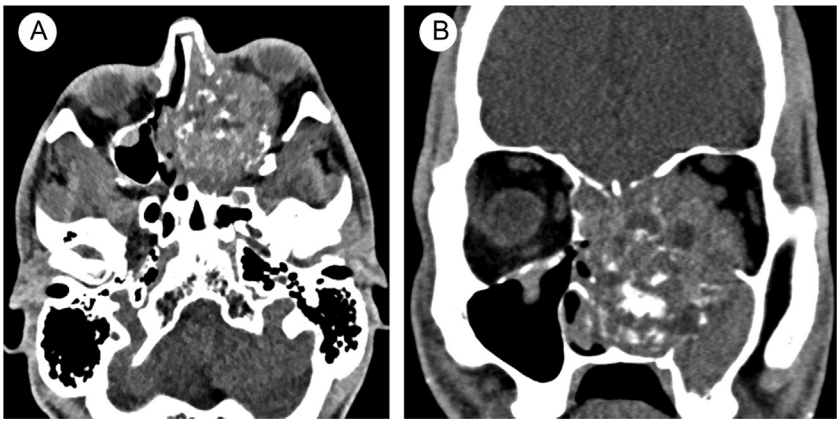

Fig. 1. A. Adamantinoma-like Ewing sarcoma. There is a large expansile soft tissue mass with internal rings and arcs pattern mineralization. The mass is centered in the left nasal cavity and extends into the left maxillary sinus and left orbit, resulting in proptosis. Bone windows demonstrate extensive bony destruction. Axial CT. B. Adamantinoma-like Ewing sarcoma. The mass invades the right nasal cavity, ethmoid sinuses, left maxillary sinus, and left orbit, with lateral displacement of the medial and inferior rectus muscles, and abutment of the optic nerve. Bone windows demonstrate extensive bony destruction and thinning of the ethmoid roof. Coronal CT.

Table 1
List of primary antibodies used in the study.

Antibody	Manufacturer	Species	Clone	Dilution
Actin, muscle-specific	Cell Marque	mouse	HHF-35	predilute
Caldesmon	Dako	mouse	h-CD	1:100
Calretinin	Cell Marque	rabbit	SP13	predilute
CD99	Dako	mouse	12E7	1:1000
Cytokeratin AE1/3	Dako	mouse	AE1/AE3	1:50
Cytokeratin 5/6	Dako	mouse	D5/16 B4	1:10
Chromogranin	Ventana	mouse	LK2H10	predilute
Desmin	Dako	mouse	D33	1:40
EMA	Dako	mouse	E29	1:50
Fli-1	Cell Marque	mouse	MRQ-1	1:25
Ki67	Ventana	mouse	30–9	predilute
NUT	Cell Signaling	rabbit	C52B1	1:45
p63	Ventana	mouse	4A4	predilute
S100	Ventana	mouse	4C4.9	predilute
Synaptophysin	Cell Marque	rabbit	MRQ-40	1:25
Vimentin	Dako	mouse	V9	1:100
WT1	Cell Marque	mouse	6F-H2	1:20

Biosystems, Buffao Grove, Il) and BondRefinePolymerTM biotin-free DAB detection kit. The antibodies applied in the study are listed in Table 1. A positive nuclear, cytoplasmic and/or membranous expression in 10% or more of neoplastic cells qualified as "positive (+)".

EWSR1 (22q12) fluorescence in situ hybridization (FISH) studies were performed at Mayo Clinic on formalin-fixed, paraffin-embedded tumor tissue using a break-apart probe. The test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements.

4. Results

4.1. Histology and immunohistochemical findings

Histologically, the tumor exhibited distinctive areas of nested growth pattern with prominent stromal fibrosis and metaplastic bone formation (Fig. 2A). The tumor cells were small and uniform with minimal amount of pale eosinophilic to clear cytoplasm and round or oval nuclei with finely dispersed chromatin and small nucleoli (Fig. 2B). Approximately 20% of the tumor parenchyma comprised of small clusters of basaloid cells within an osteofibrous background resembling the so-called osteofibrous dysplasia-like variant of adamantinoma (Fig. 2C and D). Rare foci of overt keratinization in the form of squamous pearls were also noted (Fig. 3A). Primary tumor mitotic rate was 7 mitoses/10 high power fields. No tumor necrosis was identified. The tumor exhibited areas of intraepithelial growth in the overlying sinonasal epithelium.

The initial immunohistocmical diagnostic panel showed strong expression of keratins (AE1/AE3, CK5/6) and p63 in tumor (Fig. 3B and C). The Ki67 proliferative index was 17%.

The tumor was initially misdiagnosed as possible NUT midline carcinoma due to anatomic location and strong cytokeratin expression. Additional immunohistochemical studies showed strong diffuse, membranous CD99 (Fig. 3D) and Fli-1 immunoreactivity while NUT-1, WT1, synaptophysin, chromogranin, S100, EMA, vimentin, p16, smooth muscle actin, caldesmon, and desmin immunostains were negative in lesional cells.

4.2. Fluorescence in situ hybridization

FISH assay showed *EWSR1* rearrangement. The tumor was subsequently reclassified as adamantinoma-like Ewing sarcoma.

4.3. Overall treatment plan

The patient is treated with chemotherapy, vincristine + doxorubicin + cyclophosphamide alternating with ifosfamide + etoposide. He will return to the clinic after completion of induction chemotherapy for radiotherapy planning.

5. Discussion

The EFT includes a spectrum of small round blue cell tumors such as osseous and extraosseous Ewing sarcoma, peripheral neuroectodermal tumor and Askin's tumor of the chest wall [1,2]. Because of their similar histologic and immunohistochemical characteristics and shared nonrandom chromosomal translocations, these tumors are considered to be derived from a common cell of origin, although its histogenic origin is debated [1].

Primary EFT of head and neck is uncommon and primary sinonasal EFT is even rarer [1]. Recent studies have advocated the genotypic and phenotypic delineation of a novel Ewing sarcoma histologic variant showing epithelial features defined as "adamantinoma-like Ewing sarcoma" [2,3,5,6,9]. Similar to classic EFT, head and neck adamantinoma-like EFT appears to generally affect young patients and may arise in a wide range of anatomic subsides including periorbital soft tissues, thyroid gland, parotid gland, and even mucosal sites like the sinonasal tract [1].