3.1 Rhinologic Emergencies

3.1.1 Acute Invasive Fungal Rhinosinusitis

◆ Key Features

- A rapidly progressive sinonasal fungal infection can be fatal.
- Acute invasive fungal infections occur almost exclusively in immunocompromised or debilitated patients,
- Successful treatment requires early detection, wide surgical débridement, and correction of the underlying predisposing condition.

In the debilitated patient, certain fungal infections can become angioinvasive with tissue necrosis, cranial nerve involvement, and possible orbital or intracranial extension. The most common organisms are *Mucor* or *Aspergillus* species. High-risk patients include those with neutropenia from any cause (e.g., leukemia, bone marrow transplantation), other oncology patients undergoing chemotherapy, chronic immunosuppressive therapy or corticosteroid use, diabetes mellitus and diabetic ketoacidosis, or acquired immunodeficiency syndrome (AIDS). Acute invasive fungal rhinosinusitis is a distinct and rapidly aggressive disease process that is distinguished by its fulminant course from other forms of fungal sinusitis, such as mycetoma, allergic fungal rhinosinusitis, or chronic invasive (indolent) fungal rhinosinusitis.

◆ Epidemiology

Also known as rhinocerebral mucormycosis, acute invasive fungal rhinosinusitis occurs in the at-risk populations described above: patients with hematologic malignancies, patients status post solid organ or bone marrow transplant, diabetics, those on chronic steroid therapy, neutropenic patients, and patients with AIDS.

◆ Clinical

**Signs and Symptoms**

A high index of suspicion in any at-risk patient is required, as early diagnosis improves prognosis. A fever of unknown origin should raise suspicion, as should any new sign or symptom of sinonasal disease. Facial edema, periorbital swelling, pain, or numbness are common findings. However, the leukopenic patient may be unable to mount a febrile response. Other findings may include epistaxis, headache, mental status change, or crusting/eschar at the naris that can be mistaken for dried blood. One should consider
unilateral cranial neuropathy, acute visual change, or altered ocular motility in an immunocompromised patient to be acute invasive fungal rhinosinusitis until proven otherwise. A black intranasal eschar on exam is considered pathognomonic for invasive *Mucor*.

**Differential Diagnosis**

A noninvasive sinonasal infection, such as acute bacterial sinusitis, should be considered. An acute bacterial sinusitis complication, such as orbital cellulitis or intracranial suppurative spread may present similarly. Radiographically similar processes may include squamous cell carcinoma, sinonasal lymphoma, and Wegener granulomatosis.

◆ **Evaluation**

See Fig. 3.4 for a diagnostic and treatment algorithm.

**Physical Exam**

The patient suspected to have acute invasive fungal rhinosinusitis should be seen without delay. The head and neck examination should focus on cranial nerve function and should include nasal endoscopy. Avoid tetracaine spray or other topical anesthetics. Insensate mucosa noted during an endoscopic exam is consistent with invasive fungal infection. Dark ulcers or pale, insensate mucosa may appear on the septum, turbinates, palate, or nasopharynx. Early infection may appear as pale mucosa; the presence of dark eschar has been considered to be pathognomonic. Signs of cavernous sinus thrombosis include ophthalmoplegia, exophthalmos, and decreased papillary responses.

Biopsy of suspicious areas such as the middle turbinate or septal mucosa is required for diagnosis. It is important to obtain actual tissue at biopsy, not just overlying eschar or necrotic debris. These specimens should be sent fresh for immediate frozen section analysis as well as silver stain. Patients may be thrombocytopenic, and although a low platelet count may lead to profuse bleeding after biopsy, the risk of this must be balanced with the high mortality associated with a delay in diagnosis. If necessary, platelet transfusion should be ordered early. As a rule, a platelet count of 50,000 is desired.

Acceptable hemostasis can usually be obtained with chemical cautery and Avitene (Davol, Inc., Cranston, RI), Gelfoam (Pfizer Pharmaceuticals, New York, NY), or other hemostatic packing.

**Imaging**

CT findings may be nonspecific. However, the presence of bone erosion and adjacent soft tissue edema on contrast-enhanced maxillofacial CT strongly suggests the diagnosis if clinical correlation is present. Unilateral edema of the nasal mucosa has also been associated with invasive fungal sinusitis, as well as obliteration of the retroantral fat planes. Both soft tissue and bone windows, as well as high-resolution axial and coronal views are necessary. Magnetic resonance imaging (MRI) is useful to evaluate intracranial extension and extension beyond the paranasal sinuses.
Cultures are inadequate and play no role in the initial diagnosis and management of suspected acute invasive fungal rhinosinusitis. Positive culture results will most likely be available late in the course of the disease. Useful labs to assess risk factors include a complete blood count (CBC), absolute neutrophil count, chemistries, blood glucose and hemoglobin A1C (HbA1c) in the diabetic, and human immunodeficiency virus (HIV) testing with CD4 lymphocyte counts and viral load in AIDS patients.

**Fig. 3.4** Treatment algorithm for acute invasive fungal rhinosinusitis. Note that there should be a very low threshold to proceed with biopsy, as rapid diagnosis and treatment is critical to patient survival. CT, computed tomography; MRI, magnetic resonance imaging.

**Labs**

Cultures are inadequate and play no role in the initial diagnosis and management of suspected acute invasive fungal rhinosinusitis. Positive culture results will most likely be available late in the course of the disease. Useful labs to assess risk factors include a complete blood count (CBC), absolute neutrophil count, chemistries, blood glucose and hemoglobin A1C (HbA1c) in the diabetic, and human immunodeficiency virus (HIV) testing with CD4 lymphocyte counts and viral load in AIDS patients.
Pathology

Biopsy of the middle turbinate or other suspicious lesions with immediate frozen section analysis is the gold standard test to confirm the presence of tissue-invasive fungus. *Mucor* is identifiable within the mucosa as large, irregularly shaped nonseptate hyphae that branch at right angles. *Aspergillus* is identifiable as smaller hyphae that are septate and branch at 45-degree angles. Methenamine silver stain is performed to confirm the diagnosis; however, these results may not be available for several hours.

◆ Treatment Options

This is a surgical emergency: complete surgical resection and the reversal of underlying immune dysfunction are critical. The diabetic patient can be successfully treated with early diagnosis, insulin drip, and wide surgical resection. In the oncology patient, if neutropenia cannot be reversed, mortality is high. Granulocyte-macrophage colony-stimulating factor (GM-CSF) may improve survival. Surgical goal is resection of all involved tissue. This may be accomplished endoscopically in select cases. However, an extended total maxillectomy with orbital exenteration may be necessary in advanced disease. Systemic antifungals as well as intranasal nebulized amphotericin are administered, but should be considered adjuvant therapy.

◆ Outcome and Follow-Up

Prognosis is very poor with intracranial involvement. A bone marrow transplant patient with uncorrectable neutropenia has a poor prognosis. Overall survival in diabetic patients may approach 80% if ketoacidosis is corrected.

◆ ICD-9 Codes

117.7 Zygomycosis (phycomycosis or mucormycosis)
117.3 Aspergillosis
461 Acute sinusitis
473 Chronic sinusitis

Further Reading


3.1.2 Orbital Complications of Sinusitis

◆ Key Features

- Sinusitis is a common cause of orbital infection.
- Significant morbidity and even mortality can result.
- Orbital extension of sinusitis is most common in pediatric patients.
- Combined otolaryngology and ophthalmology care is required.

Orbital extension of sinonasal disease requires immediate attention, as rapid progression and blindness may occur. Anatomically, the orbit is bounded by all paranasal sinuses and infection may spread to the orbit directly or via retrograde thrombophlebitis. The Chandler classification system is heuristically useful in staging and managing orbital complications of sinusitis (Table 3.2). Hospital admission and intravenous antibiotic therapy are required for treatment; surgical drainage is necessary for abscess formation, vision compromise, or lack of improvement with medical therapy.

Table 3.2 Chandler Classification

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Preseptal cellulitis</td>
</tr>
<tr>
<td>II</td>
<td>Orbital cellulitis</td>
</tr>
<tr>
<td>III</td>
<td>Subperiosteal abscess</td>
</tr>
<tr>
<td>IV</td>
<td>Orbital abscess</td>
</tr>
<tr>
<td>V</td>
<td>Cavernous sinus septic thrombosis</td>
</tr>
</tbody>
</table>

◆ Epidemiology

Orbital complications occur in ~3% of sinusitis cases. This is most common in children but can occur at any age. Subperiosteal abscess is present in ~20% of cases of orbital extension of sinusitis. Cavernous sinus thrombosis is rare. Immunosingulated patients are at increased risk and require aggressive treatment.

◆ Clinical

Signs and Symptoms

The most common findings are orbital edema, pain, proptosis, and fever. Orbital disease may be the first sign of sinusitis in children. In more advanced cases, there may be gaze restriction and visual acuity change.
Differential Diagnosis

In the pediatric age group, orbital pseudotumor consists of painful proptosis without a fever or leukocytosis. Orbital rhabdomyosarcoma may present with inflammatory changes in 25% of patients. An ethmoid mucocele may present with proptosis, and CT will reveal an expanded sinus in this instance. Other sinonasal causes of proptosis or orbital edema include allergic fungal rhinosinusitis and neoplasm, as well as iatrogenic injury. Abnormal thyroid state may cause ophthalmopathy.

◆ Evaluation

Physical Exam

Examination requires the combined input of the otolaryngologist and the ophthalmologist. In general, the patient will have a history of preceding sinusitis or current complaints consistent with acute sinusitis. Fever is usually present. Head and neck exam reveals lid or periorbital edema, erythema, and tenderness. In cases of preseptal (periorbital) cellulitis, the remainder of the eye exam is normal. The presence of proptosis, chemosis extraocular muscle limitation, diplopia, or decreased visual acuity suggests orbital cellulitis or subperiosteal abscess. With cavernous thrombosis or intracranial extension, findings may include a frozen globe (ophthalmoplegia), papilledema, blindness, meningeval signs, or neurologic deficits secondary to brain abscess or cerebritis. Superior orbital fissure syndrome is a symptom complex consisting of retroorbital pain, paralysis of extraocular muscles, and impairment of first trigeminal branches. This is most often a result of trauma involving fracture at the superior orbital fissure, but dysfunction of these structures can arise secondary to compression. Orbital apex syndrome adds involvement of the optic nerve.

Imaging

Contrast-enhanced CT scanning with coronal and axial views is the imaging study of choice if there is any suspicion of postseptal involvement (i.e., other than simple periorbital cellulitis). A subperiosteal abscess is identifiable as a lentiform, rim-enhancing hypodense collection in the medial orbit with adjacent sinusitis. The medial rectus is displaced. In the absence of abscess formation, there may be orbital fat stranding, solid enhancing phlegmon, or swollen and enhancing extraocular muscles, consistent with orbital cellulitis. A lid abscess may be present less commonly. Suspicion of cavernous sinus thrombosis is better evaluated with MRI.

Labs

A CBC with differential may be useful. Preoperative labs should be ordered as indicated.

Pathology

In younger children, microbiology is often single aerobes including alpha Streptococcus, Haemophilus influenzae, or coagulase-positive Staphylococcus. In those over 10 years old, organisms are often mixed and may include anaerobes.
◆ Treatment Options

Medical

All patients should be admitted and treated with serial ophthalmologic exams and intravenous (IV) antibiotics that have good cerebrospinal fluid (CSF) penetration. Generally, a third-generation cephalosporin is used. Oxacillin is often used in children. Older patients are often double-covered with clindamycin for anaerobes. Alternatives include ampicillin/sulbactam, vancomycin, or aztreonam. Antibiotics are adjusted according to cultures, if possible. Systemic steroids are not recommended. Topical nasal vasoconstrictors are useful (i.e., oxymetazoline).

Surgical

A majority of patients with orbital complications require surgery. This is an area of some controversy. Clearly, surgical drainage is required urgently for abscess formation or decreased visual acuity. If the clinical setting allows for close follow-up (i.e., frequent serial ophthalmologic assessment), many clinicians will observe certain cases of preseptal or early postseptal cellulitis. If there is any progression or lack of resolution with medical therapy over 48 hours, surgery is recommended. Surgical drainage may be accomplished endoscopically by experienced surgeons; however, consent for an external ethmoidectomy approach is recommended. Regardless of approach, the abscess should be drained and the underlying sinus disease should be addressed. For cavernous thrombosis, involved sinuses including the sphenoid must be drained; systemic anticoagulation remains controversial.

◆ Outcome and Follow-Up

The natural history of untreated disease (all stages) results in blindness in at least 10%. Most cases of Chandler stage I–IV disease recover well with treatment. There remains up to an 80% mortality rate with cavernous sinus involvement, although new literature reports suggest this figure is high.

◆ ICD-9 Codes

376.01 Orbital cellulites
461 Acute sinusitis
473 Chronic sinusitis
325 Phlebitis and thrombophlebitis of intracranial venous sinuses

Further Reading


5.2.2 Radiotherapy for Head and Neck Cancer

◆ **Key Features**

- Definitive radiotherapy is a safe and effective means to treat various cancers of the head and neck, either in inoperable patients or as an alternative to surgery for organ preservation.
- Postoperative radiotherapy decreases local failure in select high-risk patients.
- Palliative radiotherapy can reduce local symptoms in an incurable setting.
- Radiation can be improved by sensitizing tumor cells preferentially or by decreasing radiation damage to normal tissues.

Ionizing radiation is a locoregional therapy whereby photons (gamma rays or x-rays), electrons, neutrons, protons, or heavier particles (mesons, α particles, carbon ions) cause cells to either undergo death during mitosis or apoptosis, primarily through the creation of DNA double-strand breaks. The therapeutic ratio of radiation depends on the difference in sublethal repair between normal tissues and tumor cells, the use of radioprotectors and/or radiosensitizers, and the use of advanced methods to limit the irradiation of normal tissues.

◆ **Fundamental Concepts of Radiation**

Radiation dose is defined as the amount of energy (joule) imparted per unit mass (kg). The SI metric unit of dose is the Gray (Gy), defined as 1 J/kg. Historically, the unit used was the rad, which is equivalent to 0.01 Gy, or 1 cGy. Each radiation treatment is called a fraction because for most situations the total radiation dose is given over multiple sessions. A standard fraction is 1.8 to 2 Gy per fraction, and a standard course is five fractions per week with one fraction given per day. Fractionation is biologically advantageous because of the processes of tumor reoxygenation and reassortment into more radiosensitive parts of the cell cycle. Increasing the number of fractions preferentially spares normal tissues by giving them more time to repair sublethal damage. Increasing the number of fractions cannot be
extended indefinitely because of tumor repopulation, which significantly reduces radiation’s efficacy if the total treatment time exceeds 7 weeks.

Various alternative fractionation strategies have been used to try to enhance radiation’s effectiveness. Accelerated radiation delivers treatment faster than standard fractionation (>10 Gy per week). Hyperfractionated radiation is the use of fraction sizes smaller than 1.8 Gy. Hypofractionated radiation is the use of fraction sizes larger than 2.0 Gy. These strategies can be combined, as in accelerated hyperfractionation.

◆ Methods of Radiation Delivery

Radiation is broadly divided into brachytherapy and teletherapy. Brachytherapy is the placement of radioisotopes near or inside the target. In SCC of the head and neck, this is most commonly done by placing catheters in a tumor or operative bed and using an afterloading device to push the source into the catheters for predetermined periods of time to deliver a prescribed dose to the entire target volume. The exposure time ranges from over 2 to 3 days in low-dose rate applications, most commonly with cesium-137, to 10 to 30 minutes in high-dose rate applications, most commonly with iridium-192. With differentiated thyroid cancer, orally administered iodine-131 (\(^{131}\text{I}\)) preferentially binds to tumor cells, with ablative doses of 100 to 150 mCi delivering 250 to 300 Gy.

Teletherapy, or external beam radiation, is the delivery of radiation by pointing an external source of radiation at the target. The most common source in modern radiotherapy is the linear accelerator, which can generate high energy (4 to 25 MeV) photons and electrons. Gamma knife radiosurgery units use cobalt-60 sources that emit 1.25-MeV photon beams. Intraoperative radiation can be focally delivered to internal structures with a linear accelerator or portable x-ray generator in the operating room. External beam radiation is further subdivided by the technology used.

Conventional radiation planning uses x-ray films to define the target volume. Plans are generally limited to a small number of angles and radiation beams are shaped by fabricating Cerrobend blocks. Three-dimensional (3D) conformal radiation uses CT-based treatment planning systems to improve target identification and evaluate dose distribution more accurately. This increases dose conformality to the target by making it easier to use more fields from virtually any beam angle. IMRT improves dose conformality further by delivering different doses to different sections within the same beam, and optimizes the choice and intensity of beams by using a software algorithm to simultaneously test more plans than a human could do within a reasonable period of time. Image-guided radiotherapy (IGRT), further improves dose conformality by using real-time imaging to confirm the patient is in the appropriate position on the couch before delivering radiation, thereby decreasing set-up error and allowing for tighter margins. Stereotactic radiosurgery, or SRS, is the use of a highly conformal large single fraction of external beam radiotherapy, either using a gamma knife or linear accelerator. A gamma knife uses cobalt-201 sources aimed at the same point in space to produce a small area with a high dose and sharp dose drop-off. A common
trait of all modern systems is that increased dose conformality to the target requires a high level of patient set-up consistency, and this is achieved using custom masks or external frames that connect to the patient couch.

◆ **Rationale for Definitive (Curative) Radiotherapy**

Primary radiotherapy in the treatment of SCC of the nasopharynx, oropharynx, oral cavity, and glottis has long been considered an option even in resectable disease. The primary justification for this is not increased efficacy over surgery but organ and functional preservation without compromising long-term efficacy. This is an option for patients with both early (stage I or II) and advanced (stage III or IV) disease. For patients with advanced disease, definitive radiation with chemotherapy with or without planned neck dissection, with surgery to the primary reserved for salvage, had an equivalent survival compared with surgery followed by radiation in randomized trials of cancers of the larynx, hypopharynx, and other areas of the pharynx. For patients with early-stage lesions of the larynx, no randomized trials of laryngectomy versus other modalities exist, but a large series of mature data exists regarding the long-term efficacy of definitive radiation. The results of these trials cannot be extrapolated to all cases, and it is likely that surgery should be the primary modality in some patient subsets. Tumor control, functional outcome, and quality of life should be considered by a multimodality treatment team before choosing an individual patient’s treatment plan.

Definitive radiation, with or without chemotherapy depending upon the histology, is also used in mucosal melanoma, skin cancer, salivary gland cancer, lymphoma, and plasmacytoma. In select cases, conformal radiation using IMRT, SRS, or brachytherapy can be used in previously irradiated sites to salvage locally recurrent cases.

◆ **Rationale for Adjuvant Radiotherapy**

Postoperative radiotherapy is used if there is residual disease or a significant risk of occult residual disease. Randomized evidence supports the use of postoperative radiation for SCC that is stage III or IV or that has close or positive margins. The addition of current chemotherapy to adjuvant radiation has proven to be better than radiation alone in large randomized trials. Randomized data for other tissue types does not exist, but postoperative radiation is commonly given in high-risk cases of Merkel cell carcinoma, salivary gland carcinoma, skin cancer, and thyroid cancer. Preoperative radiation is generally reserved for marginally unresectable disease, but is more standard in esthesioneuroblastomas to make the definitive surgery smaller and less morbid.

◆ **Rationale for Palliative Radiotherapy**

In the noncurative setting, radiotherapy is used to treat areas that are causing local symptoms or at a high risk to cause local symptoms. Common indications in head and neck cancer to treat the primary lesion include uncontrolled bleeding, pain, dysphagia, and a compromised airway. Metastatic disease to the bone, brain, and lung can also be palliated effectively using radiation.
Complications

Radiation side effects can be characterized as acute or late. Acute effects occur during or within the first few weeks after radiotherapy and tend to be transient. Late effects occur months to years after treatment and tend to be permanent. Common acute side effects include dermatitis, mucositis, taste changes, xerostomia, fatigue, facial hair loss, decreased sweating, anorexia, and weight loss. Less common acute effects include cough, hoarseness, nausea, and sialadenitis. Common late effects include xerostomia, trismus, hypothyroidism, soft tissue fibrosis, dysphagia, and taste changes. Less common late effects include soft tissue necrosis, osteoradionecrosis, laryngeal edema, spinal cord myelopathy, carotid stenosis, and second malignancy. Acute effects are generally managed supportively because of their transient nature. Aggressive dental support, stretching exercises, and proper skin care can minimize some late effects. Routine evaluation for hypothyroidism and xerostomia should also be performed, as pharmacologic interventions can improve these conditions.

Improving the Therapeutic Ratio of Radiation

Radiation can be improved by sensitizing tumor cells preferentially or by decreasing radiation damage to normal tissues. Hyperfractionation and accelerated radiation regimes have improved outcomes in stage III or IV SCC compared with standard fractionation, and hypofractionation has improved local control in early-stage glottic lesions. Radiation sensitizers with proven efficacy in randomized trials include concurrent platinum agents, mitomycin C, and cetuximab. Normal tissues can be spared using IMRT, submandibular gland transfer, and amifostine. Future improvements are expected as imaging, radiation delivery, and new agents continue to be further developed.

Further Reading

5. Head and Neck

5.2.3 Sinonasal Cancer

◆ Key Features

- Sinonasal cancer initially may mimic benign sinus disease.
- Tumors of the paranasal sinuses often present with advanced disease.
- Cure rates are generally ≤50%.
- Most patients die of direct extension into vital areas.

Malignant tumors of the sinonasal tract are extremely rare, accounting for 0.2% of all invasive cancers and 3% of head and neck cancers. Cancers of the maxillary sinus are the most common. Tumors of the ethmoid sinuses are less common (20%), and cancers of the sphenoid and frontal sinuses are rare (<1%). Local extension often makes it difficult to access the sinus of origin.

◆ Epidemiology

Chemical carcinogens such as chromium, nickel, thorium dioxide, and tanning chemicals have been implicated in the development of carcinoma of the paranasal sinuses. Exposure to wood dust has been implicated specifically in adenocarcinoma of the ethmoid. Interestingly, tobacco use was previously thought not to play a role in sinonasal carcinogenesis. However, up to a fivefold increased risk of sinonasal carcinoma has been observed with heavy smoking. Rarely, sinonasal cancers may present as a second primary tumor in tobacco users with other head and neck cancers.

◆ Clinical

Signs and Symptoms

Clinical presentation of sinus malignancies is nonspecific and often mimics benign disease, thus diagnosis is often delayed for months. Key indicators of malignancy are cranial neuropathies, proptosis, and pain of maxillary dentition; trismus, palatal, and alveolar ridge fullness; or frank erosion into the oral cavity. Symptoms include nasal obstruction, discharge, stuffiness, congestion, epistaxis, unilateral tearing, diplopia, exophthalmos, infraorbital nerve hypesthesia, cheek swelling, facial asymmetry, hearing loss, and serous otitis media due to nasopharyngeal extension may occur.

Differential Diagnosis

The differential diagnosis includes benign sinus disease, benign sinus tumors, and metastatic tumors to the sinus.
Evaluation

History
The patient history should include known carcinogen exposure, tobacco usage, and prolonged benign sinus symptoms and signs.

Physical Exam
A complete head and neck examination, including nasal endoscopy, should be performed. The sinonasal, ocular, and neurologic systems should be studied in detail. Evidence of nerve hypesthesia, diplopia, proptosis, and loose dentition should be carefully evaluated. Suspicious lesions should be biopsied.

Imaging
Imaging should include either a contrast enhanced CT scan or MRI. There may be a role for integrated FDG-PET/CT.

Other Tests
A definitive diagnosis requires a biopsy. Special attention should be paid to CN function because malignant paranasal tumors are associated with a high incidence of cranial neuropathies compared with inflammatory or benign sinus disease.

Pathology
SCC is the most frequent type of malignant tumor in the paranasal sinuses (70–80%). Minor salivary gland tumors constitute 10 to 15% of these neoplasms. Some 5% of cases are lymphomas. Other tumors include sinonasal undifferentiated carcinoma (SNUC), chondrosarcoma, osteosarcoma and malignant melanoma, and esthesioneuroblastoma.

Inverted papilloma, a benign tumor with a tendency to recur (see Chapter 3.4), may transform into a malignant SCC of the paranasal sinuses in a small percentage of cases.

Treatment Options
Most stage T1 or T2 maxillary sinus carcinomas are treated by surgery alone, provided adequate resection margins are obtained. This may be en bloc surgical resection or endoscopic sinus surgery, depending on the extent of disease and experience of the surgeon. The specific approach is determined by the location of disease and histology (FIG. 5.6).

T3 and T4 lesions are treated by combination therapy with surgery and radiation. The issue regarding whether radiation is more effective before or after surgery remains controversial. Chemotherapy alone is generally used as a palliative measure.
Malignancy behind Öhngren’s plane is regarded to carry a much poorer prognosis because of the rapid spread to the orbit and middle cranial fossae (Fig. 5.7). Despite improvements in surgical ablative and reconstructive techniques, radiation delivery modalities, and imaging technologies, disease-free survival at 5 years remains <50%, independent of stage. Five-year disease-free survival for patients with advanced stage cancer drops to 25%.

**ICD-9 Codes**

160.2 Malignant neoplasm of maxillary sinus
160.3 Malignant neoplasm of ethmoidal sinus
160.4 Malignant neoplasm of frontal sinus
160.5 Malignant neoplasm of sphenoidal sinus

Fig. 5.7 Öhngren’s plane passing through the medial canthus and the mandibular angle. It divides the maxillary sinus into a superoposterior part and an inferoanterior part. Cancer limited to the latter part typically carries a better prognosis. (From Becker W, Naumann HH, Pfaltz CR. Ear, Nose, and Throat Diseases: A Pocket Reference. 2nd ed. Stuttgart/New York: Thieme; 1994:293.)
**Staging of Nose and Paranasal Sinus Cancer: For All Carcinomas Excluding Mucosal Malignant Melanoma**

**Primary Tumor: Maxillary Sinus**

TX: Cannot be assessed  
T0: No evidence of primary tumor  
Tis: Carcinoma in situ  
T1: Tumor limited to the maxillary sinus mucosa with no erosion or destruction of bone  
T2: Tumor causing bone erosion or destruction including extension into the hard palate and/or middle nasal meatus, except extension to posterior wall of maxillary sinus and pterygoid plates  
T3: Tumor invades any of the following: bone of the posterior wall of maxillary sinus, subcutaneous tissues, floor or medial wall of orbit, pterygoid fossa, or ethmoid sinuses  
T4a: Tumor invades anterior orbital contents, skin of cheek, pterygoid plates, infratemporal fossa, cribiform plate, or sphenoid or frontal sinuses  
T4b: Tumor invades any of the following: orbital apex, dura, brain, middle cranial fossa, cranial nerves other than maxillary division of trigeminal nerve (V2), nasopharynx, or clivus

**Primary Tumor: Nasal Cavity and Ethmoid Sinus**

TX: Cannot be assessed  
T0: No evidence of primary tumor  
Tis: Carcinoma in situ  
T1: Tumor restricted to any one subsite, with or without bone invasion  
T2: Tumor invading two subsites in a single region or extending to involve an adjacent region within the nasoethmoidal complex, with or without bone invasion  
T3: Tumor extends to invade the medial wall or floor of the orbit, maxillary sinus, palate, or cribiform plate  
T4a: Tumor invades any of the following: anterior orbital contents, skin of nose or cheek, minimal extension to anterior cranial fossa, pterygoid plates, or sphenoid or frontal sinuses  
T4b: Tumor invades any of the following: orbital apex, dura, brain, middle cranial fossa, cranial nerves other than maxillary division of trigeminal nerve (V2), nasopharynx, or clivus

**Regional Lymph Nodes**

NX: Cannot be assessed  
N0: No regional lymph node metastasis  
N1: Metastasis in a single ipsilateral lymph node, $\leq 3$ cm in greatest dimension
N2: Metastasis in a single ipsilateral lymph node, >3 cm but not >6 cm in greatest dimension, or in multiple ipsilateral lymph nodes, none >6 cm in greatest dimension, or in bilateral or contralateral nodes, none >6 cm in greatest dimension

N2a: Metastasis in a single ipsilateral lymph node, >3 cm but not >6 cm in greatest dimension

N2b: Metastasis in multiple ipsilateral lymph nodes, none >6 cm in greatest dimension

N2c: Metastasis in bilateral or contralateral lymph nodes, none >6 cm in greatest dimension

N3: Metastasis in a lymph node >6 cm in greatest dimension

*Metastases at level VII are considered regional lymph node metastases. Midline nodes are considered ipsilateral nodes.

Distant Metastasis

M0: No distant metastasis
M1: Distant metastasis

Stage Groupings: For All Cancers Except Mucosal Malignant Melanoma

Stage 0
Tis N0 M0

Stage I
T1 N0 M0

Stage II
T2 N0 M0

Stage III
T1 N1 M0
T2 N1 M0
T3 N0,N1 M0

Stage IVA
T1,T2,T3 N2 M0
T4a N0,N1,N2 M0

Stage IVB
T4b Any N M0
Any T N3 M0

Stage IVC
Any T Any N M1
Further Reading

American Joint Committee on Cancer. AJCC Cancer Staging Handbook. 7th ed. New York: Springer-Verlag; 2010

5.2.4 Nasopharyngeal Cancer

◆ Key Features

- There is a high frequency of nasopharyngeal cancer (NPC) among patients of Chinese ethnicity and descent.
- It is associated with EBV exposure.
- The diagnosis must be excluded in patients with asymptomatic cervical lymphadenopathy and unilateral serous otitis media.

NPC is a distinct type of head and neck cancer that differs from other malignancies of the upper aerodigestive tract with respect to epidemiology, pathology, clinical presentation, and responses to treatment. NPC is an uncommon neoplasm in most parts of the world but is endemic in East Asia. Seventy percent of patients with newly diagnosed NPC present with locally advanced disease. Latent EBV infection seems to be crucial in the pathogenesis of NPC. Studies have established that NPC cells express two distinct EBV latent membrane proteins, LMP-1 and LMP-2. These proteins are attractive targets for adaptive immunotherapy.

◆ Anatomy

The nasopharynx is bounded superiorly by the basiocciput and basisphenoid, posteriorly by the C1 and C2 cervical bodies, anteriorly by the choanae, and inferiorly by the soft palate. The lateral walls are occupied primarily by the eustachian tube orifice. Immediately posterior to the eustachian tube orifice is Rosenmüller’s fossa, where most nasopharyngeal carcinomas originate.

◆ Epidemiology

NPC occurs most often in China where it is the third most common malignancy among men, with an incidence rate of 15 to 50 per 100,000.