Monophasic Synovial Sarcoma of the Ethmoid Sinus: An Uncommon Differential of a Nasal Mass.

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Abstract

Sino-nasal synovial sarcomas are rare mesenchymal tumors, with most reports describing those arising primarily from the paranasal sinuses. Very few have been described with an extension to the nasal cavity. Due to a range of non-specific symptoms and local aggressiveness, there tends to be confusion in diagnosis. Here we describe a case of primary sino-nasal monophasic synovial sarcoma, diagnosed by histopathology and treated by excision and adjuvant chemoradiotherapy. On follow-up, the patient remains symptom-free to date for over two years. A wide range of diagnoses should be kept in mind for nasal masses since all tissue types coexist in this region. Initial definitive surgical excision can be considered a prudent plan of management in very limited nasal sarcomas confined to one or two paranasal sinuses.

Introduction

The nasal cavity and the paranasal sinus system are a subsite under the otolaryngologists' field of work with extreme heterogeneity in tissue structure. A wide variety of pathologies can arise from the nasal cavity owing to the range of epithelial, mesenchymal, glandular, neuroectodermal, and bony components that comprise the anatomy of this region (1). Synovial sarcomas (SS), in general, are known to comprise 5–10% of all soft tissue sarcomas. The head and neck region is the second most common site of involvement after the extremities (2). SS of the paranasal sinuses is extremely rare, with few isolated reports in the literature. Here we present a case report of a monophasic synovial sarcoma, with an atypical clinical picture, which was initially treated with surgical excision, followed by adjuvant chemoradiotherapy.

Case Description

A 63-year-old female, a known diabetic on adequate therapy, presented to the ENT outpatient clinic with the primary complaints of left-sided nasal obstruction for the past three months. It was associated with left-sided nasal discharge for two weeks. It was mucoid, non-purulent, and non-blood stained. There was no antecedent history of any breathing difficulty or any visual complaints. There was no history of pain, cheek numbness, blood-stained nasal discharge, or loosening of teeth.

On clinical examination, there was no apparent distortion of the external osseocartilaginous nasal framework. Facial symmetry was maintained with no obliteration of the nasolabial groove. On anterior rhinoscopy, a red polypoidal mass was visualized occupying the entire left nasal cavity, pushing the nasal septum to the right, and reaching the floor of the cavity. It was insensitive to touch. On probing, the mass did not bleed and appeared to be attached to the lateral wall of the nasal cavity. There was no extension to the nasopharynx. All cranial nerves appeared intact. There was no obvious palpable cervical lymphadenopathy. Visual, dental, and systemic examinations were unremarkable.

After the initial blood workup, the patient underwent a contrast-enhanced computed tomography scan (CECT) of the nose, paranasal sinuses, orbit, and neck. It depicted a well-defined 3x3x2cm enhancing soft tissue density in the left nasal cavity and the anterior ethmoids, with some extension to the posterior ethmoids. The growth was abutting the medial wall of the left maxillary sinus and the orbit with no apparent bone erosion (**Figure 1a**). It obstructed the drainage of the left frontal recess (**Figure 1b**). A subsequent contrast-enhanced magnetic resonance imaging (MRI) showed a T2 intermediate intense irregularly enhancing lesion in the left ethmoid sinuses, with no intracranial extension (**Figure 2**).

Keeping in mind the age and the clinical presentation of the patient and the endoscopic appearance, the following diagnoses were broadly considered.

1. Epithelial malignancy of the nasal cavity: Squamous cell carcinoma remains the first differential because it is more common. Squamous cell carcinoma comprises almost 50% of all sinonasal tumors in general (3).
2. Adenocarcinoma was a possibility keeping in mind the age of the patient.
3. Inverted papilloma of the nasal cavity: Also known as Schneiderian papilloma, it is a benign, locally aggressive tumor with malignant potential. Histopathology provides the mainstay of diagnosis, showing the invasion of the epithelium into the stroma.
4. Fibrosarcoma, leiomyosarcomas, and schwannomas were considered due to the preliminary spindle cell histopathology.

A diagnostic nasal endoscopy under local anesthesia revealed the mass attached to the middle turbinate, with dilated vessels on the surface (**Figure 3**). An endoscopically guided biopsy was undertaken, which was reported as spindle cell morphology with nuclear atypia, possibly a sarcomatous lesion.

The case was discussed in the multidisciplinary tumor board meeting and due to the limited nature of the disease, a primary surgery, followed by adjuvant chemoradiotherapy was planned. The patient was offered endoscopic excision under general anesthesia. The red fleshy mass was visualized occupying the middle meatus on the left. Partial middle turbinectomy was done. Middle meatal antrostomy and anterior ethmoidectomy were done using a microdebrider, sparing as much of the nasal mucosa as possible. The tumor mass was seen to be arising from the ethmoid sinuses. Bleeding was encountered which was controlled with nasal packing and bipolar diathermy. The mass was removed and sent for histopathology. Routine postoperative care was administered.

The patient was discharged a day after the procedure with antibiotics and instructions on nasal douching. Post-operative histopathology showed spindle-shaped tumor cells arranged in fascicles with nuclear atypia and hyperchromatism. Blood vessels were found interspersed within the lesion (**Figure 4a, 4b, and 4c**). Immunohistochemistry was positive for nuclear TLE-1 and bcl-2 (**Figure 5a and 5b**) and was negative for EMA and CD34 (**Figure 6a and 6b**). Thus, melanoma and epithelial tumors were ruled out. A tissue diagnosis of monophasic synovial sarcoma was thus finalized. She was referred for adjuvant chemoradiotherapy. She received intensity-modulated radiotherapy of 66Gy in 33 fractions to the nasal

cavity and the surrounding tissues along with palliative two agent chemotherapy with Doxorubicin and Ifosfamide throughout her treatment. She remains symptom-free on follow-up of two years.

Discussion

Synovial sarcomas (SS) of the nose and paranasal sinuses are misnomers in the true sense as they are undifferentiated carcinosarcomas arising from mesenchymal tissues, with no connection to synovial membrane or joints (4). They are so named only due to the morphologic similarity with normal synovial membrane, because of the presence of epithelial and stromal cells. These are considered high-grade malignant tumors. 5–12% of all SS have been reported in the head and neck region (5). Only isolated reports of sinonasal SS exist. Comprising less than 0.1% of all soft tissue malignancies, SS of the nose and paranasal sinuses are rare, with no clear-cut consensus regarding treatment options (6).

A wide range of non-specific clinical features is associated with this tumor. Nasal obstruction, pain, and epistaxis are similar to any other malignancy arising from the nasal cavity. Locally aggressive spread results in epistaxis, orbital invasion, and skull base erosion. A limited number of published reports mention a gradually enlarging mass of the sinuses which caused erosive effects on the surrounding bone. This causes a diagnostic dilemma pre-operatively due to similar presentations seen in primary epithelial malignancies.

Synovial sarcomas are a heterogeneous group of tumors with two types of tissues histologically: Spindle cells and epithelial components. Monophasic fibrous (MFSS) is one out of four subtypes of SS, the others being monophasic epithelial (MESS), biphasic, and poorly differentiated (7). The classification is based on the relative proportions of the two types of tissues present in the tumor. Immunohistochemistry of the excised mass plays an important role in diagnosis, although no specific markers exist for confirmation. Cytogenetic analysis and molecular diagnosis help to differentiate the rarer monophasic fibrous type from other sarcomas. Synovial sarcomas are usually positive for epithelial membrane antigen (EMA), S-100, vimentin, cytokeratin, and bcl-2, showing a mixed immunoreactivity.

The patient's histopathology depicted spindle-shaped tumor cells arranged in tight fascicles with minimal intervening stroma. Nuclear atypia with hyperchromatism and scanty cytoplasm is suggestive of the fibrous type, rather than the epithelial type. It is usually non-reactive to CD34 and CD31 (7). Synovial sarcomas, in general, arise due to the balanced chromosomal translocation $t(X;18)$, producing SYT-SSX, responsible for the malignant proliferation. Diagnosis of this chimeric gene by fluorescent in-situ hybridization (FISH) or reverse transcriptase-polymerase chain reaction (RT-PCR) is considered the gold standard for diagnosis of SS of any subsite (8). For poorly differentiated SS, this helps confirm the diagnosis along with routine histopathology. FISH/RT-PCR was not performed in our case.

Transducin-like- Enhancer of split-1 (TLE-1) has also been identified as a consistent and reliable marker of synovial sarcomas in particular. TLE-1 specifically differentiates SS from other spindle cell tumors such as malignant peripheral nerve sheath tumors (MPNST) which can also arise in the region of the nose and sinuses (8). Ultrastructural electron microscopic studies are contributory for diagnosis,

depicting tightly bound spindle cells in a hypocellular stroma, surrounded by collagen fibrils (9). In our case, strong nuclear positivity was obtained after epithelial and mesenchymal antigens were suggestive of SS.

After a nasal endoscopy and radiologic investigations, a prudent surgical plan of management usually consists of wide local excision of the mass with an adequate margin according to standard practice. This often proves difficult for primary tumors arising within the nasal cavity as the benefit of wide surgical clearance has to be weighed against functional and peri-operative complications. An endoscopic approach is preferred due to cosmetic reasons. Limited tumors can be resected with the addition of postoperative radiotherapy (10). Definitive proof of its efficacy in reducing recurrence or distant metastases is yet to be obtained. A longer period of follow-up is recommended for obtaining concrete evidence of the efficacy of definitive therapy. Both neoadjuvant and adjuvant chemotherapy has shown benefit (5), causing a clinically significant reduction in locally aggressive tumors. The approach of primary surgery was adopted in our case keeping in mind the limited extent of the disease, with no breach of orbital or maxillary compartments. A conservative approach towards surgery can be considered in such cases, although further studies are warranted in this direction.

Conclusions

Sarcomas are difficult to treat and defining operative margins is challenging within the nasal cavity. The case is significant as sino-nasal SS has rarely been described in the sixth decade, with a majority of cases seen in the second to third decade. There is a need for further reporting and research of such rare tumors to formulate a definitive plan for a cure. There exists only empirical evidence of adjuvant chemoradiotherapy. Surgery could be considered the primary modality for treatment. Difficulty in obtaining margins for oncological safety could be a cause of residual disease. Molecular cytogenetic analysis and immunostaining are the cornerstones for the diagnosis of such rare tumors. Generation of unfixed tissue samples should be prioritized during the surgical excision of suspected sarcomatous nasal masses.

Declarations

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest regarding the publication of this article.

Conflicts of interest

All authors have declared that there is no conflict of interest among them.

Ethical approval

All procedures performed in studies involving human participants were by the ethical standards of the institutional and/or national research committee, and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent

Informed consent was obtained from all the individuals involved and included in the study.

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Figures

Figure 1

Pre-operative CECT axial section (Figure 1a) and coronal section (Figure 1b), depicting the heterogeneously enhancing mass within the nasal cavity and the ethmoid sinuses. The black star denotes the mass in both Figure 1a and 1b.

Figure 2

Pre-operative MRI T2 weighted image in coronal view depicting the tumor as an intermediate intense mass. The black arrow depicts the mass. The black star depicts an incidentally detected mucus retention cyst in the right maxillary sinus.

Figure 3

Pre-operative diagnostic nasal endoscopy image depicting the suction tip in contact with the nasal mass. Dilated veins over the surface of the mass are marked with the black arrow. The black star denotes the middle turbinate. The nasal septum medially is marked by the black circle.

Figure 4

Photomicrographs stained with hematoxylin and eosin. Figure 4a depicts a highly cellular tumor with overlying stratified epithelium (40x magnification). Figure 4b shows tumor cells arranged in fascicles and sheets (100x magnification). The blue arrowhead in Figure 4c shows plump spindle-shaped cells with hyperchromatic nuclei (400x magnification).

Figure 5

Photomicrographs of immunohistochemistry stained with diaminobenzidine (DAB). Figure 5a depicts strong positivity with bcl-2 (DAB 100X magnification). Figure 5b shows strong nuclear positivity with TLE-1 (DAB 200x magnification).

Figure 6

Photomicrographs of immunohistochemistry stained with diaminobenzidine (DAB). Figure 6a shows tumor cells negative for EMA (DAB 100x magnification). Figure 6b depicts tumor cells staining negative for CD 34 (DAB 100x magnification).

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