

TITLE: Neoplasms of the Nose and Paranasal Sinuses

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Neoplasms of the paranasal sinuses are very rare, comprising less than 3% of all aerodigestive tract tumors. Nasal cavity cancers account for only a fraction of these tumors. Symptoms of nasal cavity and paranasal sinus tumors are similar to those of common benign disorders, such as chronic rhinosinusitis, causing a delay in diagnosis. Tumors of the nasal cavity are approximately evenly divided between benign and malignant neoplasms; inverting papilloma is the most common benign tumor and squamous cell carcinoma is the most common malignant tumor. In contrast, most paranasal sinus tumors are malignant with squamous cell carcinoma being the most common.

Survival analysis of these tumors is lacking due to the fact that 1) they are infrequent, which requires long periods of time for institutions to collect enough data to study, 2) there are many different histologic tumor types that are encountered within the nasal cavity and paranasal sinus, and 3) there is a lack of a universally accepted staging system for malignant nasal cavity tumors.

Due to the advanced stage at time of presentation, multimodality treatment has been the mainstay of therapy. Recent studies of selective orbital preservation are proving that under certain circumstances, orbital preservation is both oncologically and functionally acceptable. The advancements in endoscopic sinus surgical techniques have also opened new surgical approaches to primary and adjunctive treatments of both benign and malignant lesions.

Epidemiology

Malignant tumors of the nasal cavity and paranasal sinuses occur predominately in the 5th to 6th decade. They are most commonly found in whites, with the incidence in males being twice that of females. Exposure to industrial fumes, wood dust, nickel-refining processes, and leather tanning have been implicated in the carcinogenesis of certain types of sinonasal malignant tumors. Other industrial exposures associated with an increased incidence of sinonasal cancer include mineral oils, chromium, lacquer paint, soldering and welding. Cigarette smoking and heavy alcohol consumption have long been known to increase the risk of head and neck malignancy, but no significant association has been shown with sinonasal cancers.

The maxillary sinus is the most commonly involved location (70%), with the ethmoid sinuses as the second most common (20%). The sphenoid sinus (3%), and the frontal sinus (1%) are the least common locations for primary tumors.

Diagnosis

The diagnosis of sinonasal malignancies is challenging. Not only are they rare, but they are difficult to distinguish from their benign counterparts. Benign sinonasal disorders account for a significant proportion of visits to the otolaryngologist. The similarities of benign and malignant disorders at initial presentation leads to a significant delay in the diagnosis of malignancy. It is estimated that a span of 6 to 8 months passes on average from the time of initial symptoms until diagnosis is established. Key indicators of malignancy such as cranial neuropathies and proptosis are uncommon at initial presentation and signify advanced disease. A high index of suspicion must be maintained for patients who do not respond to medical treatment of their sinonasal symptoms.

Signs and symptoms of maxillary sinus carcinoma fall into several major categories: oral, nasal, ocular, facial, and auditory. Oral presentations occur in 25-35% and include pain involving the maxillary dentition, trismus, palatal and alveolar ridge fullness, and frank erosion into the oral cavity. Nasal findings are seen in up to 50% of patients and include obstruction, discharge, stuffiness, congestion, epistaxis, and extension into the nasal cavity. Ocular findings occur in approximately 25% and arise from upward extension into the orbit, where unilateral tearing, diplopia, fullness of lids, pain, and exophthalmos are seen. Facial signs include infraorbital nerve hypesthesia, cheek swelling, pain, and facial asymmetry. Auditory complaints include hearing loss secondary to serous otitis media due to nasopharyngeal extension.

Any suspicious lesions noted on nasal endoscopy should be biopsied with attention given to their bleeding potential. Radiologic imaging should be considered prior to biopsy to prevent distortion of tumor margins and to assess for vascularity and possible intracranial connection. Maxillary sinus masses should be biopsied via nasoantral windows or antrostomies so that that any future maxillectomy will remove the biopsy site. Anterior antrostomies should be avoided due to the oncologic feasibility of seeding the gingivobuccal sulcus and cheek skin with tumor.

Radiography

Radiographic studies are essential as the full extent of a sinonasal neoplasm cannot be established even with modern endoscopic technology. Plain radiographs are rarely used and have been replaced by computed tomography (CT) and/or magnetic resonance imaging (MRI) as the initial studies performed. These complementary studies assist in the evaluation of patients who have a malignancy of the nasal cavity or paranasal sinuses and are the most effective way to delineate the extent of tumor extracranially and intracranially.

The true value of CT scanning is its ability to detect bone erosion. Key areas include the bony orbital walls, cribriform plate, fovea ethmoidalis, posterior wall of the maxillary sinus, pterygopalatine fossa, the sphenoid sinus, and the posterior table of the frontal sinus. Despite the significant amount of information that can be gained from CT, it has certain limitations: it

cannot always determine whether tumor has invaded or just approached the periorbita and it is difficult to differentiate tumor from soft tissue swelling and secretions because of their similar densities. Contrast administration offers only marginal assistance with these two dilemmas.

MR imaging provides excellent delineation of tumor from surrounding inflammatory tissue and secretions within the sinuses. This, along with its multiplanar ability and lack of radiation exposure gives advantage to MRI in evaluation of these lesions. Typically, edema of inflamed tissue and retained secretions would be of low intensity on T1 and high intensity on T2 secondary to increased water content. However, because of the often chronic nature of these secretions at the time of diagnosis a certain amount of free water will have been absorbed and a variable pattern of intensity may be seen. On the other hand, 95% of sinonasal tumors are highly cellular with less water content giving low to intermediate signal intensity on both T1 and T2 imaging. Intravenous injection of gadolinium provides additional information. Most sinonasal tumors enhance in a diffuse fashion to an intermediate degree, whereas inflamed mucosa enhances more intensely and in a peripheral fashion. Perineural spread to tumor can also be shown on MRI which is most important if adenoid cystic carcinoma is being studied. Correlation of MR imaging and histologic findings at surgery has been shown to be as high as 94% with improvement to 98% with gadolinium.

Benign Lesions

Papillomas - A number of different papillomas arise within the nose and sinuses. In the vestibule, a squamous papilloma similar to that found elsewhere on the skin is found. In the sinonasal tract, three different types of schneiderian papillomas are recognized: inverted, fungiform, and cylindric. The fungiform or everted (50% of cases) occurs exclusively on the septum and can cause obstruction and bleeding. The cylindric papilloma (3% of cases) can be found on the lateral wall and in the sinuses. It is also composed of everted fronds but also has cystic mucus-containing spaces. These can recur but their malignant potential is questioned. Lastly and most importantly is the inverting papilloma (47% of cases). Its etiology, malignant potential, and optimal treatment are widely debated. Its site of origin is usually the lateral nasal wall in the region of the middle meatus. It has a tendency to recur, can be locally destructive, and is associated with malignancy. It is imperative that all specimens removed during sinus surgery be evaluated by pathology so that malignant degeneration does not go undiagnosed. Inverted papillomas are almost always unilateral, are more common in men, and are seen more commonly in the sixth and seventh decades. They are reported to comprise 0.5 to 4% of all sinonasal tumors. Association with carcinoma is seen in 10% of cases. Recurrence rate varies widely from 0 to 80% depending on the initial method of surgical control. Medial maxillectomy via lateral rhinotomy is the gold-standard to which all forms of therapy are measured as initial results with transnasal resection led to high recurrence rates (50-80%). However, with improvements in technology and significant experience, complete endoscopic excision of inverting papilloma with recurrence rates that are similar to open approach procedures have been obtained. The failure rates of recurrent lesions are generally worse regardless of whether an open or endoscopic approach is utilized. Early limitations of endoscopic resection of tumors located in the frontal sinus and the lateral maxillary sinus wall are being overcome by advanced transtrantral resection and modifications to the Lothrop procedure.

Osteomas - These are benign slow-growing tumors of mature bone. In order of

frequency, they occur in the frontal, ethmoid, and maxillary sinuses. They are extremely rare in the sphenoid sinus. They are very often discovered incidentally but can block sinus drainage leading to mucocele formation or invade the orbit leading to proptosis. They are most often seen in the 15 to 40 age group. Treatment if necessary is by local excision with a margin of normal bone.

Fibrous dysplasia - Fibrous dysplasia is characterized by the replacement of normal bone by tissue containing collagen, fibroblasts, and osteoid material. When confined to one bone it is referred to as monostotic and when more than one bone is involved it is polyostotic. It most commonly occurs before the age of 20. Swelling of one bone is the most common feature, and the maxilla is more affected than the mandible. In the maxilla, it usually affects the canine fossa area or the zygomatic area. The radiographic picture is fairly typical and described as a ground-glass appearance. It can vary from a diffuse uniform sclerosis that follows the contour of the bone to a maxillary lesion that shows obliteration of the maxillary sinus with involvement of the infraorbital margin and malar bones. The best treatment is to do as little as possible. The use of radiation is not recommended as malignant transformation has been seen into fibrosarcoma.

Neurogenic tumors - These tumors are commonly seen within the head and neck and up to 4% of these are seen in the paranasal sinuses. Schwannomas have been described within facial bones and along the branches of the trigeminal nerve and nerves of the autonomic nervous system. They arise from the surface of the nerve fibers and seldom undergo malignant degeneration. Neurofibromas arise from within nerve fibers, and usually occur as part of von Recklinghausen's disease. They have been described within facial bones and undergo malignant change in 15% of cases. These tumors should be treated by complete surgical excision unless vital surrounding structures are involved in which case partial excision is acceptable.

Malignant Lesions

Squamous Cell Carcinoma - Squamous cell carcinoma is the most common tumor affecting the maxillary and ethmoid sinuses. It has been said to account for up to 80% of the tumors in this area. The maxillary sinus is involved 70% of the time followed by the nasal cavity in 20% of the cases with the ethmoids comprising the remainder. Primary lesions from the frontal and sphenoid sinuses are uncommon. It is primarily a disease of males and presents most commonly in the sixth decade. Spread outside the sinuses is almost the rule at presentation. More than 90% will have invaded through at least one wall of the involved sinus when discovered. If metastasis does occur, the first echelon of nodal drainage is via the pretubal plexus into the retropharyngeal nodes and then into the subdiaphragmatic nodes. Most of these cancers present in advanced stages (88% T3/T4). Surgical resection followed by postoperative radiation therapy is recommended for treatment in resectable cases. The complex three dimensional anatomy makes surgical margins very difficult to assess which emphasizes the important role for adjuvant XRT in these advanced lesions.

Adenoid Cystic Carcinoma - Adenoid cystic carcinoma can arise within the major and minor salivary glands or mucous glands of the oral cavity and upper respiratory tract. The most common site of occurrence is the palate, followed by the major salivary glands and the paranasal sinuses of which half occur at the maxillary antrum. Despite aggressive surgical resection and radiotherapy, most adenoid cystic carcinomas grow insidiously over several years, resulting in

multiple local recurrences and distant metastases. The paranasal sinuses comprise 14-17% of all cases. Perineural spread in both anterograde and retrograde fashion along cranial nerves is believed to be responsible for the high rates of local recurrence even with negative surgical margins. Because of this, it is imperative that all patients, regardless of the status of their margins, receive regular long-term follow-up. Distant metastases most commonly occur in the lungs. Neck nodal metastases are extremely rare with this type of tumor. Tumor free margins are both difficult to obtain and can be misleading. Postoperative XRT is used to achieve better local control, but whether or not this changes overall survival is unknown.

Mucoepidermoid Carcinoma - These are extremely rare in the sinuses and tend to present in later stages. The propensity for widespread local invasion makes resection with negative margins difficult, so combination treatment with radiation is often recommended.

Adenocarcinoma - This is the second most common malignant tumor in the maxillary and ethmoid sinuses accounting for 5 to 20% of cases. These tend to be more superiorly located with the ethmoid sinuses most commonly involved. Most are related to occupational exposures as it is believed that dust particles will travel along the middle turbinate and the larger particles will be deposited there. They present similarly to squamous cell carcinoma and are divided histologically into high and low grades.

Hemangiopericytoma - Hemangiopericytoma is a well-recognized but uncommon vascular tumor that arises from the pericytes of Zimmerman. These are unique cells found spiraling around the outside of blood capillaries and postcapillary venules. Less than one-third occur in the head and neck, with the minority involving the sinonasal tract. More than 80% of these are said to involve the ethmoids. Sinonasal hemangiopericytomas are considered neither malignant nor benign, but "intermediate" in behavior. Metastases are rare. Clinically, intranasal hemangiopericytomas manifest as pale, gray-white, well-circumscribed masses with a soft, rubbery consistency, resembling nasal polyps. Nasal obstruction with epistaxis is common. The mean age of onset is 55, and the gender distribution is roughly equal. Treatment is complete surgical resection followed by radiation if the margin is positive.

Melanoma - Between 0.5 and 1.5% of all melanomas are said to originate from the nasal cavity and paranasal sinuses, where they constitute about 3.5% of all sinonasal neoplasia. The highest incidence is in patients in their fifth to eighth decades. The nasal cavity is most frequently involved with the anterior septum being the most common site. The maxillary antrum is the most frequently seen sinus location. Typically it is seen as a polypoid fleshy mass and its pigmentation varies. Treatment is primarily surgical resection with or without postoperative radiation therapy. Due to the low incidence of occult neck metastasis, elective neck dissection is currently not recommended. For recurrent lesions, surgical salvage, radiation, chemotherapy or a combination may be required. Overall, the prognosis is poor. In the AFIP study, 5yr survival was 11% and 20 year survival was 0.5%.

Olfactory neuroblastoma or esthesioneuroblastoma - These are rare lesions arising from in the upper part of the nasal cavity from stem cells of neural crest origin that differentiate into olfactory sensory cells. The tumor differs clinically from sympathetic neuroblastoma in that all ages are affected and urinary VMA and HVA are not detectable. It occurs in two age peaks, namely around 20 and 50 years of age. It is a slow-growing tumor that forms an exophytic

polypoid or sessile mass with a congested appearance and usually a smooth surface. Larger tumors may be ulcerated. Initially it is unilateral but extension to the opposite side of the nasal cavity and paranasal sinuses occurs with growth. Kadish proposed a clinical staging system with group A tumors being confined to the nasal cavity, group B involving the paranasal sinuses, and group C extending beyond these limits. The UCLA T staging system is thought to provide a better prognostic prediction regarding local recurrence. Rosettes of the neuroblastoma cells are the hallmark of diagnosis but the histology varies widely and these tumors are sometimes classified mistakenly as undifferentiated carcinoma. The tumor manifests an aggressive behavior. Local recurrences can be expected in about 50 to 75% of patients and metastases in 20 to 30%. Most often metastases are to regional lymph nodes, lungs, and bones. Treatment is primarily surgical resection which often requires en bloc resection of the cribriform plate. Post operative XRT is usually indicated.

Osteogenic sarcoma - Osteosarcoma is the most common primary malignant tumor of bone but is rare in the sinuses. Only about 5% occur in the head and neck where the mandible is more commonly affected than the maxilla. Radiographically the sunray appearance is classic but is only seen in about 25% of cases. There is a 30-40% chance of distant metastases and the five-year survival is 15-20%.

Fibrosarcoma - These are extremely rare in the head and neck and even more so in the paranasal sinuses. The most important determinant of prognosis is the degree of differentiation.

Chondrosarcoma - These are seen in the third to fifth decades with an equal male:female incidence. Histological differentiation between benign and malignant types can be difficult but the malignant variety predominates. Distant metastases are rare. Death is by slow erosive destruction of the skull base. Treatment is often inadequate because of difficulty in establishing margins.

Rhabdomyosarcoma - This is the most common paranasal sinus malignancy seen in children but can affect older individuals as well. They arise in the head and neck in 35 to 45% of cases. Ten percent of these are found in the sinonasal tract, which are classified as a nonorbital, parameningeal site. They are traditionally more aggressive than those arising from other sites. Three types are described: embryonal and alveolar, which are most common in children, and pleomorphic, more commonly seen in adults. Triple therapy with surgery, chemotherapy, and irradiation is often necessary. Aggressive use of chemotherapy and radiation therapy has shown remarkable improvements in survival- from 51% to 81%.

Lymphoma - Sinonasal lymphoma has a bimodal presentation, affecting the very young but more frequently seen in men between the fifth and seventh decades. They are usually of the non-Hodgkins type and seventy percent of the lesions are stage 4 at presentation. Treatment is by radiation, with or without chemotherapy. Children do remarkably better than adults who suffer relapse frequently. If there is recurrence, ultimate survival drops to around 10%.

Extramedullary Plasmacytoma - The large majority of these occur in the head and neck with 40% developing in the nasal cavity or paranasal sinuses. Typically the lesion is "benign" and does not progress to multiple myeloma. Cervical lymph nodes can be involved in 10 to 25% of cases. Successful treatment includes excision or irradiation.

Metastatic tumors - Metastases can occur from anywhere within the body but usually occur from the kidney. Renal cell carcinoma leads by a sizeable margin as the most common infraclavicular site of spread. Neoplasms of the lungs, breasts, and the rest of the urogenital and gastrointestinal tract follow. It is important to recognize these as metastatic lesions as radical surgery is not appropriate and only palliation can be offered.

Sinonasal Undifferentiated Carcinoma – SNUC was first described in 1987 by Levine as an aggressive locally destructive lesion with characteristic histologic findings. They are known for their very aggressive invasion of local structures with relatively little physical symptoms. The differential diagnosis includes esthesioneuroblastoma, lymphoma, melanoma, or rhabdomyosarcoma. The diagnosis is dependent on pathology and is very difficult to distinguish from esthesioneuroblastoma. No consensus on the best therapeutic approach has been made. Preoperative chemotherapy and radiation may offer improved survival.

Staging

Currently, the American Joint Committee on Cancer defines only the maxillary sinus in the TNM staging. An imaginary line drawn from the medial canthus to the angle of the mandible, known as Ohngren's line, is the basis for this T staging. Tumors that are below this line are within the "infrastructure" of the maxillary sinus and have better prognosis than those lying above this line or within the "superstructure" of the maxillary sinus.

Tx- primary tumor cannot be assessed

To- No evidence of primary tumor

Tis- Carcinoma in situ

T1- Tumor limited to the antral mucosa with no erosion or destruction of bone

T2- Tumor with erosion or destruction of the infrastructure, including the hard palate and/or the middle meatus

T3- Tumor invades any of the following: skin of cheek, posterior wall of maxillary sinus, medial or orbital floor, anterior ethmoid sinus

T4- Tumor invades orbital contents and/or any of the following: cribriform plate, posterior ethmoid or sphenoid sinus, nasopharynx, soft palate, pterygomaxillary or temporal fossae, or base of skull.

The AJCC recommends a different system for sarcomas based on histologic grading which is thought to be the most important prognostic factor for these patients. It is based on the number of mitoses, degree of cellularity, amount of stroma, degree of maturation, nuclear pleomorphism, and presence or absence of necrosis.

Cervical node involvement is staged similarly to other head and malignancies. Nodal involvement at the time of initial presentation is a significant prognostic factor. In patients with positive cervical disease, aggressive treatment of the neck is advocated. In the N0 neck, ipsilateral neck dissections have been some controversy as nodal disease has been shown in some studies to arise in a delayed fashion. At the least, careful extended follow-up is warranted.

Surgery

The mainstay of therapy for sinonasal malignancy is en bloc surgical resection. The specific approach is determined by location of disease and histology. Sisson detailed four specific criteria for unresectability which include extension of tumor to the frontal lobes (superior extension), invasion of prevertebral fascia (posterior extension), bilateral optic nerve involvement, and cavernous sinus extension (lateral extension).

Nasal septal lesions can be treated by wide-local excision of the lesion. Medial maxillectomy was described by Sessions and Larsen in 1977 and is most amenable to inverting papilloma or limited lesions involving the lateral nasal wall. Maxillectomy has been the standard approach toward sinus neoplasia with bone cuts through the palate, lateral maxilla, and ethmoids below the skullbase. Tumors with extensive spread or tumors of the ethmoids and frontal sinuses with involvement of the skullbase require craniofacial resections with neurosurgical assistance. There are numerous approaches and procedures described for these more complicated resections which are beyond the scope of this discussion.

Treatment of the Orbit

Preservation of orbital contents during surgical resection of malignant tumors remains a controversial issue. Fortunately there have been recent studies that support pushing the limits of selective orbital preservation. Before 1970, orbital exenteration was included with radical resection of tumors of the paranasal sinus. Initial studies of preoperative radiation to reduce tumor load and margins allowed for orbital preservation with clear surgical margins. Currently, the debate is centered on what degree of "orbital invasion" is acceptable for orbital preservation. Current indications for orbital exenteration include 1) involvement of the orbital apex, 2) involvement of extrocular muscles, 3) involvement of the bulbar conjunctiva or sclera, 4) lid involvement beyond a reasonable hope for reconstruction, and 5) non-resectable full-thickness invasion through the periorbita into retrobulbar fat. Using these criteria and safe oncologic techniques to obtain clear margins in those patients who underwent orbital preservation, there were no adverse affects on survival or local control and up to 90% of orbit-spared patients achieve functional eyes. Importance was placed on proper orbital rim reconstruction using rigid reconstruction techniques for larger defects and the use of Silastic stents in cases where the lacrimal system was violated.

Radiation

Radiation therapy is the primary treatment for lymphoreticular tumors, for patients who are poor surgical candidates, and for those patients who refuse surgery. In resectable cases, the use of radiation alone is no longer recommended. There is no convincing evidence as to the superiority of preoperative versus postoperative irradiation. Preoperative doses are commonly in the 50 Gy range and postoperative doses in the 60 to 70 Gy range. Most select postoperative irradiation because tumor margins are easier to discern and wound complications less. Preoperative irradiation is preferred by some when radiographic evaluation indicates tumor in proximity to the periorbita or dura mater. Frozen section sampling during the surgical procedure can then determine whether these structures have been sterilized and orbital exenteration or craniotomy can be avoided.

Chemotherapy

Chemotherapy is usually reserved for palliative treatment of advanced or recurrent paranasal malignant neoplasms. Early attempts at chemotherapy centered on bleomycin, but currently the same protocols used in other head and neck malignancies are used in sinonasal tumors with platin-based regimens for squamous cell carcinoma, and with doxorubicin or fluorouracil for glandular malignant neoplasms. Patients at high risk for recurrence such as those presenting with positive margins, perineural spread, or extracapsular spread in regional metastasis, as well as patients who represent a poor surgical risk and those who refuse surgery, could be considered for enrollment in protocols that include combinations of radiation and chemotherapy.

Conclusion

Neoplasms of the nasal cavity and paranasal sinuses are rare and require a high index of suspicion for diagnosis due to the overlapping presentation of these neoplasms with more commonly encountered infectious disease states. The rarity of these lesions in combination with the multiple histologies that are encountered have limited large scale studies. Once a paranasal sinus neoplasm is diagnosed, aggressive multimodality therapy is often necessary.

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