Hyalinizing clear cell carcinoma in the sphenoid sinus

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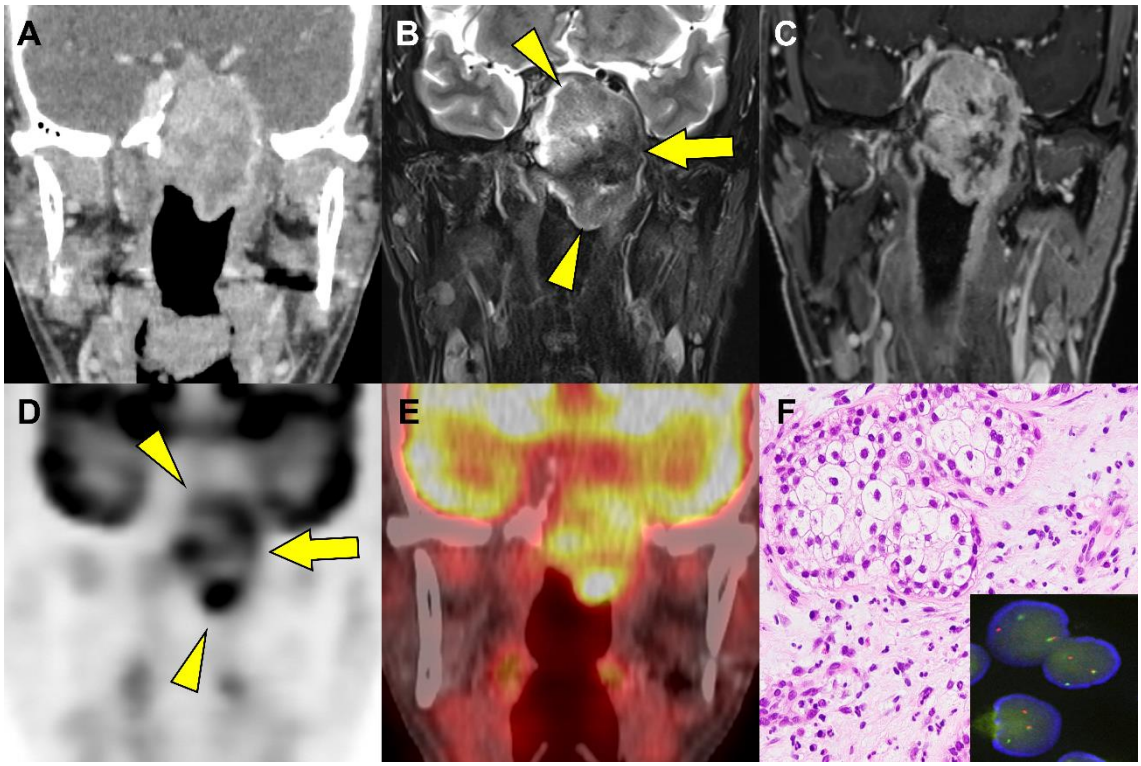
Abstract: (100 words)

A 39-year-old man presented with a one-month history of headaches. Imaging revealed a mass with extensive destruction. T2-weighted imaging (T2w) displayed mixture of low and sponge-like high intensities and also dark area, with FDG PET/CT showing uneven but intense accumulation. Biopsy confirmed *EWSR1* rearrangement, and hyalinizing clear cell carcinoma (HCCC) was diagnosed. HCCC, recently renamed from clear cell carcinoma in the fifth edition of the World Health Organization Classification of Head and Neck Tumors, is a rare tumor. This case describes the features of T2w and FDG PET patterns in HCCC, possibly contributing to their consideration in the differential diagnosis.

Figure Legend: 472 words



A 39-year-old man presented to our hospital with a one-month history of headaches. CT and MRI revealed a sphenoid sinus mass lesion, approximately 5 cm in diameter, which extends into the left nasopharynx (A-C) and caused destruction of nearby structures, including the clivus and bottom and left side of the sphenoid bone (A). Despite its extensive spread, the lesion had clear boundaries. T2-weighted imaging (T2w) revealed that the tumor comprised several features (B). Predominantly low and sponge-like high intensities with uniform enhancement was shown mainly in the cranial aspect and caudal end of the lesion (B, arrowhead). Meanwhile, a dark T2w area was mainly observed in the middle level (B, arrow), showing enhancement with only its edges. In the FDG PET/CT scan shown in range with standardized uptake value (SUV) 0-8, the tumor displayed uneven accumulation

(D, E). The high signal areas observed in T2w showed intense accumulation (SUVmax =11.4), while the low signal areas exhibited relatively weaker accumulation. Low signal intensity on T2w indicated the presence of distinctive features of the tumor, such as fibrosis. However, FDG accumulation still pointed towards a malignant tumor.

The biopsy specimen shows irregular nests of tumor cells with clear cytoplasm, and mitotic figures are rare (F). Immunohistochemically, the tumor cells were p40- and p63-positive. Break-apart fluorescence *in situ* hybridization (FISH) confirmed *EWSR1* rearrangement (F, lower right corner). Based on these findings, the tumor was diagnosed as a hyalinizing clear cell carcinoma (HCCC). Owing to the extent of invasion, the patient was considered inoperable and subsequently referred for proton beam therapy at an alternative medical facility. Three months after the end of the treatment, the tumor reduced in size.

HCCC, recently renamed from clear cell carcinoma in the latest fifth edition of the World Health Organization Classification of Head and Neck Tumors, (1) is a rare tumor that originates from the minor salivary glands, mainly in the oral cavity. Its occurrence in the paranasal sinuses is extremely rare, with only a limited number of reported cases. (2-4) HCCC typically shows a slow progression and has a favorable prognosis if completely resected; however, chemoradiotherapy may be an option for recurrent or unresectable cases. (5) Assessment of *EWSR1* rearrangement is useful for identifying HCCC because its diagnosis is sometimes challenging based on histopathology. (1) In our biopsy

sample, there were no hyalinizing or fibrous tissue, which are pathognomonic features of HCCC. (6) Nevertheless, *EWSR1* break apart in p40-positive clear cells enable us to confirm the diagnosis of HCCC.

Although imaging findings, especially the FDG PET findings of HCCC, are unclear, hypermetabolic activities in the lesions have been described in the literature, (7,8) similar to ours. This case suggests that if we observe both T2w low-signal intensity areas that may have reflected hyalinization and intense accumulation of FDG, indicating suspicious malignancy, HCCC could be considered as a differential diagnosis.

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