Case Report

Sino nasal undifferentiated carcinoma: A rare entity

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Abstract

Malignant neoplasms of the paranasal sinuses and nasal cavity are rare, comprising only 3% of all head and neck malignancies. This includes both primary sinonasal neoplasms and metastatic disease. We present the case of a patient with a maxillary soft tissue swelling, which proved to be a rare malignant tumor of maxillary sinus origin, a sinonasal undifferentiated carcinoma

Key words: Maxilla, Sino-Nasal Undifferentiated Carcinoma, sinonasal undifferentiated carcinoma

INTRODUCTION

Sino-Nasal Undifferentiated Carcinoma (SNUC) is a rare malignancy first described by Frierson *et al.*, as an aggressive neoplasm that was clinico-pathologically distinct from other poorly differentiated malignancies of the nasal cavity and sinuses.[1,2] SNUC is believed to originate from schneiderian epithelium or from the nasal ectoderm of the paranasal sinuses.[1] SNUC typically presents as a rapidly enlarging tumor mass involving multiple (sinonasal tract) sites, often with an evidence of extension beyond the anatomic confines of the sinonasal tract.

Given the undifferentiated nature of this malignancy, however, immunohistochemical analysis is extremely helpful.[3] With the use of a panel of markers, positive staining for neuron-specific enolase and chromogranin, cytokeratins 7, 8 and 19, nonreactive to S-100 and non-expression of vimentin. These findings suggest that the tumor is of epithelial origin and lacks any evidence of neuroendocrine, muscle, melanocyte or leukocyte differentiation.[3,4] This allows proper classification of the tumor as an SNUC - a malignant tumor of the sinus (sinonasal) that is of epithelial origin (carcinoma), but lacks evidence of keratin production (undifferentiated).[3]

Since the initial recognition of SNUC as a distinct clinicopathological entity, treatment regimens have evolved to include the current recommendation of combined radial resection, radiotherapy and chemotherapy. Despite this aggressive therapy, outcome has remained dismal, with the mean survival time being less than a year after diagnosis.[5]

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CASE REPORT

A 63-year-old man came to the outpatient department of Saveetha Dental College and Hospital, Chennai with the chief complaint of pain and swelling in the left side of face since two months along with pain on mouth opening. He also gave history of nasal obstruction with occasional epistaxis. His past medical and surgical history is non-contributory. He had the habit of tobacco, betel nut chewing for the past eight years. He had also undergone uneventful extractions.

Extra oral examination revealed a diffuse swelling on the left side of the face, in the maxillary region. The left infraorbital region was tender on palpation. Intraorally an ulcerated proliferative growth was seen on the left alveolar maxillary region in 24-27 region along with obliteration of buccal vestibule. The surface of the growth was covered with necrotic tissue with pus discharge and bleeding [Figure 1]. Limitation of mouth opening along with bilateral ulceration, bleeding and crust formation at angle

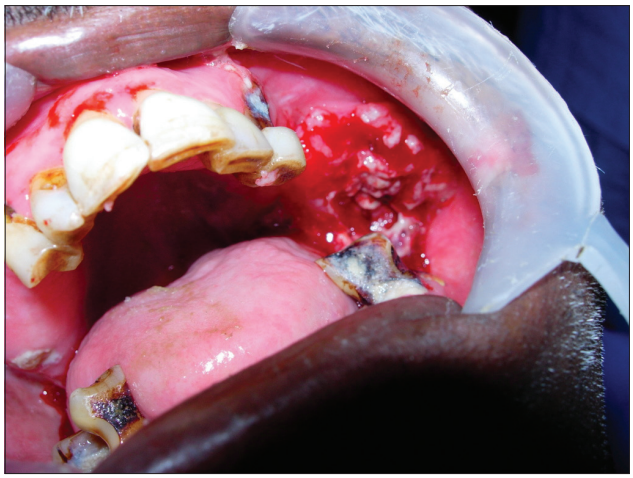

Figure 1: Clinical picture showing the ulcerated growth with bleeding

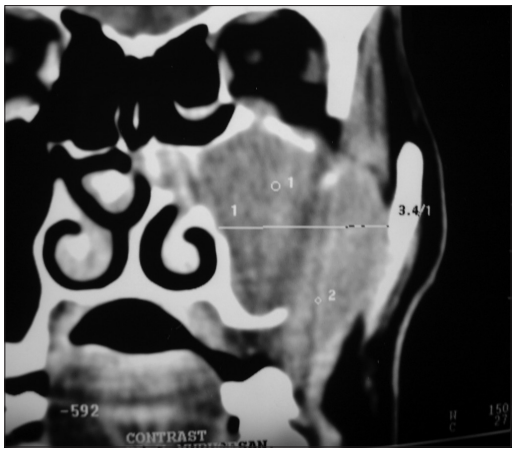

Figure 2: CT scan showing the expansile mass involving the maxillary sinus

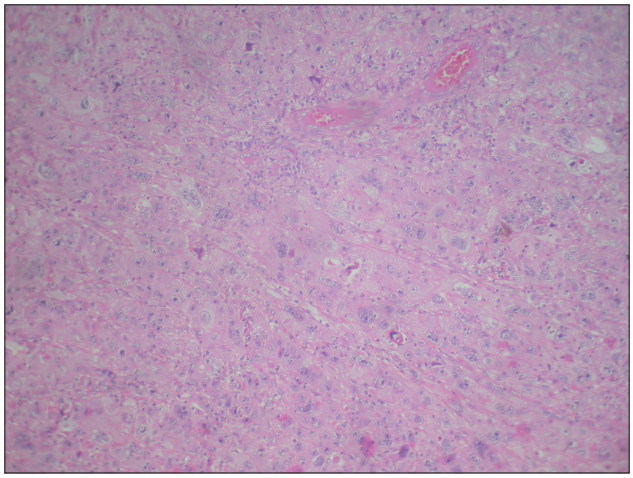

Figure 3: Pleomorphic undifferentiated epithelial cells in the form of nests and trabeculae separated by thin fibrous connective tissue septa (H&E, ×10)

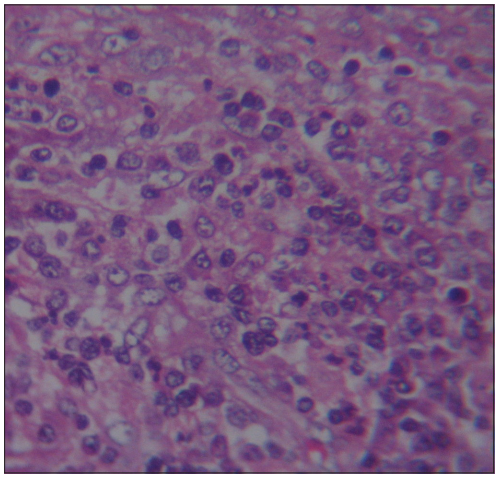

Figure 4: Photomicrograph showing large cells with pleomorphic nuclei (H & E, ×40)

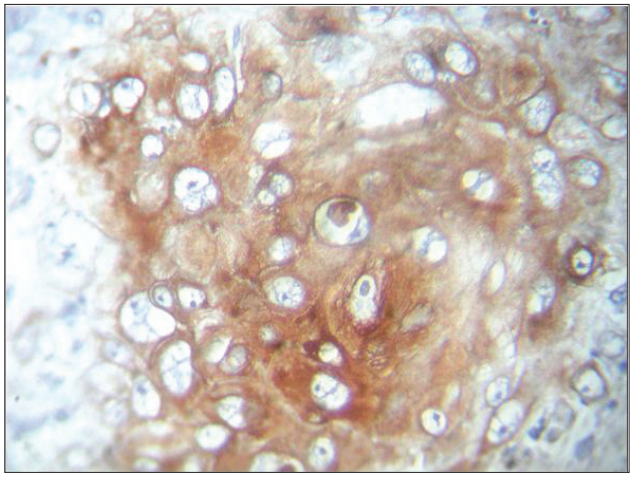

Figure 5: Photomicrograph showing positive reactivity to cytokeratin (×40)

of mouth was also observed. Generalized mobility of the teeth was also seen.

The OPG revealed a radiolucent area with bone destruction and obliteration of antrum on the left side. The CT scan revealed a huge enhancing lesion involving the entire left maxillary sinus causing erosion of its superior, medial, and postero-lateral walls, extending up to the nasal cavity, left ethmoid sinus and retro maxillary space [Figure 2].

Microscopic examination of the biopsy specimen revealed pleomorphic undifferentiated epithelial cells in the form of nests and trabeculae separated by thin fibrous connective tissue septa [Figure 3]. The cells were of variable size and shape, large cells with amphophilic cytoplasm with round to oval diffusely hyperchromatic nuclei with or without small nucleoli are seen interspersed with cells which have vesicular nuclei and prominent nucleoli [Figure 4]. Very few areas of squamous cells were appreciated along with areas of necrosis and increased mitotic activity.

Immunohistochemical assay revealed immunoreactivity of the neoplastic cells to cytokeratin (CK7,8,19) [Figure 5] and

epithelial membrane antigen. The tumor cells were negative for S-100, vimentin and neuroendocrine markers. Thus, the final diagnosis was Sinonasal undifferentiated carcinoma.

The patient subsequently underwent maxillectomy of the left maxilla including the zygomatic process, floor of orbit, ramus of mandible with supra-omohyoid neck dissection. The patient subsequently underwent radiation therapy and is now on a regular follow-up for the past one year.

DISCUSSION

SNUC is an uncommon, highly aggressive, and clinicopathologically distinctive carcinoma of uncertain histogenesis.[6] The etiology of sinonasal carcinomas is unknown. There may be an association with cigarette smoking or a previous history of radiation therapy. In contrast to nasopharyngeal carcinoma, an association with Epstein-Barr virus infection has not been demonstrated.[4]

The most common symptoms are nasal obstruction, proptosis, cranial nerve palsies, periorbital swelling, diplopia, epistaxis, and periorbital pain. The duration of symptoms for these cases varied from a few weeks to five months. These tumors are large, involved multiple paranasal sinuses, and produced marked destruction of sinus walls. Invasion of the orbital bones occurred in along with penetration of the cranial cavity, and spread to the nasopharynx.[1,2,7] Most of these features are consistent with the findings in our case.

The computed tomography (CT) and MRI features of SNUC are bone destruction and invasion of adjacent structures, including the anterior cranial fossa, adjacent paranasal sinuses, and orbits. Obstruction of adjacent sinuses was commonly noted.[1,8] Bone destruction and involvement of adjacent structures were evident in our case.[9]

When formulating a differential diagnosis for a swelling in proximity to the jaws, it is often helpful to determine first, by radiographic examination, whether the enlargement originates primarily in bone or in the extraosseous soft tissue. Common intraosseous expansile radiolucent lesions would include central giant-cell granulomas, developmental odontogenic cysts (dentigerous cyst, odontogenic keratocyst), as well as odontogenic tumours (ameloblastoma). When faced with an expansile radiopaque or mixed radiopaque–radiolucent intraosseous lesion, the possibility of a benign fibro-osseous lesion should be considered. An infection of odontogenic origin is the most common cause of a soft tissue swelling of the maxillary buccal vestibule. Less common reactive or neoplastic lesions of connective tissue origin, such as inflammatory myofibroblastic tumour, nodular fasciitis, myofibroma and desmoplastic fibroma should also be included in the differential diagnosis. Finally, the possibility of a malignant neoplasm of the maxillary antrum, although uncommon, should be considered.[3-5] The differential diagnosis of such neoplasms includes esthesioneuroblastoma, neuroendocrine carcinoma, rhabdomyosarcoma, lymphoepithelioma, lymphoma, melanoma, and poorly differentiated adenoid cystic carcinoma. They can be distinguished by their clinical, light microscopic, electron microscopic, and immunohistochemical features.[1,2,4] Immunohistochemistry is an important tool that can be valuable in reaching a diagnosis in such a situation.

The light microscopic features of SNUC include the presence of a hypercellular proliferation with varied growth patterns, including trabecular, sheet-like, ribbon, lobular, and organoid patterns. The tumor cells are medium to large sized and round to oval and have pleomorphic and hyperchromatic nuclei, inconspicuous to prominent nucleoli, varying amount of eosinophilic cytoplasm, high nuclear-to-cytoplasmic ratio, marked increase in mitotic activity frequently with atypical mitoses, tumor necrosis, and apoptosis.[7,10] Most of these histopathological findings were consistent with our case.

The presence of squamous cell differentiation would correlate to origin in the Schneiderian epithelium, thereby conferring an ectodermal derivation to these tumors. Adjunct analyses (e.g., immunohistochemistry, electron microscopy, and molecular biologic studies) are often required in the diagnosis of SNUC and in differentiating it from other undifferentiated malignant neoplasms.[2,3,6,10] In accordance with the literature, the immunostaining for cytokeratin 7,8 and 19 and EMA were documented in our present case.

Due to the small number of reported cases, the ideal treatment regimen has not been systematically evaluated. However, treatment generally involves surgical removal of the tumor. Patients with SNUC have a high rate of both local–regional recurrence and distant metastasis. Moreover, because of the complex anatomy of the head and neck area, complete removal of the tumor with wide margins is not always possible. The treatment of SNUC includes aggressive multimodality therapy, including surgical resection and adjuvant therapy (i.e., radiotherapy, chemotherapy). The prognosis associated with SNUC is poor, and death due to disease often occurs within short periods following the diagnosis. The optimal treatment is yet to be determined. It is important to recognize and differentiate this distinct tumor from other nasal tumors because of its aggressive behavior, since early intervention may result in a successful outcome.[5,9,10] Our patient had

undergone a combination treatment protocol comprising surgery and radiotherapy and is remaining disease free for the past one year and is on a regular follow-up.

In conclusion, we describe a rare case of SNUC of the maxillary sinus confirmed by IHC markers, who had undergone combination treatment protocol and remaining disease-free for the past one year.

REFERENCES

1. Frierson HF Jr, Mills SE, Fechner RE, Taxy JB, Levine PA. Sinonasal undifferentiated carcinoma: Aggressive neoplasm derived from schneiderian epithelium and distinct from olfactory neuroblastoma. Am J Surg Pathol 1986;10:771-9.
2. Franchi A, Moroni M, Massi D, Paglierani M, Santucci M. Sinonasal undifferentiatedcarcinoma, nasopharyngeal-type undifferentiated carcinoma, and keratinizing and nonkeratinizing squamous cell carcinoma express different cytokeratin patterns. Am J Surg Pathol 2002;26:1597-604.
3. Ejaz A, Wenig BM. Sinonasal Undifferentiated Carcinoma: Clinical and Pathologic Features and a Discussion on Classification, Cellular Differentiation, and Differential Diagnosis. Adv Anat Pathol 2005;12:134-43.
4. Jeng YM, Sung MT, Fang CL, Huang HY, Mao TL, Cheng W, *et al*. Sinonasal undifferentiated carcinoma and nasopharyngeal-type undifferentiated carcinoma: Two clinically, biologically, and histopathologically distinct entities. Am J Surg Pathol 2002;26:371-6.
5. Day TA, Beas RA, Schlosser RJ, Woodworth BA, Barredo J, Sharma AK, *et al*. Management of paranasal sinus malignancy. Curr Treat Options Oncol 2005;6:3-18.
6. Edwards PC, Hess SJ, Saini T. Sinonasal Undifferentiated Carcinoma of the Maxillary Sinus. J Can Dent Assoc 2006;72:163-7.
7. Kim B, Vongtama R, Juillard G. Sinonasal undifferentiated carcinoma: Case series and literature review. Am J Otolaryngol 2004;25:162-6.
8. Phillips CD, Futterer SF, Lipper MH, Levine PA. Sinonasal undifferentiated carcinoma: CT and MR imaging of an uncommon neoplasm of the nasal cavity. Radiology 1997;202:477-80.
9. Raja V, Campbell GA. Unusual Cases Involving the CNS and Nasal Sinuses case 2. sinonasal undifferentiated carcinoma. *J Clin Oncol* 2003;21:3877-80.
10. Danny J. Enepekides- Sinonasal undifferentiated carcinoma: An update. Curr Opin Otolaryngol Head Neck Surg 2005;13:222-5.

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