
LCA Operational Policy

Anterior Skull Base Tumours

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1 Introduction

This operational policy should be read in conjunction with the LCA Brain/CNS Cancer Clinical Guidelines.

Tumours in the sinonasal region are rare, affecting fewer than 1 in 100,000 people/year. They are histologically the most diverse group and potentially pose significant management problems due to their close proximity to the orbit and intracranial cavity. Squamous cell carcinoma (SCC) is the most commonly encountered of malignant tumours, but tumours of every histological type can occur. The commoner epithelial tumours include adenocarcinoma, olfactory neuroblastoma, malignant melanoma and adenoid cystic carcinoma. Sarcomas include chondrosarcoma and rhabdomyosarcoma. Benign tumours include inverted papilloma, osteoma, juvenile angiofibroma, haemangiopericytoma, haemangioma, schwannoma, pleomorphic adenoma and meningioma. All areas of the nasal cavity and paranasal sinuses can be affected but the lateral wall, ethmoids and maxillary sinus are the most common primary sites. The frontal and sphenoid sinuses are rare primary sites for reasons that are unknown.

Initial symptoms such as nasal blockage, blood-stained discharge and loss of smell are often overlooked though their unilateral nature should raise suspicion. Delayed presentation is common. Subsequent extension into the orbit, nasolacrimal system, anterior cranial cavity, cavernous sinus, pterygomaxillary fissure, palate, skin and infratemporal fossa may produce symptoms such as proptosis, diplopia and epiphora, trismus, pain, oroantral fistula, paraesthesia, or other neurological deficits or a mass.

Investigation should include computerised tomography (CT) and magnetic resonance imaging (MRI), which are complementary in the skull base, and biopsy. CT scans give excellent bony details and are helpful in determining whether a tumour remains confined within these natural boundaries or has eroded through the surrounding bone. They also provide details of the extent of local bony invasion and are useful in assessing the lamina papyracea, orbital floor, cribriform plate and pterygoid plates. MRI allows better distinction of tumour from adjacent soft tissues and retained mucus and is particularly useful for determining invasion of the orbital contents, dura, brain and cavernous sinus. An MRI may also be better for assessing carotid artery invasion.

Discussion about management of these rare tumours should ideally occur in a skull base multidisciplinary team (MDT). All decisions about treatment will involve the patient, their family and carers at every point in the pathway.

Lymph node involvement at diagnosis is low. Rates are higher with increasing T stage, and squamous and undifferentiated histology. In T3–T4 SCC maxillary tumours, elective nodal treatment of ipsilateral levels Ib and II has been advocated. In contrast, ethmoid sinus tumours have been associated with low rates of both lymph node involvement at diagnosis and nodal recurrence (~2% and 7%, respectively).

Follow-up is required to detect recurrence and to manage surgical sequelae (nasal crusting, epiphora etc). Follow-up should be extended as some tumours can recur many years after treatment and should include careful examination of the cavity with the endoscope and MR scans.

Recommendation

Sinonasal tumours are best treated de novo and unusual polyps should be imaged and biopsied prior to definitive surgery.

(Recommendation grade D)

Treatment of sinonasal malignancy should be carefully planned and discussed at a skull base MDT meeting with available histology and all of the necessary imaging.

(Recommendation grade D)

2 Endoscopic Resection of Sinonasal Tumour

The accepted method of resecting tumours of the anterior skull base is craniofacial resection. However, recent technological advances have facilitated endoscopic resection of malignant tumours of the lateral nasal wall and anterior skull base with safety and precision.

In some cases, tumour resection may be entirely endoscopic, but the endoscope may also be combined to enhance surgical resection with craniotomy, mid-facial degloving and lateral rhinotomy.

Patients with sinonasal malignancy undergoing purely endonasal resection are reported to have outcomes as good as conventional external surgical techniques with the potential for lower morbidity and shorter hospital stays.

Endoscopic resection of sinonasal tumours should be managed in units that have comprehensive skull base expertise and that can manage all facets of the patient's care.

2.1 Indications for endoscopic endonasal resection

Prior to undertaking this means of treatment, a clear operative plan must be considered by an MDT with the full range of expertise in the management of sinonasal malignancy. Surgeons undertaking endoscopic resection must be experienced in both endoscopic techniques and the full range of other surgical options with which they may be combined and must also be familiar with the natural history of the wide range of malignant sinonasal tumours.

Once a decision has been made to treat a tumour surgically, the aim should define whether this is with curative intent or palliation.

2.2 Contraindications to endoscopic resection

- Tumours invading facial soft tissues should not be attempted endoscopically.
- Tumours that are very vascular would pose a considerable problem if resected endoscopically. Embolisation within days of definitive surgery should be considered in these cases.
- Relative contraindications to endoscopic resection include extension to the orbital apex or laterally to the pterygomaxillary space and infratemporal fossa. Malignant tumour invasion of the cavernous and sagittal sinuses and brain parenchyma is difficult to clear endoscopically, but a decision to operate under these circumstances would mainly be for palliation rather than cure.

2.3 Surgery

Intra-operative computer-assisted navigation should ideally be available. Some systems incorporate CT–MR fusion and 3-dimensional CT angiography.

Powered instruments should also include a microdebrider and high-speed drill systems with long diamond burrs and curved drills designed for intranasal use.

Diathermy instruments designed for endoscopic intranasal use should be available, bipolar diathermy being preferable.

Resecting tumours endoscopically is aided by having two surgeons using a 3–4-handed technique via both sides of the nose. This technique is facilitated by partial excision of the nasal septum.

Recommendation

Essential equipment is necessary and must be available prior to commencing endonasal resection of skull base malignancy.

(Recommendation grade D)

En bloc resection is usually not possible in the skull base. The most important principle is to obtain clearance of tumour margins, confirmed with frozen section when necessary. The incidence of positive tumour margins is reported to be similar in patients with advanced anterior skull base disease undergoing either endoscopic resection or traditional craniofacial resection.

Dura may be resected if invaded by tumour, but if extensive, an open approach may be more suitable.

The extent of resection is determined by the histology: for olfactory neuroblastoma, the olfactory bulbs and tracts may be resected, but for high-grade malignancy invading critical structures such as the cavernous sinus, complete resection is not possible.

Recommendation

Endoscopic skull base surgery may be facilitated by two surgeons working simultaneously, utilising both sides of the nose.

To ensure the optimum oncological results, the primary tumour must be completely removed and margins checked by frozen section if necessary.

(Recommendation grade D)

Reconstruction of the skull base defect is essential if the skull base or dura has been included in the resection. A multilayered technique is recommended and graft materials include autologous fascia, cartilage, fat, split calvarial bone and local mucosal flaps and grafts.

Large pedicled septal mucosal flaps based on the sphenopalatine artery have been described but are suitable only if the mucosa is not invaded by the tumour.

Recommendation

It is essential to perform a careful, substantial repair of any skull base or dural defect at the time of the primary surgery.

(Recommendation grade D)

2.4 Results

Five-year disease-specific survival rates of 85% after endoscopic resection of sinonasal malignancy are reported though selection bias needs to be taken into account. Encouraging results with good local control are reported following the endoscopic resection of olfactory neuroblastoma.

The overall survival of adenocarcinoma after endoscopic resection is reported at 92% with a median follow-up of 30 months. The results following endoscopic resection of SCC are significantly worse.

The outcome is dependent on the histology of the primary tumour as well as the presence of intracranial spread and positive surgical margins. With more recent larger series, it appears that survival is worse with increasing T-stage.

Survival is best for patients who have not undergone previous surgery with incomplete resection.

3 Craniofacial Resection

3.1 Approaches

Type 1 craniofacial or trans-orbital cranial facial uses the lateral rhinotomy incision extended up into a Lynch incision. There is no need to extend this incision around the nasal alar, so avoiding any asymmetry of the alar base. Wide release of the orbital periosteum and lacrimal duct allows gentle lateral reflection of the orbital contents, giving excellent exposure of the ethmoids and cribriform plate, lateral nasal wall, fronto-nasal duct, lamina papyracea and orbital periosteum – all of which can be resected. Small areas of ethmoidal roof, cribriform plate and the olfactory bulb can be resected from below and dura can be resected and repaired as necessary.

The type 2 craniofacial includes a shield-shaped window craniotomy over the frontal sinus allowing excellent exposure of the superior surface of the cribriform plates allowing en bloc resection of dura, cribriform plate and early brain involvement. It allows robust repair of the dura under direct vision with fascia lata or pericranium.

The type 3 craniofacial involves an approach to the ethmoids via a lateral rhinotomy-type incision and a large frontal craniotomy approached by a bicoronal incision. This is required only for significant intracranial disease requiring neurosurgical input.

3.2 Orbital management

An understanding of the anatomical barriers to the disease is very important. Both the dura and the orbital periosteum provide significant barriers. In particular, the orbital periosteum may still be intact despite considerable intra-orbital tumour with proptosis.

Although care must be taken to avoid attempting orbital preservation at the potential cost of decreased local disease control and survival, at present the most commonly performed approach with frozen section control is to resect involved orbital periosteum and preserve the orbital contents in cases where there is no invasion through the periosteum into orbital fat, orbital musculature or orbital apex. There does, however, remain some debate about the oncological basis for this. Although, psychologically, the loss of an eye is often very difficult for patients to consider, it must be remembered that preservation of a painful eye with diplopia and poor vision following radiotherapy is a significantly worse outcome than orbital clearance with an excellent prosthesis.

3.3 Contraindications to surgery

Anatomical areas which preclude surgical intervention differ with the aggressiveness of the pathology. An aggressive tumour invading the cavernous sinus, particularly if it reaches the internal carotid artery or with massive intracranial extension, would be deemed incurable and the morbidity of surgical intervention would outweigh any potential benefits. These, however, are probably the only anatomical contraindications to surgery. With slower growing tumours quite significant intracranial disease may well still be amenable to surgical intervention with a hope of long-term survival. Significant involvement of both eyes or the loss of an only seeing eye is a devastating consequence of surgery and this would be a relative contraindication to any surgical resection.

3.4 Results

Results from combined surgery and radiotherapy are dependent on pathology and the anatomical areas involved by tumour, with results if orbit and brain are involved being extremely poor. Involvement of the periorbita or dura also reduces survival.

- SCC: overall 5-year survival is in the region of 30–50%
- Adenocarcinoma: a 5-year survival is of the order of 45–60%
- Olfactory neuroblastoma: a 5-year survival rate of 75% is attainable.

4 Radiotherapy and Chemotherapy for Sinus Cancer

4.1 The role of radiotherapy

Sinonasal tumours are often advanced at presentation, invading adjacent structures, and lie in close proximity to many organs at risk of damage from radiation (lens, retina, optic nerve and chiasm, pituitary gland). This makes irradiation to a radical dose difficult. If orbital or brain invasion occurs, survival rates are extremely poor despite aggressive treatment.

The most common management approach is surgery followed by post-operative radiotherapy, although some protocols have used chemotherapy.

Following surgery that involves a dural repair, a longer interval before radiotherapy may be preferred to allow healing.

The sequence of surgery and radiotherapy remains open to debate, with no significant differences in outcome found. Pre-operative chemo-radiotherapy may allow for less extensive surgery in advanced tumours.

The implementation of new advanced radiation techniques, such as intensity modulated radiotherapy (IMRT), is especially attractive in sinus tumours as the dose distributions achieved with conventional techniques are rather inhomogeneous, with areas of low dose that can potentially contribute to local recurrence. IMRT has demonstrated improved coverage of the tumour bed and potential sites of spread, while ensuring that levels of radiation exposure are kept within the tolerance of adjacent neurological structures. Prospective studies with mature outcome data, however, are not yet available.

Dose escalation above conventional dose levels is achievable with IMRT and this will be an active area of future study to improve local control, since the majority of local failures occur within the radiation field. Patients with the most advanced tumours, previously thought to be suitable only for palliation, may then become treatable radically.

Proton therapy is currently under evaluation and may have a role in treating small volume disease, e.g. low-grade tumours at the skull base or close to radiosensitive structures, due to rapid dose fall-off. Sub-volumes may also be potentially treated using protons as a boost to residual tumour masses within a larger photon field, as mixed plans.

4.1.1 Radiation toxicity

Doses delivered with conventional radiotherapy are of the order of 60–70Gy and are known to cause blindness in up to a third of patients; too often, sacrifice of the sight in one eye is unavoidable.

Care must be taken to avoid a dry eye, caused by radiation injury from quite modest doses to the lacrimal gland (30Gy), as optic pain, perforation and even enucleation may ensue.

Brain radio-necrosis is a potentially devastating complication of radiotherapy and the risk depends on total dose, dose per fraction, overall treatment time and volume, with tolerance for partial volume irradiation set at 60Gy. There is, however, very little information on the effect of irradiating large volumes of tissue to lower doses, as occurs with IMRT, due to the multiple radiation portals.

Conventional dose prescriptions include 60–70Gy in 30–35# over 6 to 7 weeks for SCC, adenocarcinoma, undifferentiated carcinoma and olfactory neuroblastoma. Doses for lymphoma are ~40–50Gy in 20–25# over 4 to 5 weeks. Accelerated, hyper- and hypo-fractionated regimens remain investigational.

Recommendations for radiotherapy

The most common management approach is surgery followed by post-operative radiotherapy ideally within 6 weeks.

(Recommendation grade C)

Radiation is given first if a response to radiation may lead to organ preservation.

(Recommendation grade C)

Radiotherapy should be delivered within an accredited department using megavoltage photons from a linear accelerator (typical energies 4–6MV) as an unbroken course.

(Recommendation grade B)

3D conformal radiotherapy is the standard technique but IMRT can improve target coverage, allow for dose escalation and facilitate organ sparing to reduce toxicity.

(Recommendation grade D)

4.2 The role of chemotherapy

Consensus statements are difficult due to the lack of adequately powered, randomised evidence.

Small-scale observational studies have reported on topical and intra-arterial chemotherapy but are not recommended. Neo-adjuvant systemic chemotherapy, usually cisplatin based, in the phase II setting produces a response in about two thirds of patients and has been used prior to surgery or chemo-radiation. Concomitant chemotherapy using various regimes has suggested improved disease-free and overall survival

at 5 years to ~70% and ~67% respectively. In this setting the chemotherapy agent, usually cisplatin, is acting as a radiation sensitiser.

Chemotherapy has also been reported to be of use in undifferentiated carcinomas, neuroendocrine and small cell carcinomas. Excellent local and distant control rates for olfactory neuroblastoma have been demonstrated with local therapy alone, and chemotherapy in this setting is experimental but often given in the presence of locally advanced disease.

For sinonasal SCC there is no randomised evidence in favour of the use of concomitant chemo-radiation. Evidence supporting its use both in the primary and adjuvant setting can be extrapolated from other head and neck malignancies.

Chemotherapy may improve quality of life and offer a modest survival benefit in the palliative setting, translating from benefit seen in other head and neck SCC sites.

Molecular targeted treatments are under investigation but none has proven benefits to date.

Recommendations for chemotherapy

Chemotherapy may be given in the following settings:

- as part of triple therapy, e.g. embryonal rhabdomyosarcoma.
(Recommendation grade B)
- in concurrent combination with radiation in locally advanced disease, e.g. SCC of maxilla.
(Recommendation grade D)
- for palliation, e.g. poorly differentiated SCC with disseminated disease.
(Recommendation grade B)

4.3 Palliation

Some patients present with advanced disease where radical treatment is not appropriate. Surgery, radiotherapy and chemotherapy all have a potential role in palliation.

Palliative radiotherapy treatment requires high doses to achieve any significant tumour control, and short fractionation regimes are associated with marked acute toxicity. Regimens that can be considered on an individual basis include 50Gy in 20# over 4 weeks, 27Gy in 6# over 3 weeks and 36–39Gy in 12–13# over 2½ weeks.

If patient has a localised disease recurrence, then retreatment with IMRT or the CyberKnife may be considered, especially if there has been a long disease-free interval.

5 Key Points

- Endoscopy and imaging (CT and MRI) are key to assessing tumour extent and planning surgical approach.
- Endoscopic techniques enable low morbidity and low recurrence rates to be achieved in suitable tumours and may be performed for curative or palliative reasons.

- A high level of expertise in endoscopic sinus surgery and skull base/dural reconstruction is a necessity before undertaking endoscopic resections.
- Patients should be discussed at a skull base MDT meeting supported by all the necessary expertise. A multidisciplinary approach is paramount. The majority of patients will require adjuvant radiotherapy. Likewise, many patients require either an immediate prosthesis or staged dental or orbital rehabilitation with osseo-integrated implants.
- Neurosurgical support and neuronavigation should be routinely available in centres undertaking this surgery.
- Diligent tumour surveillance with nasal endoscopy and interval MRI scans are a necessity following treatment of sinonasal malignancy.
- Craniofacial resection should be undertaken in centres carrying out 10–20 procedures a year.

6 Key References

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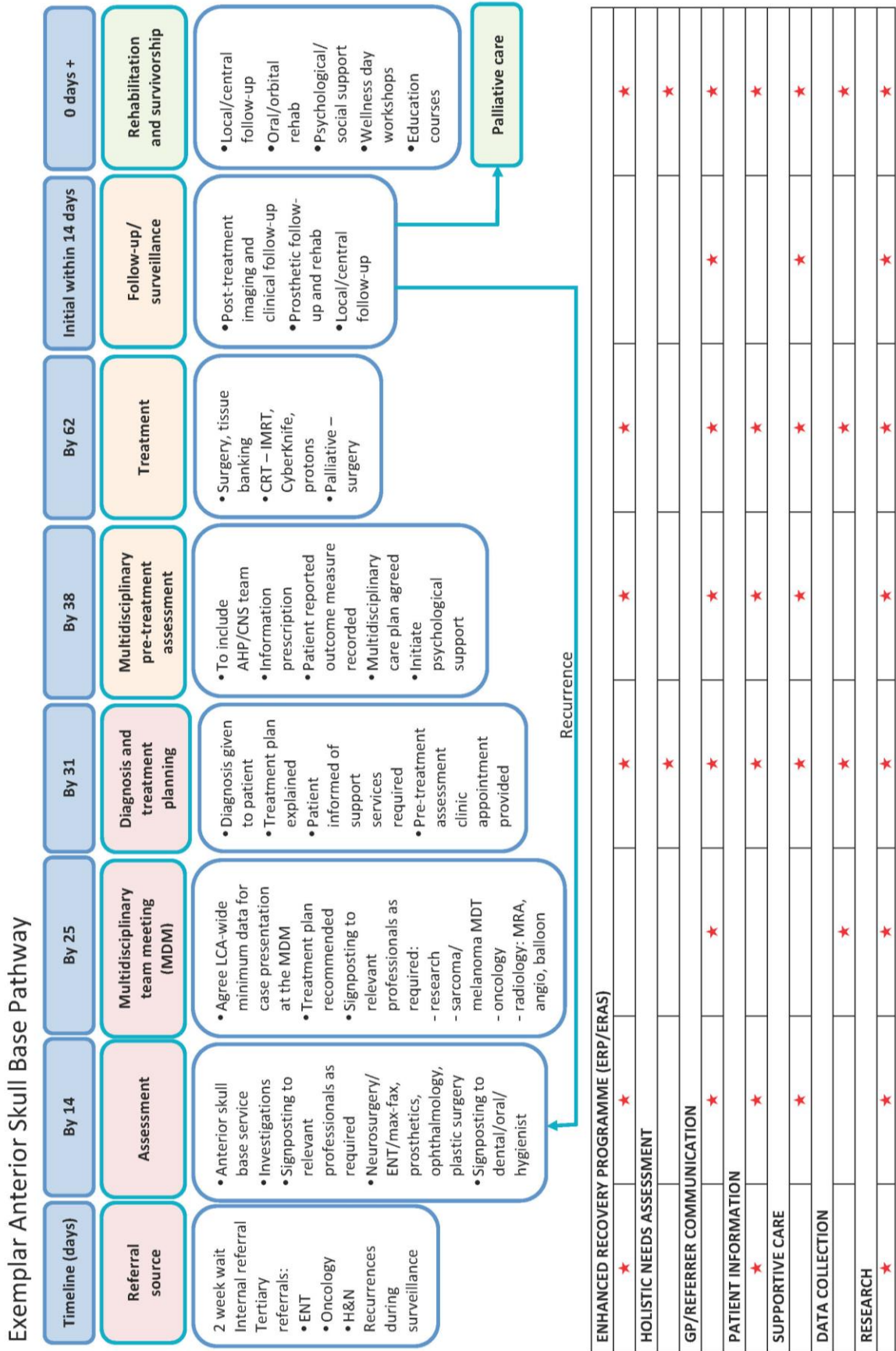
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Appendix: Exemplar Anterior Skull Base Pathway



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