

A rare case of SMARCB1 (INI-1)-deficient sinonasal carcinoma: First case report from Nepal

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Title Page:

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The data supporting the findings in this case report is available within the article and its supplementary materials.

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The authors declare that there is no conflict of interest.

ETHICS STATEMENT

None

WRITTEN CONSENT FROM THE PATIENT

Written informed consent was obtained from the patient before the submission of the report. The patient understands that her name and initials won't be mentioned and in the images only the histological sections' slides will be used.

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KEYWORDS

carcinoma; case report; histopathology; sinonasal; SMARCB1

INTRODUCTION

SMARCB1-deficient sinonasal carcinomas are locally aggressive rare malignant tumors of the nasal cavity and paranasal sinuses. They represent only about 1% of total head and neck malignancies.^{1,2} SMARCB1-deficient sinonasal carcinoma is also called as integrase interactor-1 (INI-1) deficient carcinoma.^{2,3}

It was first reported in 2014 and was described as a subset of sinonasal undifferentiated carcinoma.^{1,2,4} Most of the cases are present lately when the condition is already locally aggressive at diagnosis. Probably, the reason for late diagnosis is due to the similarity of clinical symptoms to other benign conditions. As per our knowledge, only around 200 cases of SMARCB1 deficient sinonasal carcinomas have been reported so far in the medical literature and this is the first case that has been reported from Nepal.⁵

In this case report, we present a case of SMARCB1-deficient sinonasal carcinoma in a 54-year-old male with the lesion occupying the right ethmoid sinus and extending up to the right frontal sinus and nasal cavity.

CASE HISTORY/EXAMINATION

A 54-year-old male patient presented with a complaint of right-sided nasal obstruction of several months associated with occasional nasal bleeding and hyposmia. The family status of carcinoma was unknown.

METHODS

His laboratory findings were unremarkable. A non-contrast-enhanced computerized tomography followed by contrast-enhanced computed tomography scan of the paranasal sinus revealed an ill-defined soft tissue density lesion measuring 3.2x2.6x2.1cm in the right posterior ethmoid sinus extending up to the right frontal sinus and nasal cavity causing erosion of adjacent bones involving right fovea ethmoidalis, lateral lamella, vertical lamella and middle turbinate with an indistinct floor of right olfactory groove. Minimal mucosal thickening is noted in the right maxillary sinus. No definite intracranial or intraorbital extension was noted.

A preliminary diagnosis of right-sided sinonasal mass was made and the patient underwent endoscopic sinus surgery. Intraoperative findings include a friable mass occupying the ethmoid and frontal sinus and extending up to the nasal cavity and lamina papyracea dehiscence was also noted. The resected mass was then sent for histopathological examination. The patient was discharged on the first postoperative day with no complaints.

Histopathological examination revealed atypical cells arranged in papillary patterns, sheets, and clusters infiltrating into the fibrotic stroma. These atypical cells are basaloid and exhibit pleomorphism. Individual cells have a high nucleo-cytoplasmic ratio, hyperchromatic nuclei, few visible nucleoli, and a scant amount of cytoplasm. **(Figure 1)** Mitosis and areas of necrosis were seen. Tumor tissue was subjected to further immunohistochemistry (IHC) analysis showed tumor cells positive for CK5/6, EBV, CK, and P40 and negative for S-100. **(Figure 2a-2d)** INI showed loss of expression. **(Figure 3)** Based on the overall histomorphological features combined with the immunohistochemical profile, a final diagnosis of SMARCB1-deficient sinonasal carcinoma was made.

CONCLUSION AND RESULTS

Subsequently, concurrent chemoradiotherapy (CCRT) was started with an injection of Cisplatin 50mg IV weekly during radiotherapy. On follow-up magnetic resonance imaging(MRI) of the brain and the neck, the patient has no features of recurrence. So far, the patient has received six cycles of CCRT and currently is in stable condition.

DISCUSSION

Sinonasal tract carcinoma accounts for about 3-5% of total malignancies in the head and neck.⁶ SMARCB1 is a tumor suppressor gene which is located on chromosome 22q11. It is present in the nucleus of all normal cells and is responsible for the regulation of gene transcription and proliferation.⁷ SMARCB1 mutation is responsible for the pathogenesis of other malignancies, which include atypical teratoid and malignant rhabdoid tumors, epithelioid sarcoma, renal medullary carcinoma, myoepithelial carcinoma of soft tissue, epithelioid malignant peripheral nerve sheath tumor, and extraskeletal myxoid chondrosarcoma.^{2,8}

SMARCB1-deficient carcinoma commonly arises in the nasal cavity or ethmoid sinus. However, multiple sites are also frequently involved. The most common clinical presentations are nasal obstruction, headache, epistaxis, proptosis, or visual defects owing to the mass effect. Most of the cases present in the late T4 stage with the involvement of the bone, skull base, or periorbital invasion.⁹ Our patient presented with complaints of right-sided nasal obstruction for several months along with associated occasional nasal bleeding and hyposmia. The carcinoma is involved in the right posterior ethmoid sinus and right frontal sinus reaching up to the nasal cavity along with the erosion of adjacent bones involving right fovea ethmoidalis, lateral lamella, vertical lamella, and middle turbinate. Due to the clinical presentations similar to benign conditions such as allergic rhinitis, nasal polyps, and chronic sinusitis, the cases are identified at a late stage when the carcinoma is already locally aggressive and invasion of the bones owing to challenges in the complete surgical removal.⁵

Histomorphological examination of the SMARCB1-deficient sinonasal carcinomas shows round tumor cells and anastomosing nests of tumor cells which are separated by bands of fibrous stroma. The tumor cells have enlarged round nuclei with prominent nucleoli. The cytoplasm of tumor cells can be scant to abundant. In the tumor cells with scant cytoplasm, they have basaloid morphology; while other tumor cells have abundant, eccentric, eosinophilic cytoplasm depicting a rhabdoid appearance.² Tumors with the basaloid morphology are characterized by undifferentiated or “blue cell” tumors with high nuclear: cytoplasmic ratios, prominent nucleoli, scant cytoplasm, and sheet-like, nest-like, or palisading arrangements while the rhabdoid tumors are characterized by “pink cell tumors” with abundant eosinophilic cytoplasm and eccentric nuclei.^{1,2,9,10} In our case, tumor cells are arranged in papillary patterns, sheets, and clusters infiltrating into the fibrotic stroma. These tumor cells are basaloid in appearance and exhibit pleomorphism. Cells have a high nucleocytoplasmic ratio, hyperchromatic nuclei, few visible nucleoli, and a scant amount of cytoplasm. Mitosis and areas of necrosis seen.

On IHC analysis, tumor cells of SMARCB1 deficient sinonasal carcinoma are diffusely positive for pancytokeratin. Some cases of SMARCB1-deficient sinonasal carcinoma show diffuse p63/40 stains while neuroendocrine markers synaptophysin/chromogranin are positive in around 30% of cases. Tumor cells show loss of SMARCB1 (INI-1) expression while S100, SMA, calponin, CD99/NKX2.2, and NUT1 are usually negative.^{9,11,12} In our case, on IHC, the tumor cells are positive for CK5/6, EBV, CK, and P40 and negative for S-100 while INI-1 showed loss of expression. Differential diagnoses include Sinonasal undifferentiated carcinoma, NUT carcinoma, Myoepithelial carcinoma, and HPV-related multi-phenotypic sinonasal carcinoma:

The standard recommended treatment of potentially resectable disease for this condition is surgery followed by postoperative adjuvant RT or CCRT. However, some authors recommend that if there is >50% response to induction therapy then it is recommended to continue chemoradiation. But if there is < 50% response to induction chemotherapy, then surgery followed by chemoradiation is advised.^{5,13} Also, there have been different ongoing randomized clinical trials regarding the treatment modality of SMARCB1-deficient sinonasal carcinoma. One of the ongoing studies is the phase II clinical trials to investigate a specific EZH2 inhibitor therapy as a target therapy for SMARCB1-deficient cancers.¹⁴

Loss of SMARCB1(INI-1) expression has a poor prognosis compared with tumors in which SMARCB1

expression is retained.¹⁵ The rate of recurrence and mortality is also high in SMARCB1(INI-1)-deficient tumors. 5-year survival rate of these patients is only 34.9%.^{16,17} The reported distant metastasis is to the lungs, brain, pleura, bone, and liver.⁵

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FIGURE LEGENDS

Figure 1: Hematoxylin and Eosin stained section show sheets of undifferentiated atypical cells having high nucleo-cytoplasmic ratio, round to oval nuclei, conspicuous nucleoli and moderate cytoplasm.

Figure 2a: IHC shows tumor cells are positive for CK.

Figure 2b: IHC shows tumor cells are positive for P40.

Figure 2c: IHC shows tumor cells are positive for EBV.

Figure 2d: IHC shows tumor cells are positive for CK5/6.

Figure 3: IHC shows loss of expression of INI.







