Sinonasal Undifferentiated Carcinoma: A Rare Entity

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ABSTRACT
Malignant tumors of sinonasal tract are rare, representing only 3% of head and neck cancers. Sinonasal undifferentiated carcinoma (SNUC) is a rare entity recently described by Frierson et al. in 1986. Many clinical and pathological aspects of this disease remain misunderstood. We report the case of 52-year-old male suffering from a rapidly fatal SNUC of the right nasal cavity. We tried to focus on the clinical and histological presentations of the disease, and we discussed the different possible treatment modalities, which are still guided by small retrospective studies. SNUC is a rare entity. Its management is challenging due to its local aggressive behavior and high propensity to metastasis. There is no evidence that aggressive therapy offers better survival. A better comprehension of the disease is necessary.

Keywords: Chemoradiation, Immunohistochemistry, Malignant tumor, Sinonasal tract, Surgery.

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INTRODUCTION
Malignant tumors of sinonasal tract are rare, representing less than 1% of all cancers and 3% of all upper aerodigestive tract cancers.1 Sinonasal undifferentiated carcinoma (SNUC) is a relatively rare entity specific to the nasal cavities and paranasal sinus. According to the World Health Organization, SNUC is defined as a highly aggressive and clinicopathologically distinct carcinoma of uncertain histogenesis composed of pleomorphic tumor cells with frequent necrosis and should be differentiated from other carcinomas or olfactory neuroblastoma. SNUC usually presents with vague symptoms, such as nasal obstruction, headache, and epistaxis for a short duration.2 Therefore 70–100% of tumors are T4 at presentation.3,4 Since it was first described by Frierson et al. in 1986,5 few cases of SNUC were reported; thus, management of these tumors is still unclear and guided by small series with small number of patients.6,7 Long-term survival rates are deceiving reaching 50% in the best cases.2

CASE DESCRIPTION
In June 2014, a 52-year-old painter sought medical consultation in Salah Azaez Oncology Institute, Department of Head and Neck Surgery, with unilateral epistaxis as chief complaint. Cluster pain of the right hemi-face and ipsilateral recent swelling were also reported. The patient was a heavy smoker, and only a benign prostatic hypertrophy in medical history has been noted. Clinical examination showed a right 2-cm paranasal swelling erasing the nasolabial fold, hypoesthesia in the right V2 territory, and an ipsilateral 2-cm cervical lymph node in the level II. Endoscopy found a fungating white formation filling the right nasal cavity. Computed tomography (CT) scan of the facial massif concluded a tissular process in the right nasal cavity respecting the floor and the palatine vault with a little invasion of the adjacent medial wall of the orbit. Two biopsies have been performed under local anesthesia. Histological examination coupled with immunohistochemistry (IHC) concluded SNUC with PS100-, cytokératine +, EMA +. Magnetic resonance imaging (MRI) showed a tissular process of right nasal cavity and the ethmoid with hyposignal in T1 and hypersignal in T2 with gadolinium enhancement (Figs 1 and 2). Chest CT scan showed a suspicious pulmonary node. The patient was classified T3N1M1 following the UICC TNM Classification 2009, 7th edition. Three cycles of SFU-CDDP chemotherapy were administrated to the patient. Evolution was marked by rapid growth of the facial swelling complicated with blindness in an interval of 2 months. Flash irradiation in an analgesic purpose was administrated. The patient died after several months after a cataclysmic bleeding.

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**Fig. 2:** T2-gadolinium-enhanced MRI coronal section showing a nasal right process infiltrating the ethmoid with retention image in the ipsilateral maxillary sinus

**Discussion**

In 1986, Frierson et al. reported the first SNUC series, including eight patients all with advanced disease with orbital and cranial extension, all were treated with chemoradiation therapy. Only three patients were alive after 1 year. Since then, fewer than 200 cases were reported in the literature. Recently, Kuo et al. reported 435 cases in a multicenter American review. This is to our knowledge the largest cohort ever reported. Worthy improvements in the management of SNUC were achieved, but many clinical and therapeutic features are still unclear. In addition to its uncertain histogenesis, the etiology of SNUC is to date unknown. The role of cigarette smoking and previous radiation therapy was not demonstrated. Unlike undifferentiated nasopharyngeal carcinoma (UCNT), it seems that there is no correlation between SNUC and Epstein Barr virus (EBV).

Males are more affected by the disease than females, with broad age range. According to Kuo et al., there was more males with a sex ratio near to 1.7, age range between 18 years and 85 years, and half of patient were younger than 55 years.

For a short duration, symptoms are vague, such as nasal obstruction epistaxis and headache. Therefore, 70–100% are staged T4 at presentation, and 10–30% had metastatic cervical lymph nodes. According to an American review by Caroline C Xu et al., headache and neurologic symptoms are present in 45% of cases and epistaxis in 25%. The same review reports 42.3% of patient had orbital involvement at diagnosis. In our case, cluster trigeminal pain, headache, and epistaxis, concomitant to the paranasal swelling, were present at the first consultation with a cerebral node metastasis. A distant metastasis in the lung was identified which classifies the patient as stage IV according to the TNM classification.

Histological examination coupled with IHC is necessary for the diagnosis. The immunostaining for the cytokeratine 7, 8, and 19 and the EMA, like in our case, is documented in the literature.

Imaging is fundamental in dealing with malignant tumor of sinonasal tract. While CT scan is very contributive in highlighting bone destruction, MRI is interesting in studying extension to soft part. Tumor limits visible in CT scan are correlated in only 78% of cases to surgical and histological findings. These correlations reach 94% with MRI and 98.4% with gadolinium-enhanced MRI. Imaging is necessary in diagnosis, staging, and follow-up.

According to Kuo et al., SNUC is difficult to treat for many reasons including, advanced stage at presentation, proximity to critical structures, and rarity. No ideal treatment strategy has been systematically evaluated due to the small number of reported cases. Most authors recommend an aggressive therapy to eradicate the diseased tissues. Surgery, when possible, is indicated. It consists usually of mutilating craniofacial resection with maxillectomy, orbital exenteration, and occasionally neurosurgical involvement. Neoadjuvant chemotheraphy associating cyclophosphamide, doxorubicin, and Vincristine, followed by surgical resection and postoperative or preoperative radiotherapy, is the most common regimen described in the literature. According to Musy et al., these tumors are no longer surgical if one or many of the following structures are involved: cavernous sinus, infratemporal fossa, the brain, or the orbital cone bottom. Systematic irradiation of the cervical lymph node compartments for N0 patients is recommended by some authors due to the disease aggressiveness. The 5-year survival rates are low. According to Kuo et al., the cumulative 5-year survival rate was 41.5%. Close survival rates were found in other series. Surgery associated with chemotherapy or chemoradiation therapy is correlated with the best survival rates in univariate and multivariate analysis according to the same authors. No chemotherapy regimen has been selected as specific to the management of the SNUC. Docetaxel + 5-fluorouracil (5-FU) + cisplatin (TPF), cisplagine + 5-FU (PF), cisplagine + Taxotere, and cisplagine alone were used.

In our case, a palliative chemotherapy was administrated to the patient due to the distant pulmonary metastasis.

**Conclusion**

SNUC is a rare tumor of sinonasal tract with uncertain histogenesis. It remains challenging due to its aggressive local behavior and its high propensity to regional and distant metastasis. Only small retrospective series of patients were reported in the literature making the management of this disease unclear. There is no evidence that aggressive therapy offers better survival. Therefore, a better comprehension of the disease and the search of new modalities for the treatment is necessary.

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