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REPORT



Sinonasal undifferentiated carcinoma with metastasis to the extradural spine

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ABSTRACT

Sinonasal undifferentiated carcinoma (SNUC) is a rare and aggressive cancer of the sinonasal tract and is often characterized by intracranial invasion. However, SNUC rarely metastasizes to the spine. In this paper, we present a case of extradural metastasis and invasion of the adjacent spine by SNUC. A 42-year-old man presented to our hospital with two-month history of anosmia and nosebleeds. Imaging studies showed a neoplasm of the ethmoid sinus with extension into the anterior cranial fossa. The patient underwent resection of the carcinoma and began chemoradiotherapy. After completing chemoradiotherapy the patient complained of neck pain radiating down the right arm, and imaging showed an extradural mass at the C5 vertebral level. The patient underwent laminectomy for debulking of this tumor. One month later, the patient complained of recurrent weakness and pain in the right shoulder and arm. Imaging showed an extradural tumor wrapping around the C7 and C8 nerve roots, as well as a separate tumor at C2 adherent to the dura. The extradural tumor at C2 was surgically resected. Further imaging showed multiple new soft tissue masses at the thoracic level. We present a case of SNUC metastasis to the extradural spine representing the second case reported in the literature. Peri-dural metastasis and resulting symptoms should be included in the differential diagnosis and assessment of patients with SNUC.

ARTICLE HISTORY

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Extradural; SNUC; sinonasal
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Case

A 42-year-old Caucasian man experienced sudden anosmia and nosebleeds, which he initially attributed to seasonal allergies. When these symptoms did not subside after two months, he referred himself to our hospital. Computed tomography (CT) showed a large nodular mass extending from the superior nasal cavity to the skull base with erosion of the anterior skull base and cribriform plate. Magnetic resonance imaging (MRI) showed a 5 × 4 cm neoplasm of the ethmoid sinus with extension into the cranium through the cribriform plate (Figure 1). Biopsy and histopathological examination resulted in the diagnosis of sinonasal undifferentiated carcinoma (SNUC). A positron emission tomography (PET) scan on day +20 showed no metastasis and the tumor was surgically resected on day +40. The patient underwent chemoradiotherapy and a subsequent surgery for a cerebrospinal fluid (CSF) leak on day +74. After completing chemoradiotherapy, the patient presented with neck pain radiating down the right arm. A PET scan post-treatment on day +206 showed fluorodeoxyglucose (FDG) uptake along the superior margins of the ethmoid sinus, as well as at the area of the C6 spine (Figure 1H). MRI on day +213 showed a 0.4 × 1.4 × 2.7 cm extradural lesion at C5-C6, correlating with exam findings. Day +256 MRI showed an increasing size of the C5-C7 lesion (Figure 1E & F). There was also a new lesion adherent to the dura at C2. The extradural lesion at C6 was debulked with laminectomy and instrumented fusion on day +262 but was histologically indeterminate. About a month after the surgery, the patient began

experiencing increasing weakening and radicular pain in the right shoulder and arm. Subsequent imaging showed a progressive extradural mass at C5-T1. The tumor doubled in size with complete engulfment of the C7 and C8 spinal nerve roots. The patient presented with 0/5 strength in the right triceps with 3/5 grip strength. There was also enlargement of the C2 lesion. On day +302 the patient underwent a re-exploration of the cervical laminectomy site to decompress the affected nerve roots with post-operative improvement in arm strength. Pathology was reported at this time as metastatic, poorly differentiated carcinoma with identical cell morphology to the previous ethmoid SNUC resection specimen. On day +306, MRI showed multiple new extradural masses in the thoracic spine at T7-T8 and T9-T10. The patient underwent further chemoradiotherapy for the new metastases.

Discussion

SNUC is an aggressive neoplasm of the nasal cavity and paranasal sinuses, often diagnosed in patients with sinonasal obstruction, epistaxis and facial pain. Patients may have neurocognitive or cranial nerve involvement, given the tumor's propensity to locally invade the cranial cavity; however, distant metastasis is a rare occurrence. Because of the rarity of spinal cord metastasis of SNUC, a treatment protocol for such patients has not been established. Further, it is critical to recognize the clinical signs and symptoms of spinal cord or nerve compression that can be secondary to metastasis of SNUC due to the proximity of the original tumor to the central nervous system (CNS).

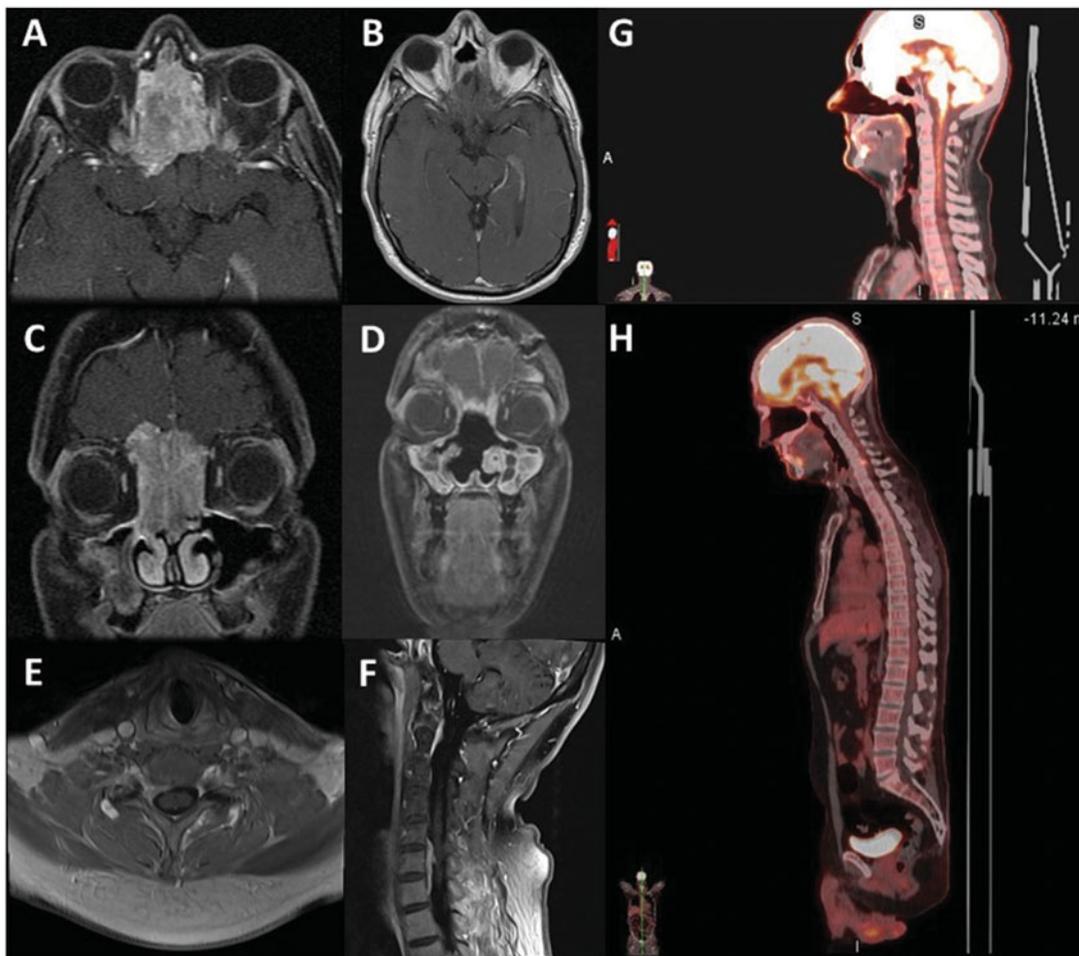


Figure 1. Radiological progression of SNUC metastasis. Contrasted axial (A, B) and coronal (C, D) T1 MR images of the nasal tumor at presentation and after resection by otolaryngologist. Contrasted sagittal T1 flair (E) and contrasted axial T1 VIBE (F) MR cervical spine images through C6 showing tumor prior to spinal surgery. PET images negative (G) for metastasis at initial nasal tumor diagnosis but present (H) at C6 obtained by otolaryngologist after development of radicular symptoms.

In this paper, we document a case of extradural spine metastasis of SNUC and the first to the cervical spine ever reported in the English literature, as determined by review of PubMed results from relevant search terms. The initial clinical presentation was typical of SNUC. Most patients with SNUC will present with symptoms resulting from cranial nerve and orbital involvement of the mass.¹ SNUCs are typically large tumors that invade the surrounding cranial structures, as observed in this case.² While SNUC is a rare malignancy, metastasis to the spinal cord is extremely uncommon. It is common, however, for SNUC to interact with the dura due to intracranial extension of the primary tumor.³ There have only been a handful of documented cases of SNUC metastasis to the intradural spinal cord. Ghosh *et al.* presented a novel case of intradural extramedullary metastasis of SNUC to the spinal cord.⁴ They concluded that dural violation by the original neoplasm lead to distant metastases through seeding of the CSF.⁴ A similar case of SNUC leptomeningeal carcinomatosis was also reported, but implicated CSF seeding as the probable cause of the metastasis.⁵ Indeed, the interaction of the tumor with CSF is of clinical concern and can lead to intradural metastasis, but it would likely not explain an extradural metastasis as is presented in this case. By our search, there is only one other case of extradural metastasis of SNUC reported in

the English literature. In that case, a compressive thoracic tumor was identified, and the mechanism of spread was hypothesized to be via venous dissemination through the valve-less Batson's paravertebral, epidural plexus but histopathology was not presented.⁶

SNUC is diagnosed by histopathological examination. Grossly, these tumors are usually larger than four centimeters with fungating, ill-defined margins. Invasion into adjacent structures and anatomic compartments with bone destruction is common. Histologically, the tumor is characterized by a sub-mucosal cellular proliferation with lobular and trabecular growth patterns predominating. The cellular infiltrate consists of polygonal medium- to large-sized cells with a high nuclear-to-cytoplasmic ratio, eosinophilic cytoplasm, and well-defined borders. The nuclei can be hyperchromatic or vesicular with variably prominent nucleoli. SNUCs have a high mitotic rate with prominent confluent tumor necrosis and individual cell apoptosis. As seen in our case, lymph-vascular and perineural invasion are common.⁷ These tumors are consistently positive for neuron specific enolase.⁸ About 50% of cases will also express epithelial membrane antigen.⁷ We present here the histopathological features of this SNUC tumor (Figure 2) from the original resection specimen (day +8) and the cervical spine metastasis (day +302).

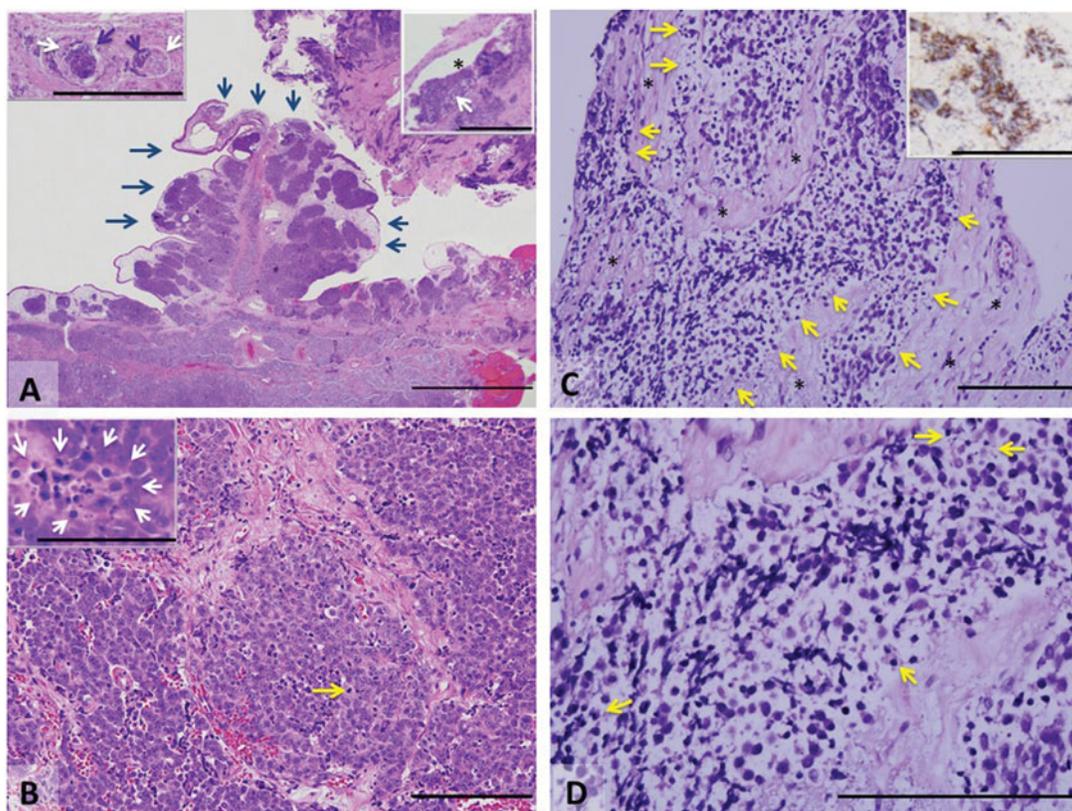


Figure 2. Histopathological characteristics of sinonasal undifferentiated carcinoma (SNUC). Images A–B are from the original resection specimen and images C–D are from the extradural spinal metastasis. A. Respiratory epithelium infiltrated by a lobular and trabecular growth pattern of medium sized polygonal cells with round, hyperchromatic nuclei, prominent nucleoli, and eosinophilic cytoplasm, creating a polypoid growth protruding from the respiratory mucosa (blue arrows). These tumors frequently invade nerves and vascular channels as seen in the two photo insets. The top left photo inset is of two nerves (white arrows) with perineural and endoneurial invasion by tumor cells (purple arrows) and the top right photo inset is a vessel (asterisks) with tumor cells attached to the vascular wall (white arrow). [Objective = 20×; left photo inset objective = 100×; right photo inset objective = 40× scale bars = 2 mm] B. SNUCs are aggressive tumors with rapid growth that quickly outgrow their blood supply as evidenced by prominent tumor necrosis and numerous mitotic figures. The yellow arrow highlights one of the mitotic figures in metaphase. Tumor necrosis is highlighted in the photo inset illustrating a cluster of apoptotic/pyknotic nuclei (white arrows) [Objective = 200×; photo inset objective = 400×; scale bars = 2 mm] C. Trabecular growth pattern of metastatic tumor cells (yellow arrows) with eosinophilic cytoplasm infiltrating the fibroconnective tissue of the spinal dura (asterisks). The inset is a cyto keratin immunohistochemical stain, CAM 5.2. The tumor cells express CAM 5.2 as evidenced by the brown nuclear staining in the neoplastic cells. The staining pattern is consistent with a SNUC. [Objective = 100×, photo inset objective = 100×; scale bars = 2 mm] D. Metastatic tumor cells within the spinal dura. The metastatic tumor cells have similar characteristics to the primary tumor with medium sized neoplastic cells, a high nuclear to cytoplasmic ratio, hyperchromatic nuclei, and eosinophilic cytoplasm. Areas of tumor necrosis are seen as evidenced by apoptotic nuclei (yellow arrows). [Objective = 400×; scale bar = 2 mm]

Therefore, we speculate that lymph-vascular invasion of tumor cells is the mechanism of extradural metastasis. Atypical SNUC metastasis should be considered in cases of advanced SNUC, especially when patients demonstrate radicular pain and other symptoms of a spinal cord lesion. Tumors may develop quickly and surgery for preservation of neurologic function may be necessary.

Disclosure statement

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