Cancer of the nasal vestibule, nasal cavity and paranasal sinuses

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All these recommendations are evidence level 3 (expert opinion) and they are therefore grade C recommendations. Where this is not the case, this is stated in these guidelines.

Key-words. Guidelines; cancer; nasal vestibule; nasal cavity; paranasal sinuses

Abstract. The usual clinical presentation of sinonasal tumours includes symptoms that are indistinguishable from inflammatory sinus disease, namely nasal airway obstruction, pain, and epistaxis. Abnormal V1 and/or V2 sensations are a strong indication of the possibility of tumour. Computed tomography is the most reliable and informative imaging tool for evaluating the cancers of the paranasal sinuses. Magnetic resonance imaging is essential for tumour mapping because of the excellent tissue characterisation and the possibility of differentiating between neoplasms and retained secretions. A wide variety of histologies may be encountered, although squamous cell carcinoma (SCCA) is the most common. Radiation is a common adjuvant to surgery. The response of sinonasal tract tumours to radiation therapy varies with the stage and histology of the tumour. Rehabilitation after surgical resection may be accomplished with prosthodontics or reconstructive flaps. Bony erosion of the orbital walls does not constitute an indication for orbital exenteration. Patients with tumour involvement of the skull base, either in the infratemporal fossa or at the fovea ethmoidalis and cribiform plate, should be considered for craniofacial resection. Management of these tumours requires a multimodal approach, involving surgery, radiation therapy and, increasingly in recent years, chemotherapy. Management should therefore be entrusted to multidisciplinary teams only.

Introduction

Neoplasms of the paranasal sinuses and nasal cavity account for 3% to 4% of head and neck cancers. The male to female ratio for all sites and histologies is approximately 3:2. Most tumours are advanced at presentation, and the exact site of origin may be uncertain. Tumours may arise from any of six separate anatomic locations: maxillary sinus, ethmoid sinus, frontal sinus, sphenoid sinus, nasal cavity, or nasal vestibule. Non-squamous-cell malignant tumours comprise about half of all malignant tumours of these sites. In addition to squamous cell carcinoma, numerous other histologic subtypes are encountered with some frequency: aesthesioneuroblastoma, sinonasal undifferentiated carcinoma (SNUC), small cell carcinoma, adenocarcinoma, adenoid cystic carcinoma, mucoepidermoid carcinoma, lethal midline granuloma (nasal natural killer/T-cell CD56-positive lymphoma), malignant melanoma, sarcoma, plasmacytoma, and T-cell or B-cell lymphoma. The occasional occurrence of metastatic adenocarcinoma (particularly renal cell, lung or breast) in this region should be also kept in mind. Anatomic complexity, a high frequency of tumour unresectability, patient refusal to undergo mutilating resection, and tumour proximity to vital structures (brain, brainstem, pituitary, cavernous sinus, optic nerve, orbit) constitute additional challenges in the management of these tumours. Surgical resections are often piecemeal; even when resection margins are deemed negative, local recurrence occurs in more than 50% of patients after surgery alone. Management of these tumours requires a multimodal approach, involving surgery, radiation therapy and, increasingly in recent years, chemotherapy.

1. Diagnostic evaluation

The usual clinical presentation of sinonasal tumours includes symptoms that are indistinguishable from inflammatory sinus disease, namely nasal airway obstruction, pain, and epistaxis. Abnormal V1 and/or V2 sensations are a strong indication of the possibility of tumour. A good clinical evaluation requires the collection of a com-
complete history of the disease including the professional activities (for example, wood worker) of the patient and any recent weight loss. An assessment is required of a performance status as Karnofsky or the ZU BROD-ECOG-WHO scale. Generic, multidimensional questionnaires have been developed and validated to assess quality of life in varying cancer populations. All of them evaluate, at minimum, physical, psychological, and social well-being. The Head and Neck Cancer Module of the EORTC QLQ-C30 is designed to be used in conjunction with the generic, multidimensional QOL measure developed by the European Organisation for Research and Treatment of Cancer; this is a well-validated scale that assesses symptoms prevalent in head and neck cancer and some functional concerns.

The nasal cavity and the nasopharynx should be inspected using a nasal speculum and a 30° rigid fibre-optic nasendoscope after the use of a topical decongestive agent and anaesthetic to shrink the mucosa. A flexible nasopharyngoscope is less suitable for examination of the nasal cavity. A 90°-degree Hopkins laryngopharyngoscope provides an excellent panoramic view of the nasopharynx and posterior nares, especially when tumour bulk makes direct inspection using a 30° nasendoscope difficult or impossible. Examinations, including audiometry, should be conducted of the cranial nerves. Facial asymmetry should be noted. Vision and oculomotor function should be assessed. Oculomotor dysfunction can be due to cranial nerve invasion in the cavernous sinus or to the direct tumour invasion of the oculomotor muscles. Particular emphasis should be placed on the bimanual examination of the neck and, in particular, the submandibular lymph nodes, the facial lymph nodes (bimanual palpation of the cheek in the case of nasal vestibular carcinoma, and the posterior neck triangle (zone V) in the case of nasopharyngeal carcinoma.

Drawing the lesions on a standardised pre-established outline is recommended. A pathologic diagnosis can be obtained with a biopsy of the intranasal mass or the ethmoid, the sphenoid, frontal or maxillary sinuses using an endoscopic and endonasal approach.

2. Diagnostic imaging

Patients should undergo axial, coronal, and sagittal computed tomography (CT) of the paranasal sinuses and the neck, and magnetic resonance imaging (MRI) of the paranasal sinuses and brain. These are complementary examinations. A CT is better at detecting cerebral lymph nodes metastasis and bone destruction; MRI is superior in assessing the extent of intracranial or brain involvement and in distinguishing tumours from retained secretions. An MRI is also better than CT for evaluating retropharyngeal lymph nodes. MRI of the spine is indicated in patients with intracranial disease extension who have symptoms or signs of leptomeningeal spread, although such spread occurs late in the course of the disease. Both CT and MRI should be performed with contrast and should be acquired with a high-spatial-resolution algorithm, as opposed to the standard type used for brain imaging. Panoramic dental X-rays (for the purposes of future radiotherapy and optimisation of dental health), chest X-rays, and spiral CT scans of the thorax should be used to complete the diagnostic imaging. If a CT scan is performed, the chest X-ray can be omitted. In the case of oral-pharyngeal-laryngeal cancer, it is now generally agreed that early synchronous lung cancer and distant metastases are better detected using a thoracic spiral CT scan (level 2) and PET scan (level 4). In some cases, depending on previous findings, positron emission tomography (PET scan) should be recommended. PET scans may prove useful for follow-up in instances of persistent but apparently stable imaging abnormalities, mainly when recurrent disease may be difficult to detect with post-therapeutic CT or MRI examinations due to oedema, scarring, and flap reconstruction. Although PET scans are still investigational in the preoperative assessment of the sinusal malignant tumour, they should be recommended in the Belgian health-care context. In cases of deep skull-base involvement and its treatment, MRI is more valuable for the early detection of recurrence at the extracranial margin and it is more sensitive for intracranial progression.

3. Other clinical investigations

The clinical evaluation therefore requires an ophthalmologic and an oro-dental examination. Recommended laboratory tests should include a haemogram, coagulation, liver-enzyme and kidney function tests and, if radiotherapy is provided, pituitary and thyroid gland function evaluation. Neuron-specific enolase is a tumour marker that can be determined for aestheticionuroblastoma but its use has
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never been prospectively proven. EBV serology is useful in nasopharyngeal carcinoma. If present, serum IgA EBV (IgA VCA, IgA EA) concentrations have been shown to correlate with stage before treatment and disease recurrent activity following treatment.14

If maxillectomy is considered, prosthetic rehabilitation should be provided, and a visit to the prosthetic dentist (in order to make templates for an obturating plate to be used intraoperatively following resection) or anaplastologist (in cases requiring an orbital prosthesis) should precede any surgical action. Neurosurgical and cosmetic examinations are recommended, depending on the surgical approach. For pathologic examination, frozen and fixed biopsies should be carried out.

4. Clinical staging

The 2002 American Joint Committee on Cancer (AJCC) staging system for maxillary sinus and nasoethmoid lesions is shown in Table 1. The staging system used at the University of Florida for cancer of the nasal cavity, the sphenoid sinus and frontal sinus is outlined in Table 2. The system of the Massachusetts General Hospital (the Kadish system), which is widely used for aestheticneuroblastoma, is shown in Table 3. The nasal vestibule cancers are staged according to the 1997 AJCC staging system for skin cancer (Table 4). (In UICC 2002, these are staged together under the heading of nasal cavity tumours.)

<table>
<thead>
<tr>
<th>Primary tumour (T)</th>
<th>2002 American Joint Committee on Cancer Staging for Maxillary Sinus and the Nasoethmoid Complex</th>
</tr>
</thead>
<tbody>
<tr>
<td>TX</td>
<td>Primary tumour cannot be assessed</td>
</tr>
<tr>
<td>TO</td>
<td>No evidence of primary tumour</td>
</tr>
<tr>
<td>Tis</td>
<td>Carcinoma in situ</td>
</tr>
<tr>
<td>Maxillary Sinus</td>
<td></td>
</tr>
<tr>
<td>T1</td>
<td>Tumour limited to maxillary sinus mucosa with no erosion or destruction of bone</td>
</tr>
<tr>
<td>T2</td>
<td>Tumour causing bone erosion or destruction including extension into the hard palate or middle nasal meatus, except extension to posterior wall of maxillary sinus and pterygoid plates</td>
</tr>
<tr>
<td>T3</td>
<td>Tumour invades any of the following: bone of the posterior wall of maxillary sinus, subcutaneous tissues, floor of medial wall of orbit, pterygoid fossa, ethmoid sinuses</td>
</tr>
<tr>
<td>T4a</td>
<td>Tumour invades anterior orbital contents, skin of cheek, pterygoid plates, infra-temporal fossa, cribiform plate, sphenoid or frontal sinuses</td>
</tr>
<tr>
<td>T4b</td>
<td>Tumour invades any of the following: orbital apex, dura, brain, middle cranial fossa, cranial nerves other than maxillary division of trigeminal nerve (V1), nasopharynx, or clivus.</td>
</tr>
<tr>
<td>Nasal cavity and ethmoid sinus</td>
<td></td>
</tr>
<tr>
<td>T1</td>
<td>Tumour restricted to any one subsite, with or without bony invasion</td>
</tr>
<tr>
<td>T2</td>
<td>Tumour invading two subsites in a single region or extending to involve an adjacent region within the nasoethmoidal complex, with or without bony invasion</td>
</tr>
<tr>
<td>T3</td>
<td>Tumour extends to invade the medial wall or floor of the orbit, maxillary sinus, palate or cribiform plate</td>
</tr>
<tr>
<td>T4a</td>
<td>Tumour invades any of the following: anterior orbital contents, skin of nose or cheek, minimal extension to anterior cranial fossa, pterygoid plates, sphenoid or frontal sinuses</td>
</tr>
<tr>
<td>T4b</td>
<td>Tumour invades any of the following: orbital apex, dura, brain, middle cranial fossa, cranial nerves other than V1, nasopharynx or clivus.</td>
</tr>
<tr>
<td>Regional lymph nodes (N)</td>
<td></td>
</tr>
<tr>
<td>Nx</td>
<td>Regional lymph nodes cannot be assessed</td>
</tr>
<tr>
<td>N0</td>
<td>No regional lymph node metastasis</td>
</tr>
<tr>
<td>N1</td>
<td>Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension</td>
</tr>
<tr>
<td>N2a</td>
<td>Metastasis in a single ipsilateral lymph node, more than 3 cm but not more than 6cm in greatest dimension</td>
</tr>
<tr>
<td>N2b</td>
<td>Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension</td>
</tr>
<tr>
<td>N2c</td>
<td>Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension</td>
</tr>
<tr>
<td>N3</td>
<td>Metastasis in a lymph node, more than 6 cm in greatest dimension</td>
</tr>
<tr>
<td>Distant metastasis (M)</td>
<td></td>
</tr>
<tr>
<td>Mx</td>
<td>Distant metastasis cannot be assessed</td>
</tr>
<tr>
<td>M0</td>
<td>No distant metastasis</td>
</tr>
<tr>
<td>vM1</td>
<td>Distant metastasis</td>
</tr>
</tbody>
</table>

See next page
5. Selection of treatment modalities

5.1. Primary treatment for the neck

In N0, elective treatment (neck dissection (ND) or radiotherapy (RT) depending on the treatment of the primary tumour) of both sides of the neck is indicated when the tumour extends to the nasopharynx and/or the soft palate and/or the upper lip. In other N stages, appropriate ND on both side of the neck plus postoperative RT is recommended.

5.2. Maxillary sinus

In T1 and T2, partial maxillectomy is recommended. In T3, a total maxillectomy is required. In T4, a radical maxillectomy is required including the removal of the entire maxilla and ethmoid sinus. The globe and the orbital floor are preserved for lower tumours. Orbital exenteration is indicated when a tumour has spread through the periorbita and invaded the orbital fat. Craniofacial resection (CFR) may be required if the roof of the ethmoid and of the orbit is involved. Reconstructive techniques such as rectus abdominus free flap repair of maxillary defects and rib reconstruction of the orbital floor have significantly reduced long-term surgical morbidity. Primary iliac crest (with muscle) reconstruction of the palatal defect has received considerable attention lately and should be considered.15,16 Massive tumour extension to the base of skull, clivus, orbital apex, brain, middle cranial fossa and cranial nerves other than V2, nasopharynx, or sphenoid sinus (stage T4B) contraindicates surgery. Borderline resectable tumours are treated with neoadjuvant chemotherapy.
sometimes followed by surgery if feasible. Chemotherapy may have a role to play in preserving the orbital contents. It is commonly recommended as an adjunct to RT in patients who refuse surgical resection. Nevertheless, the usefulness of neoadjuvant or concurrent chemotherapy is still unknown, with the exception of its proven role in nasopharyngeal carcinoma (level 1). As stated below, reports on the role of induction chemotherapy are inconclusive.

Early infrastructure lesions (T1) may be cured by surgery alone but, in other cases (T3, T4), RT is given after surgery even if the margins are clear. RT in T2 is questionable and more controversial. The radiation treatment volume includes the entire maxilla adjacent to the nasal cavity, the ethmoid sinus, nasopharynx, and pterygopalatine fossa, and at least a portion of the adjacent orbit. Three-dimensional conformal therapy, fractionated stereotactic treatment or intensity-modulated RT are appropriate means of increasing the target dose while confining the dose to normal dose-limiting tissues, most notably the brain and visual apparatus.

We recommend elective neck RT in all patients with T2 to T4 or poorly differentiated cancers (level 2).

5.3. Ethmoid sinus

The preferred treatment for both early and advanced lesions is surgery followed by postoperative RT. Margin status is difficult to determine because of the usual piecemeal manner in which the specimen is removed. The majority of ethmoid tumours are extirpated through lateral rhinotomy and en bloc ethmoidectomy including the entire lateral wall, the ethmoid labyrinth, lamina papyracea, and middle and inferior turbinates. In trained teams engaged in endoscopic endonasal surgery, endoscopic resection could be considered for T1 and T2 classified tumours. If the tumour involves the fovea ethmoidalis or cribriform plate, then a combined CFR approach is required. Resection may include the cavernous sinus or the sphenoid sinus, but cure rates are dismal when these areas are involved. Surgery does not allow adequate en bloc resection of tumours involving the orbital apex or nasopharynx, or deeply infiltrating the pterygoid space. In US institutions, CFR is the most common procedure for these tumours. Although some early reports stressed the importance of orbital exenteration as a component of CFR, it is now performed much less frequently. Sparing the orbital contents has not proven detrimental to tumour control or survival. If the tumour does not pass through the orbital periorbita involving the orbital contents, then exenteration is not necessary, even for patients in whom there are clinical suspicions of orbital invasion (level 2). When the lesion extends through the bony skull base, the overlying dura should be left attached to the specimen. If the patient is not a surgical candidate, then RT alone controls 50% to 65% of these tumours, but there is a higher risk for the visual apparatus and brain than with lower-dose postoperative RT. The expectation that surgery will salvage RT failures is not very realistic because few failures are successfully salvaged.

Neoadjuvant chemotherapy produces a high response rate in patients with undifferentiated carcinoma of the ethmoid sinus (level 2). Some tumours that extensively involve the orbit undergo enough regression after neoadjuvant chemotherapy to make it feasible to spare the orbital contents.

5.4. Sphenoid Sinus

Some sphenoid sinus tumours are amenable to surgical resection (mostly through a transseptal or a combined lateral and anterior approach) but most are too advanced for surgery and are treated with primary RT with or without chemotherapy.

5.5. Frontal Sinus

Cure with surgery alone is unlikely and involves huge cosmetic sequelae. Combined surgery and RT produce a few cures.

5.6. Aesthesioneuroblastoma

Combined treatment for all stages of the disease is recommended.

For Kadish A and early B lesions, CFR is followed by postoperative RT (60 Gy).

For advanced B or C lesions that are resectable, there should be neoadjuvant chemotherapy (Cis-platine-etoposide), followed by CFR and neck dissection if clinically lymph nodes persist after chemotherapy, followed by RT (60 Gy). For unresectable advanced tumours or tumours that extensively invade the brain or the orbit we recommend adjuvant chemotherapy. If the tumour becomes resectable after chemotherapy, we recommend CFR followed by RT. If it remains unresectable after neoadjuvant chemotherapy, we recommend preoperative RT (60 Gy) followed by resection if feasible. If the tumour remains unresectable after the completion of RT, the RT should
be continued at higher doses depending on the size and the location of the tumour.33

Patients with direct extension into the brain should be treated with curative intent in the appropriate setting because occasional cures have been reported.26,34,35 Long-term remission is sometimes possible in cases of leptomeningeal seeding or distant metastases with a combination of chemotherapy, RT and chemotherapy, with or without autologous bone marrow transplant.1

We recommend bilateral elective neck RT for patients with advanced stage B or C, as the failure in the lymphatic occurs in at least 20% of the patients when no elective treatment is administrated (level 2).33,36-39 Chemotherapy may also reduce the risk of neck failure.

5.7. Malignant Melanoma

The treatment for malignant melanoma is the same, stage for stage, as for squamous cell carcinoma (i.e., surgery and postoperative RT) (level 2).40-42 Elective neck treatment is not indicated. As the prognosis is very bad, surgery is only indicated in selected cases.

5.8. Sinonasal Undifferentiated Carcinoma (SNUC)

The treatment of this highly aggressive tumour includes neo-adjuvant chemotherapy (cyclophosphamide, doxorubicin, vincristine), followed by preoperative RT, then surgical resection, usually CFR. The frequency of lymph node metastasis suggests that elective neck RT is advisable. The prognosis is very bad as for malignant melanoma and surgery is indicated in selected cases.

5.9. Nasal NK/T-Cell Lymphoma (Lethal Midline Granuloma)

When the disease is limited to the upper aerodigestive tract, RT is the treatment of choice. The dose recommended is 45 to 50 Gy43-46 and is delivered to the entire nasal cavity, all paranasal sinuses bilaterally, and to the entire hard palate. All areas are treated to 40 Gy, and then the site of initial disease is boosted to 50 Gy. More limited treatment volumes are associated with a 20% rate of marginal miss.47

There is no convincing evidence that chemotherapy markedly improves outcome for patients with limited disease over RT alone (level 2).43,44,47 When used as primary treatment, chemotherapy produces a lower complete response rate than primary RT.48 Conventional chemotherapy for relapsed disease is usually not successful.

5.10. Rhabdomyosarcoma

Induction chemotherapy is recommended, followed by RT or surgery plus RT depending on the tumour response.

5.11. Plasmocytoma

RT is recommended.

5.12. Nasal Vestibule

Radiation therapy is usually recommended because adequate excision often produces deformity. Early, superficial, well-demarcated lesions of the nasal septum are readily amenable to surgical excision with clear margin and repair by skin graft. Most other lesions are better treated by RT. Tumours involving the alar side of the vestibule often infiltrate the cartilage, and adequate repair of the defect after surgical excision is often less than ideal. Likewise, cancers that involve the floor of the vestibule or columella frequently extend submucosally into the upper lip; resection produces a defect that is difficult to correct. The volume of such cancers may be significant and both external beam RT as well as brachytherapy may have to be combined (level 2).39 Rhinectomy is generally avoided except as a salvage procedure after failed RT. In N0, if the tumour invades the upper lip, elective neck RT is the procedure.

6. Follow-up

We recommend cavity cleaning, fiberoptic examination, and neck palpation every 3 months during the first two years, then every six months during the next three years, and every year during the next five years. Chest X-ray every year and CT or MRI after 6 and twelve months. If RT has been delivered on the neck or on the pituitary gland, laboratory tests for thyroid and pituitary should be carried out.

7. Management of recurrence

Salvage of primary recurrence consists of surgical resection plus postoperative RT if it has not already been administered. Unresectable lesions are treated initially by chemotherapy or RT in the hope of making them resectable. If surgery is not an option, high-dose RT with or without chemotherapy will produce some cures. Neck failures are managed by neck dissection plus RT.

For the nasal vestibule, primary recurrences after RT are excised and post-surgical failures are treated by RT. Management of recurrence is often successful but
deformity may be significant. The development of lymph node metastases requires neck dissection.

References


34. Zappia JJ, Carroll WR, Wolf GT, Thornton AF, Ho L, Krause CJ. Olfactory neuroblastoma: the results of modern treatment approaches at the
CME questions

1. Which of these statements about cancers of the paranasal sinuses and nasal cavity is true?
   A - Neoplasms in these sites account for 10% of head and neck cancers.
   B - Non-squamous-cell malignant tumours account for half of all malignant tumours in these sites.
   C - The optimal management of these tumours always requires ‘en bloc’ surgical removal.

2. Which of these procedures is not systematically required for the diagnostic evaluation of these cancers?
   A - Bronchoscopy
   B - Ophthalmologic examination
   C - MRI of the sinuses
   D - Laboratory tests
   E - Oro-dental examination

3. In these cancers, PET scans have proven useful:
   A - Never
   B - Always
   C - During follow-up
   D - In the preoperative assessment
   E - When distant metastasis is suspected

4. In the 2002 AJCC (American Joint Committee on Cancer staging for maxillary sinus and nasoethmoid complex) system, TX means:
   A - That the histological determination of the tumour is dubious.
   B - That the tumour is a carcinoma in situ.
   C - That the primary tumour cannot be assessed.
   D - That the tumour is a metastatic one.
   E - That the tumour cannot be clearly staged.

5. Radiotherapy is indicated in cancer of the maxillary sinus
   A - After surgery, even if the margins are clear.
   B - Only in T4 tumours.
   C - In T1 tumours.
   D - In T2 and T3 tumours.
   E - Only in squamous cell carcinoma.

6. An anterior ethmoidal tumour which infiltrates the ground lamella and the middle turbinate is classified
   A - T1
   B - T2
   C - T3
   D - T3a
7. In ethmoidal cancers, orbital exenteration is indicated
   A - When pretreatment symptoms suggest an orbital invasion.
   B - In all tumours staged T4a.
   C - When the spread of the tumour through the orbital periosteum is minimal.
   D - Never. It is performed depending on peroperative findings.
   E - In all tumours staged T4b.

8. Elective neck radiotherapy is indicated
   A - In aesthesioneuroblastoma staged Kadish A.
   B - In aesthesioneuroblastoma staged Kadish C.
   C - In malignant melanoma.
   D - In SNUC (Sinonasal Undifferentiated Carcinoma).
   E - In every case of N0 squamous cell carcinoma of the maxillary sinus.

9. Which would be the optimal sequence in the treatment of a child of six years presenting with a rhabdomyosarcoma of the ethmoid?
   A - Surgery(S) + radiotherapy (RT) + chemotherapy (C)
   B - RT + S + C
   C - C + RT + S
   D - S + C + RT
   E - RT + C + S
   F - C + S + RT

10. Guidelines about cancers of the paranasal sinuses are
    A - Mandatory because the levels of evidence are high.
    B - Mandatory because the opinions of the teams treating these conditions are quite similar.
    C - Not mandatory because there are almost no consensus about the optimal treatment of these conditions.
    D - Not mandatory because a guideline deals with the financial or legal aspects of the medical practice rather than the strictly medical ones.
    E - Not mandatory because no better results can be expected if the physician follows the guidelines or his own experience.

Answers: 1B; 2A; 3CD; 4C; 5D; 6B; 7D; 8BD; 9C; 10B