Sinonasal neoplasms are rare, comprising less than 3% of all malignant aerodigestive tumors and less than 1% of all malignancies. Despite their infrequency, they represent both a diagnostic and therapeutic challenge because the presenting signs and symptoms may be indistinguishable from benign or inflammatory disorders. These malignancies typically affect Caucasian males in the fifth to seventh decades of life and have a 2:1 male preponderance. Although the presentation may be nonspecific, certain physical findings are often suggestive of this disease spectrum, such as cranial neuropathies, facial swelling, and epistaxis.

Tumors of the nasal cavity proper are approximately evenly divided between benign and malignant neoplasia, with inverting papilloma predominating in the benign group and squamous cell carcinoma in the malignant. On the other hand, most sinus tumors are malignant with squamous cell carcinoma being the most prevalent. The maxillary sinus is most commonly involved with tumor, followed by the nasal cavity, the ethmoids, and then the frontal and sphenoid sinuses.

Epidemiology

Because cancer of the paranasal sinuses is uncommon, it is more difficult than usual to identify promoting and initiating factors. Despite this, up to 44% are attributed to occupational exposures, including nickel, chromium, isopropyl oils, volatile hydrocarbons, and organic fibers that are found in the wood, shoe, and textile industries. In addition, human papillomavirus can be a cofactor, and in one series, human papillomavirus 6 or 12 was documented in 24% of inverting papillomas and 4% of squamous cell carcinomas. Specific associations found include squamous cell carcinoma in nickel workers and adenocarcinoma in workers exposed to hardwood dusts and leather tanning. Cigarette smoking and heavy alcohol consumption have long been known to increase the risk of head and neck malignancy. Their association with sinonasal neoplasms has been harder to establish. It has long been thought that there was no association with sinonasal cancer but Zheng et al have proposed an increased risk of nasal cancer, particularly in the maxillary sinus.

Presentation

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.

With advanced disease, the classic triad of findings for carcinoma of the nasal cavity and paranasal sinuses may be present. These include (1) facial asymmetry, (2) a visible or palpable tumor bulge in the oral cavity, and (3) tumor visible in the nose with anterior rhinoscopy. All three will be present in 40 to 60% of patients, but at least one will be present in 90% at the time of diagnosis.

**Diagnosis**

The physical examination should be thorough. The sinonasal, ocular, and neurologic systems should be studied in detail. In particular, evidence of infraorbital nerve hypesthesia, diplopia, proptosis, and loose dentition should be carefully evaluated. Nasal endoscopy should be performed after adequate topical anesthesia so that exam is not limited by patient discomfort.

Any suspicious lesions noted on nasal endoscopy should be biopsied being cognizant of their bleeding potential. It is recommended that biopsy follow radiographic exam so that tissues are not distorted. Maxillary sinus neoplasms are biopsied via antrostomies or nasoantral windows so that any future partial maxillectomy will remove the biopsy site with the specimen. Additionally, any maxillary sinus with retained secretions will need drainage via these routes if radiation therapy is entertained. Biopsy via a Caldwell-Luc approach is not recommended because of the potential to seed the gingivobuccal sulcus and cheek skin with tumor.

Radiographic studies are essential as the full extent of a sinonasal neoplasm cannot be established even with modern fiberoptic technology. Plain radiographs are rarely used currently 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.

As a general rule, malignant tumors destroy bone, whereas benign processes cause thickening or remodeling of adjacent bone. Bone changes are depicted better with computed tomography than with magnetic resonance imaging. All malignant tumors do not destroy bone, however. Most sinonasal sarcomas remodel abutting bone somewhat, as do most minor salivary gland carcinomas, extramedullary plasmacytomas, large cell lymphomas, olfactory neuroblastomas, and hemangiopericytomas.

The true value of CT scanning is its ability to detect bone erosion. Key areas include the bony orbital walls, cribiform plate, fovea ethmoidalis, posterior wall of the maxillary sinus, pterygopalatine fossa, the sphenoid sinus, and the posterior table of the frontal sinus. The accuracy of CT in determining tumor spread to these areas is on the order of 85%. 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 these lesions do not go undiagnosed. These 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 2 to 13% 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. Recently, many authors have advocated endoscopic excision for control of lesions that are accessible and easily followed postoperatively.

*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. 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. They are very vascular if operated on in the vascular phase. The use of radiation is not recommended as malignant transformation has been seen.

*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 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 maxillary tumors spread to the submandibular nodes and the ethmoidal tumors often are seen in the jugulodigastric and subdigastric nodes. The extent of disease is more important than the degree of differentiation of the tumor.

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. 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 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.

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 being seen in up to 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 the squamous cell carcinoma and are divided histologically into high and low grades.

Hemangiopericytoma - Hemangiopericytomas are 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 most commonly seen. The maxillary antrum is the most frequently seen sinus location. Typically it is seen as a polypoid fleshy mass and its pigmentation varies. Initial metastasis to regional lymph nodes is not prevalent which is misleading as 5 and 10 year survival is on the order of 38 and 17%. Long-term survival statistics are difficult to establish as patients succumb to their disease even after relatively long disease-free survivals of up to 20 years. Survival from mucosal melanoma is very poor especially from the amelanotic variety with some studies reporting 5 year survival as low as 6%.

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. 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
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extending beyond these limits. 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.

**Osteosarcoma** - 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. Histologic 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. 8% of these are found in the sinonasal tract. 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.

**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, 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.

**Staging**

Ohngren in 1933 established an imaginary line extending from the medial canthus to the angle of the mandible. Using this the maxillary sinus is divided into a "suprastructure" and an "infrastructure." He correctly reasoned that tumor above this line is harder to resect and therefore carries a worse prognosis. One caveat with this is that although inferior extension through the palate is more easily resected than other structures, some consider this to be more correctly considered an oral cavity tumor which carries a higher rate of cervical node involvement. Currently, maxillary sinus carcinoma is the only one that has been given a TNM assignment by the American Joint Committee on Cancer. It consists of the following: 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 nasal meatus; T3 - tumor invades any of the following: skin of cheek, posterior wall of maxillary sinus, floor or medial wall of the orbit, anterior ethmoid sinus; and T4 -
tumor invades orbital contents and/or any of the following: cribiform plate, posterior ethmoid or sphenoid sinuses, nasopharynx, soft palate, pterygomaxillary or temporal fossae, or base of skull. Nodal (N) and metastatic (M) designations are similar to other head and neck malignancies.

Sarcomas are evaluated based on a histologic grading system determined by the number of mitoses, degree of cellularity, amount of stroma, degree of maturation, nuclear pleomorphism, and presence or absence of necrosis.

Treatment

As stated previously, most sinonasal tumors present at advanced stages due to the relative lack of specific symptoms identifying that malignancy is present. Seventy-five percent of tumors will be of T3 or T4 status at diagnosis. This leads to difficult decisions regarding treatment. Resection of many of these lesions will lead to permanent disfigurement and still may not provide much hope of disease control. Local control is the most difficult to achieve in these tumors as they abut a number of vital structures. As many as 60% of patients recur locally. The choice of resection depends on the patient's wishes and the location of the tumor. Use of preoperative or postoperative radiation is often used for positive margins and/or attempts to limit the size of resection. Chemotherapy is usually reserved for palliation of unresectable lesions, metastatic lesions, or with recurrences.

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 is beyond the scope of this discussion.

Orbital extension of tumor sparks debate on the necessity of exenteration. All four of the major paranasal sinuses lie adjacent to the orbit and form its bony walls. These bony walls are perforated by various foramina that transmit nerves and blood vessels, all of which are potential routes of invasion into the eye. The thin bone of the lacrimal fossa is often the point of entry for tumor from the ethmoids into the orbit. Fortunately, the eye is lined by an inner periosteum or periorbita which is highly resistant to tumor invasion. In the past, radical maxillectomy with orbital exenteration was the procedure of choice for tumors that erode into the orbit. Harrison, in 1976, proposed orbital exenteration whenever there was preoperative proptosis, limitation of extraocular movement, or bony erosion of the orbit. Even in patients who exhibited small areas of bone erosion underwent exenteration because of the possibility of residual tumor on the periosteum. Sisson was one of the first to use preoperative irradiation of the orbit to prevent exenteration. He was not able to alter survival but did decrease his number of exenterations. McCary and Levine have cited experience with orbital preservation and recommend preoperative irradiation of the orbit to 50 Gy. During resection they immediately evaluate the periorbita with frozen section studies and resect periorbita if positive. The periorbital defects are repaired primarily, with temporalis fascia grafts, or with skin grafts. They have had to exenterate virtually no orbits and report adequate postoperative function.

Pterygopalatine fossa invasion varies from 10 to 20% and is a risk factor for local recurrence as resection becomes very difficult. Som has gone so far as to suggest that pterygopalatine fossa invasion precludes the possibility of local control. Despite this, there are reports of adequate local control with craniofacial techniques including resection of the middle cranial fossa. Radical surgical resection and postoperative irradiation are recommended for involvement of this area.

Neck dissection is not routinely performed and should be reserved for patients with palpable lymphadenopathy or radiographic evidence for neck metastasis. Lymphatic drainage from the paranasal
Radiation

Surgery as a single modality is generally reserved for patients with histologically small tumors in whom clear margins are easily attained and whose tumors are located in areas readily visualized by nasal endoscopy. In clinical practice, this comprises few patients. The use of adjuvant XRT is recommended if surgical margins are positive or for advanced tumors. Adjuvant XRT is thought to augment surgical 5-year cure rates by 10 to 15%. The use of XRT alone as primary treatment modality is no longer considered a viable option except for palliation. Five year survival for XRT alone is said to be 23% and for surgery and XRT 44%. The use of palliative high-dose irradiation alone for unresectable disease offers 5-year survival rates of 10 to 15%.

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.

Irradiation ports must be carefully designed and damage to the central nervous system and globe must be balanced against the need to treat the neoplasm. In those treated by irradiation alone for sinus neoplasms, useful ipsilateral vision is lost in 12 to 20% of patients and bilateral vision in 0 to 8%. Due to diplopia or other factors, postoperative vision is not useful in 10 to 20% of globes preserved at surgery, and this percentage is doubled by irradiation.

Chemotherapy

Chemotherapy is usually reserved for palliative treatment of advanced or recurrent paranasal malignant neoplasms. 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. The use of intra-arterial chemotherapy has had some promising results from Robbins et al (86% response rate of T4 lesions) and Lee et al (91% satisfactory response) but others have shown no improvement. Its use is investigational at present. 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

Paranasal sinus neoplasms constitute an enigma to head and neck surgeons because of their difficulty in diagnosis with such grave consequences for the patient when found in an advanced state. A high index of suspicion leading to more detailed studies is therefore necessary when patients do not respond to routine medical management. Once a paranasal sinus neoplasm is diagnosed, aggressive multimodality therapy is often necessary and should not be delayed.

Bibliography


