Eur Radiol (2007) 17: 2622–2630
DOI 10.1007/s00330-007-0616-z

F. Dubrulle
R. Souillard
R. Hermans

Extension patterns of nasopharyngeal carcinoma

Received: 7 November 2006
Revised: 2 February 2007
Accepted: 9 February 2007
Published online: 3 April 2007

F. Dubrulle (✉) · R. Souillard
Department of Radiology,
Centre Hospitalier Universitaire,
59037 Lille cedex, France
e-mail: f-dubrulle@chru-lille.fr
Tel.: +33-3-20446191
Fax: +33-3-20446138

R. Hermans
Department of Radiology,
University Hospitals,
Leuven, Belgium

Abstract The nasopharynx represents an intersection between the nasal choanae, the oropharynx, the deep facial spaces, the skull base and the intracranial cavity. Most nasopharyngeal neoplasms are malignant tumors showing aggressive local infiltration along well-defined routes. The primary role of imaging is accurate tumor mapping and detection of possible tumor extension, especially to the skull base and the deep facial spaces. The aim of this paper is to illustrate these extension patterns of nasopharyngeal carcinomas on imaging and to show the particular implication of imaging in the correct staging of the lesion.

Keywords Nasopharyngeal cancer · Diagnostic imaging · Tumor staging · Magnetic resonance imaging

Introduction

The nasopharynx constitutes the upper part of the pharynx and aerodigestive tract. It lies under the skull base and represents an intersection between the nasal choanae, the oropharynx, the deep facial spaces, the skull base and the intracranial cavity. Most nasopharyngeal neoplasms are malignant tumors. It is fundamental to analyze the extension of these tumors in this area, especially at the skull base foramen and the deep facial spaces.

Specific anatomy

The nasopharynx (Fig. 1) is a cuboid cavity underneath the skull base. The boundaries of the nasopharynx are as follows: superiorly, the basisphenoid and the clivus; posteriorly, the retropharyngeal and prevertebral space; anteriorly, the nasal choanae; inferiorly, the oropharynx; laterally, the parapharyngeal space. Anteriorly, the soft palate separates the nasopharynx from the oropharynx (the posterior side of the soft palate belongs to the nasopharynx, the inferior side to the oropharynx). Posteriorly, there is no clear separation between the nasopharynx and oropharynx; on imaging studies, this separation can be made by drawing a horizontal line along the superior edge of the anterior arch of C1 [1] or through the atlanto-axial articulation, depending on the author.

The nasopharyngeal mucosa consists of epithelium delineating the pharyngeal mucosal space. The submucosal space also contains lymphoid tissue, accessory salivary glands, cellular notochord remnants, and tensor and levator veli palatini muscles. There are two main mucosal-lined recesses (Fig. 2):

– the eustachian tube orifice, just in front of the torus tubarius
– the lateral pharyngeal recess or fossa of Rosenmüller, located superior and posterior to the torus tubarius

Because of the configuration of the torus tubarius, the fossa of Rosenmüller appears posterior on axial images and superior on coronal images to the eustachian tube orifice [2].

The adenoids, or pharyngeal tonsils, consist of lymphatic tissue located midline in the roof of the nasopharynx. Prominent adenoids are typically present in children.

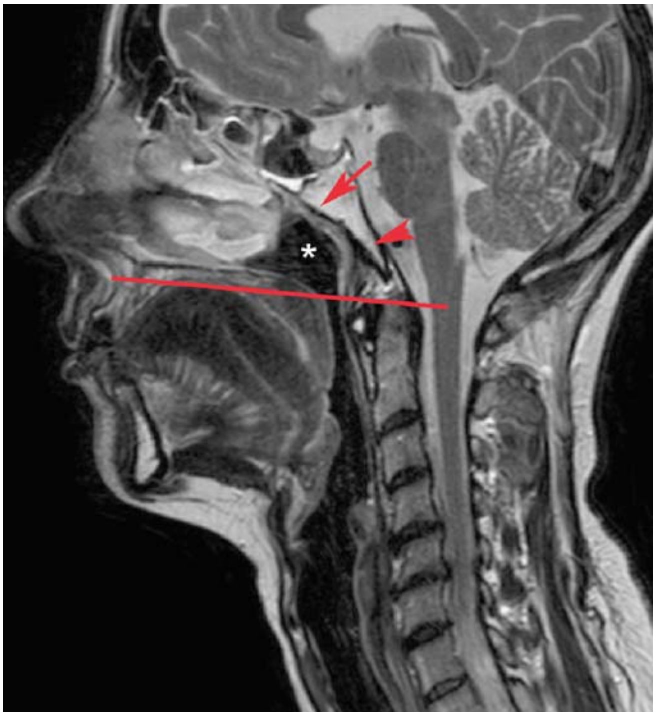


Fig. 1 Sagittal TSE T2-weighted MR image showing the nasopharynx (*asterix*) and its superior limit represented by the basisphenoid (*arrow*) and the clivus (*arrowhead*). Inferiorly, the junction between nasopharynx and oropharynx (*red line*) is represented by a line between the hard palate and the superior edge of the anterior arch of C1

Gradual adenoidal involution begins around the time of puberty; the majority of the individuals have lost most of this adenoidal tissue by 30 years of age.

The pharyngobasilar fascia (Fig. 2b), a tough aponeurosis, separates the nasopharynx from the masticator space [3]. This pharyngobasilar fascia attaches to the skull base, anteriorly to the medial plate of the pterygoid process, and superiorly to the inferior part of the petrous apex. The foramen ovale is lateral to this fascia, while the foramen lacerum is within the attachment of this fascia to the skull base (Fig. 2). Posteriorly, the pharyngobasilar fascia attaches to the occipital pharyngeal tuber and the prevertebral muscles. The eustachian tube and levator veli palatini muscle enter the nasopharynx through a posterolateral defect of the pharyngobasilar fascia; this defect is known as the sinus of Morgagni.

The strong pharyngobasilar fascia limits tumor spread, but there are two points of weakness, representing privileged pathways for tumor spread:

– skull base and intracranial spread may occur through the foramen lacerum, despite the closure of this orifice by a fibro-cartilage
– posterolateral spread may occur through the sinus of Morgagni.

The pharyngobasilar fascia separates the nasopharynx from the deep facial spaces laterally: the prestyloid compartiment of the parapharyngeal space, and the retrostyloid compartiment of this space (essentially corresponding to the carotid space). The retropharyngeal space is located posteriorly, anterior to the prevertebral space. The retropharyngeal space is more or less continuous with the retrostyloid parapharyngeal space. Within the retropharyngeal space are the retropharyngeal nodes, constituting the primary nodal drainage of the nasopharynx.

Nasopharyngeal carcinomas

Histology

Most nasopharyngeal neoplasms are malignant tumors. Undifferentiated carcinoma is the most common form of

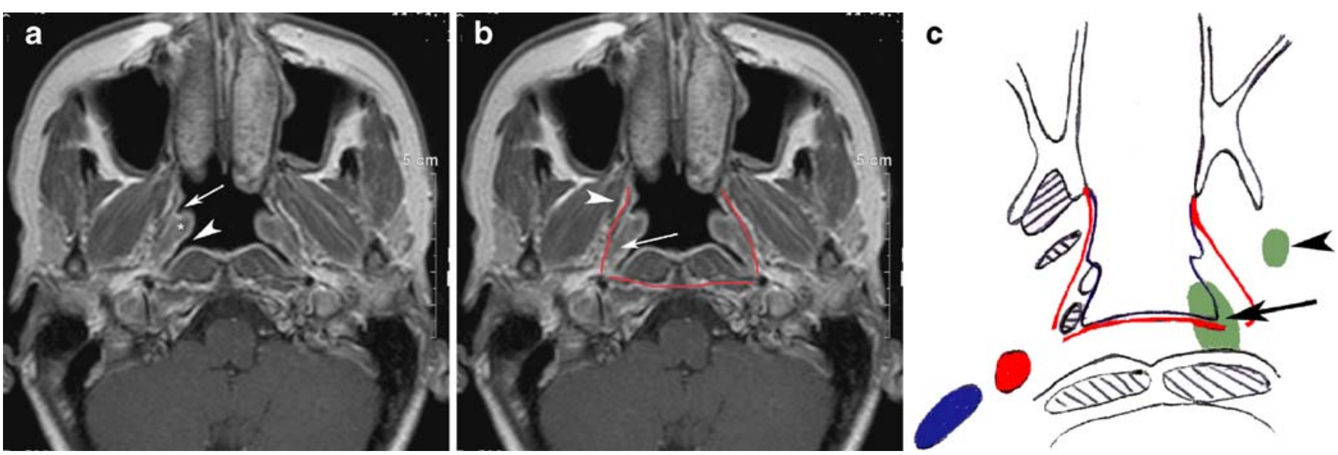


Fig. 2 **a** Axial image illustrates the nasopharynx recesses: eustachian tube orifice (*arrow*) and Rosenmüller fossa posteriorly (*arrow*head), separated by the torus tubarius (*asterisk*). **b** Pharyngobasilar fascia schematic (*red*): levator levi palatine muscle (*arrow*) is medial to the fascia whereas tensor veli palatine muscle (*arrowhead*) is lateral. **c** Schematic drawing of foramen lacerum (*arrow*) and foramen ovale (*arrowhead*). The foramen lacerum is within the attachement of the pharyngobasilar fascia, whereas the foramen ovale is lateral to this fascia

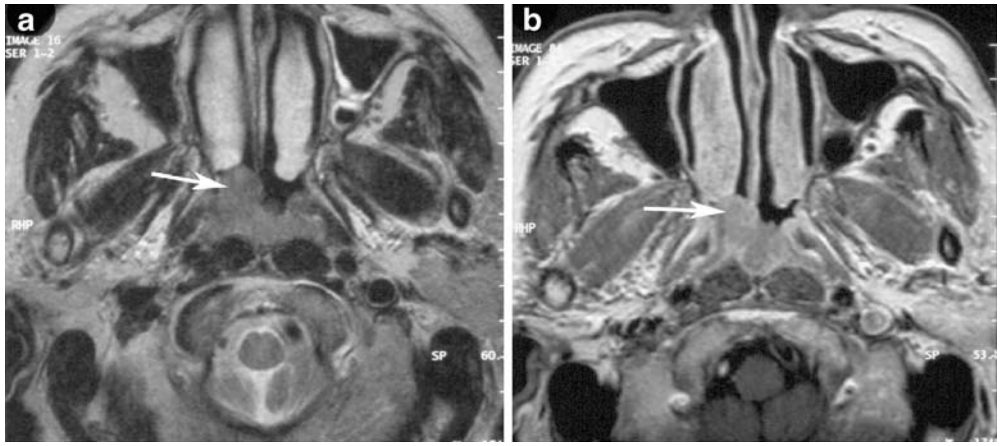


Fig. 3 Right nasopharyngeal tumor detected at an early stage in the area of the Rosenmüller fossa. The tumor (*arrow*) shows **a** intermediate signal intensity on T2-weighted MR image and **b** moderate enhancement (*arrow*) on contrast-enhanced T1-weighted MR image

malignancy, accounting for up to 98% of all nasopharyngeal malignancies in the Orient. The highest incidence rates are found in southern China and Hong Kong. Also, the southern rim of the Mediterranean is mostly affected. This represents the outcome of interactions of genetic factors, environmental factors and Epstein-Barr virus (EBV) infections. Patients with undifferentiated carcinoma show high levels of antibodies to EBV antigens [2, 5].

A variety of other malignancies arise in the nasopharynx, such as adenocarcinoma, cystic adenoid carcinoma, rhabdomyosarcomas and lymphoma.

Among benign nasopharyngeal lesions, prominent adenoids in children and teenagers are most common. Another benign lesion is a Thornwald cyst, a notochord derivative, which is a well-delineated cystic lesion, located midline in the roof of the nasopharynx.

Clinical presentation

Clinical complaints linked to nasopharyngeal tumors are usually subtle at the beginning. The average delay between the first symptoms and the discovery of the malignancy is 8–10 months.

The most common complaint at clinical presentation is cervical lymphadenopathy. In nasopharyngeal carcinoma, there is no relationship between the primary tumor size and the presence of nodal disease.

Other common presenting symptoms are otalgia, the sensation of an obstructed ear, or conductive hearing loss due to serous otitis, caused by eustachian tube obstruction. Imaging of the nasopharynx must be performed in the case of unilateral serous otitis in an adult, even if the clinical examination of the nasopharynx is normal.

Other symptoms include headaches, nasal obstruction and epistaxis.

Advanced tumors may present with neurologic symptoms such as headaches or palsies of cranial nerves.

Natural history

The fossa of Rosenmüller is a common site of origin of nasopharyngeal tumors (Fig. 3). Tumor tends to spread submucosally with early infiltration of the palatal muscles, in particular the levator veli palatini muscle. This muscle is responsible for opening of the eustachian tube orifice during swallowing, and its dysfunction results in serous otitis (Fig. 4).

The tumor will spread through areas of lesser resistance of the pharyngobasilar fascia, and into the deep spaces of the face.

Lymphadenopathy is present in up to 90% of the patients, the first involved site being the retropharyngeal nodal chain.

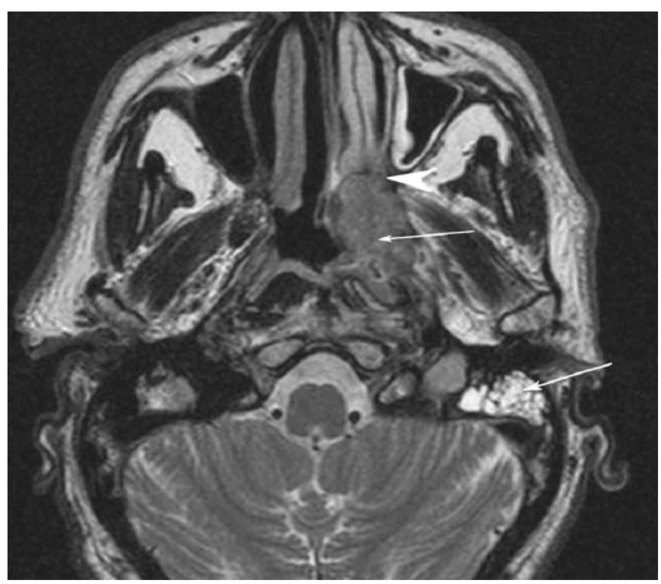


Fig. 4 Patient presenting with a left nasopharyngeal tumor (*anterior arrow*), showing intermediate signal intensity on T2-weighted MR image. Note the anterior extension to the left choana (*arrowhead*). Associated serous otitis (*posterior arrow*)

TNM classification

TNM classification was adapted in 2002, with the sixth edition of the nasopharyngeal carcinoma UICC TNM classification [6, 7] (Table 1). Some investigators have shown that tumor volume is an important prognostic factor [8, 9], and in the future, tumor volume may be incorporated into the nasopharyngeal carcinoma TNM classification.

Extension patterns on imaging

Imaging issues

The primary role of imaging is accurate tumor mapping with description of possible tumor extension to the skull base and the deep facial spaces. Magnetic resonance imaging (MRI) is more sensitive than computed tomography (CT) to detect perineural tumor spread and bone marrow changes in the skull base [3, 4]. However, early skull base erosion is best depicted on CT (Fig. 5).

Therefore, it may be useful to perform both a high resolution (HR) CT study of the skull base, and a MRI of the skull base and the neck.

The MRI study should be performed by using a dedicated head and neck coil, including the following sequences:

- HR turbo spin echo (TSE) T2-weighted sequence in the axial and coronal planes.
- HR spin echo (SE) T1-weighted sequence, without contrast or fat saturation in order to visualize skull base involvement showing modifications of the normal high signal in the bone marrow.
- Contrast-enhanced axial and coronal HR SE T1-weighted sequence with fat saturation.
  This sequence is helpful to analyze deep extension, in particular perineural spread to the skull base and the endocranium. This sequence is also very useful to depict lateral spread to the prestyloid and retrostyloid

Table 1 TNM classification of nasopharyngeal carcinoma, sixth edition (2002)

Descriptions of nasopharyngeal carcinoma based on TNM classification			
T Primary tumor			
T1	Tumor confined to the nasopharynx		
T2	Tumor extends to soft tissues of oropharynx and/or nasal fossa		
	T2a	Without parapharyngeal extension	
	T2b	With parapharyngeal extension	
T3	Tumor invades bony structures and/or paranasal sinuses		
T4	Tumor with intracranial extension and/or involvement of cranial nerves, infratemporal fossa, hypopharynx or orbit		
N Regional lymph nodes			
Nx	Regional lymph nodes can not be assessed		
N0	No regional lymph nodes metastasis		
N1	Unilateral lymph node(s) metastasis, 6 cm or less in greatest dimension, above supraclavicular fossa		
N2	Bilateral lymph nodes metastasis, 6 cm or less in greatest dimension, above supraclavicular fossa		
N3	N3a	Lymph node(s) metastasis greater than 6 cm in dimension	
	N3b	Lymph node(s) metastasis in the supraclavicular fossa	
Stage			
Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage IIA	T2a	N0	M0
Stage IIB	T1	N1	M0
	T2a	N1	M0
	T2b	N0, N1	M0
Stage III	T1	N2	M0
	T2a–T2b	N2	M0
	T3	N0, N1, N2	M0
Stage IVA	T4	N0, N1, N2	M0
Stage IVB	Any T	N3	M0
Stage IVC	Any T	Any N	M1

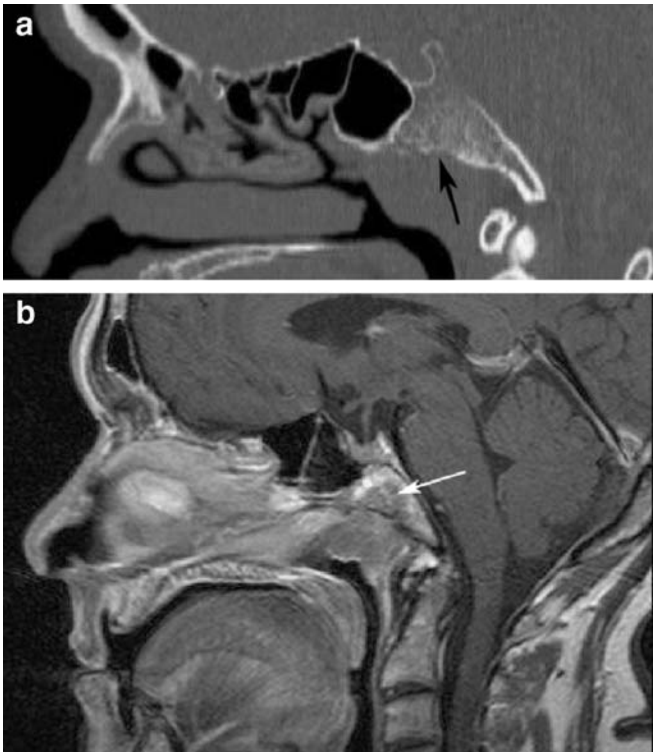


Fig. 5 Patient presenting with a nasopharyngeal tumor showing direct superior extension and infiltration of the sphenoid bone. **a** CT depicts small skull base erosions, **b** whereas MRI, in particular the non-enhanced T1-weighted sequence without fat saturation, shows a much more important infiltration of sphenoid bone marrow

compartiments of the parapharyngeal spaces, as well as the infratemporal fossa.
– TSE T2-weighted sequence in axial plane for the research of cervical lymph nodes including the supra-clavicular fossa

Nasopharyngeal tumors, and especially undifferentiated carcinomas, usually present with intermediate signal intensity, superior to the muscle signal, on T2-weighted images, low signal intensity on T1-weighted images, and moderate enhancement (Fig. 3) on contrast-enhanced T1-weighted images, best defined with fat saturation [1, 10].

Tumoral spread

As explained, nasopharyngeal tumors spread along well-defined routes.

Anterior spread

Nasopharyngeal tumors often spread to the nasal fossa, which is not separated from the nasopharynx by any anatomic barrier. From the nasal fossa, the tumor may easily infiltrate the pterygopalatine fossa through the sphenopalatine foramen (Fig. 4). The earliest sign of involvement of the pterygopalatine fossa is replacement of its normal fat content by tumoral tissue (Fig. 6).

Once tumor gains access to the pterygopalatine fossa, it can spread into (Fig. 7):

– the foramen rotundum along the maxillary nerve (V2)
– the inferior orbital fissure and further the orbital apex, from where the tumor can extend intracranially through the superior orbital fissure.
– the infratemporal fossa, where the masticatory muscles are at risk of invasion. Erosion of the pterygoid process may occur. Perineural extension along the mandibular nerve (V3) into the foramen ovale and the endocranium is also possible (Fig. 7e)
– the vidian canal along the pterygoidien nerve and further to the petrous apex.

Lateral spread

Lateral extension to the parapharyngeal spaces can occur directly through the pharyngobasilar fascia (Fig. 8), or indirectly through the sinus of Morgagni, the fascia's point of weakness. Further lateral spread involves the infratemporal fossa and the masticator space infiltrating the pterygoid muscles. From the masticator space, perineural extension along the mandibular nerve (V3) may occur, leading to infiltration of the foramen ovale and the cavernous sinus (Fig. 7e).

Fig. 6 Axial TSE T2-weighted image showing left nasopharyngeal tumor extending to the pterygo-palatine fossa (*arrow*)

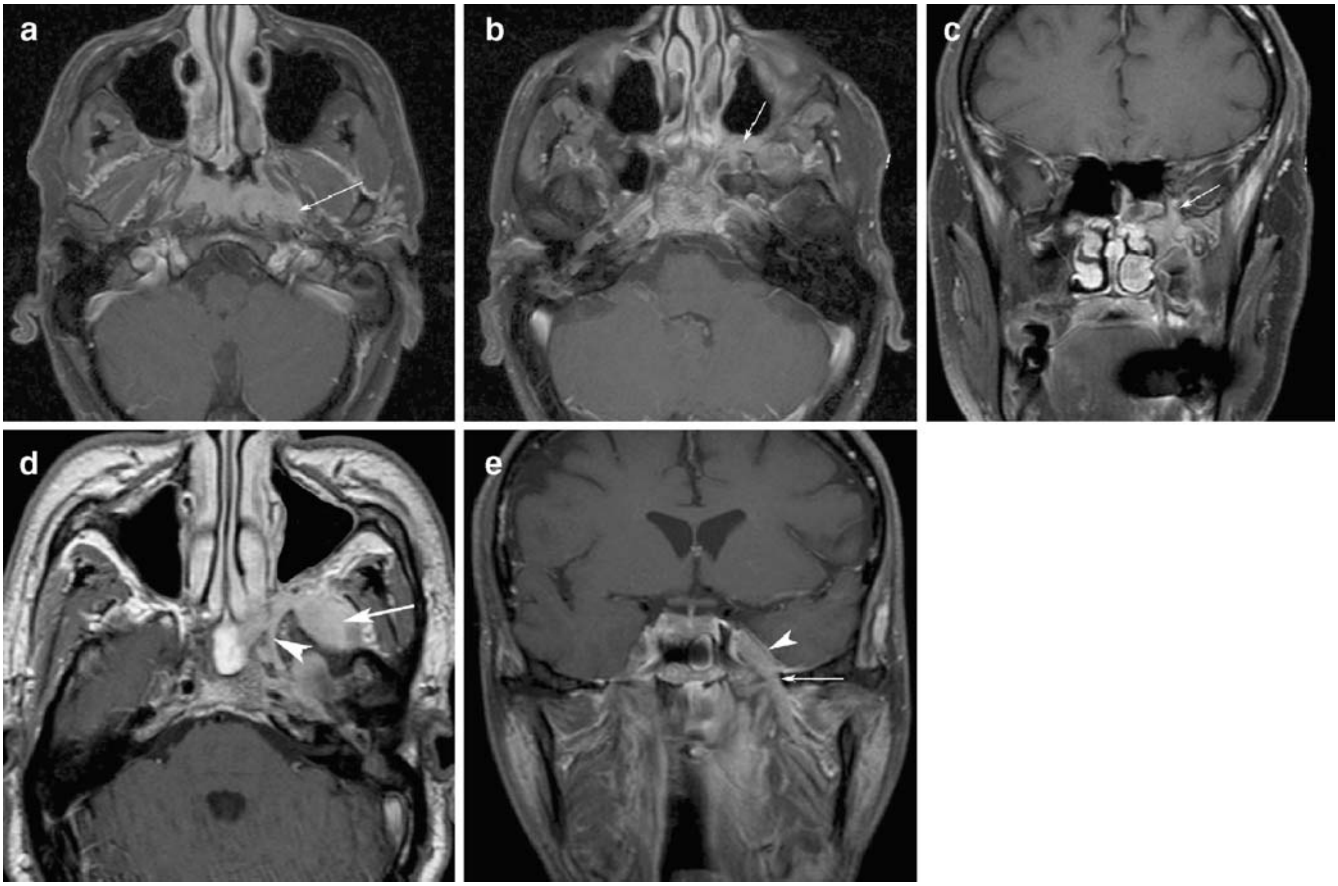
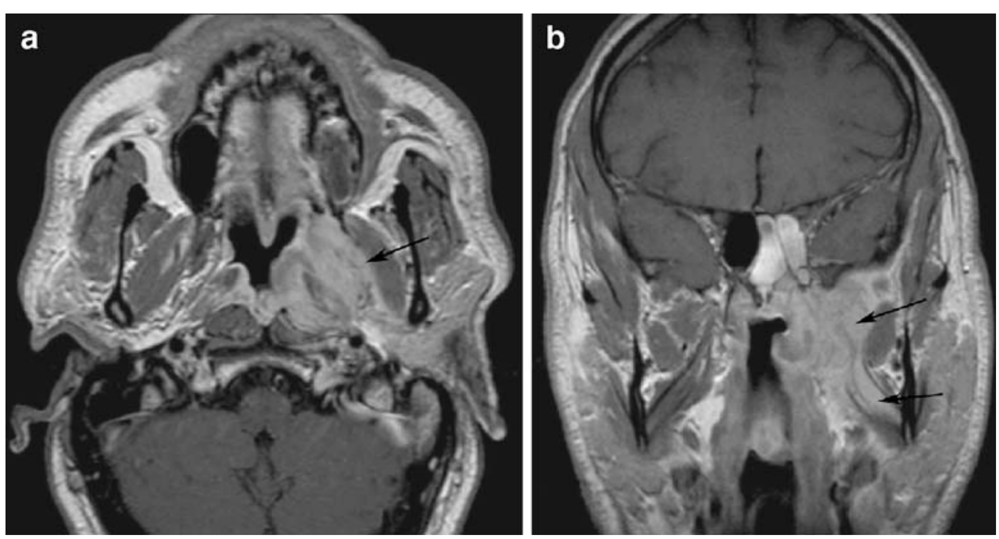


Fig. 7 Contrast-enhanced SE T1-weighted MR images with fat saturation illustrating different pathways of extension in a patient suffering nasopharyngeal tumor. **a** Extension through the sinus of Morgagni, weakness point of the pharyngobasilar fascia (*arrow*). **b** Extension into the pterygopalatine fossa (*arrow*), neural crossroad within the skull base. **c** From the pterygopalatine fossa, the tumor extends to the inferior orbital fissure (*arrow*). **d** Extension to the infratemporal fossa (*arrow*) and to the pterygoid canal with perineural spread along the vidian nerve (*arrowhead*). **e** Perineural spread along the mandibular nerve (V3) extending to the foramen ovale (*arrow*) and the cavernous sinus (*arrowhead*)

Fig. 8 Contrast-enhanced T1-weighted MR images in a patient presenting with direct lateral extension through the pharyngobasilar fascia to the prestyloid compartiment of the parapharyngeal space (**a**, *arrow*), and the infratemporal fossa, with infiltration of the pterygoid muscles (**b**, *arrow*)



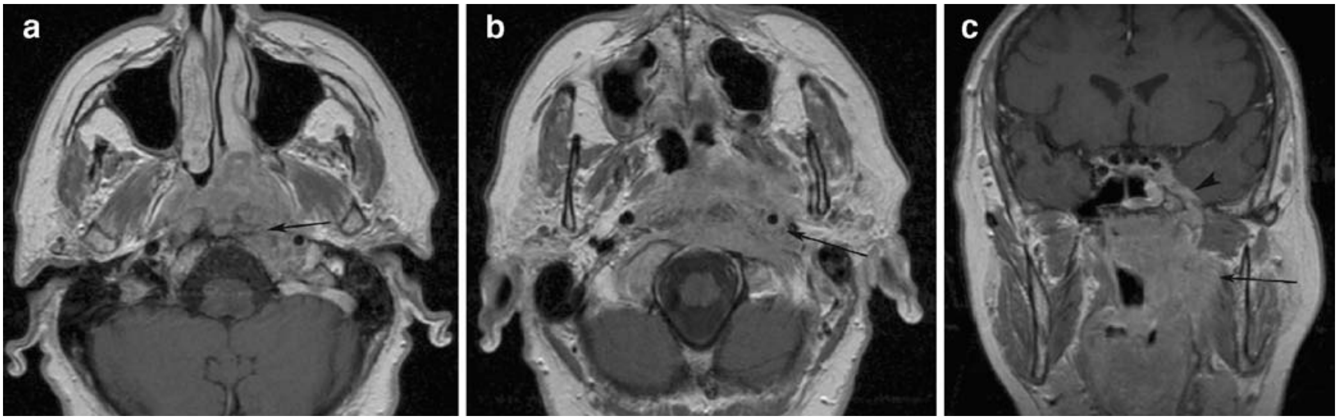


Fig. 9 Spread of an advanced nasopharyngeal tumor. **a** Posterior extension to the retropharyngeal space and prevertebral muscles (*arrow*). **b** Lateral extension to the retrostyloid compartiment of the parapharyngeal space, with encasement and narrowing of the internal carotid artery (*arrow*). **c** Extension to the infratemporal fossa (*arrow*) with intracranial spread into the cavernous sinus through the foramen ovale (*arrowhead*)

Posterior spread

Nasopharyngeal tumors can extend posteriorly to the retropharyngeal space and the prevertebral muscles (Fig. 9). Destruction of vertebral bodies is occasionally seen in very advanced tumors. Posterolateral extension may involve the jugular foramen and the hypoglossal canal (Fig. 10b), with possible but rare spread to the posterior fossa. This posterior extension may result in hypoglossal nerve (XII) palsy.

Inferior spread

Some nasopharyngeal tumors present with submucosal spread into the oropharynx, involving the tonsillar fossa (Fig. 11c). This extension may take place submucosally and thus escape detection by endoscopy, although not detection by imaging.

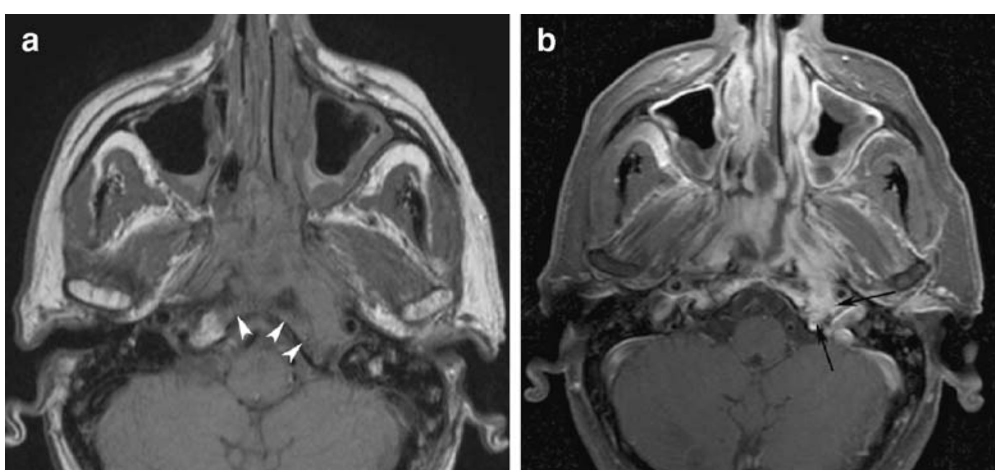
Superior spread

Nasopharyngeal tumor can spread through the foramen lacerum, even if it is contained by the pharyngobasilar fascia. If the tumor extends to the tough fibrous cartilage which closes the foramen lacerum, intracranial extension may occur (Fig. 12).

Superior spread with erosion of the clivus and the sphenoid sinus is also possible leading to intracranial extension (Fig. 5).

Intracranial extension of nasopharyngeal tumors is possible via different pathways such as the foramen lacerum, the foramen ovale and erosion of the skull base. Many studies have illustrated the good sensitivity of MRI to detect such extension, which is usually perineural. The frequency of intracranial abnormalities on MRI is 30% [2]. Nasopharyngeal tumors with intracranial extension are classified as T4 tumors according to the TNM staging system [2, 11]. Intracranial spread is usually extra-cerebral, resulting in involvement of the cavernous and temporal meninges.

Fig. 10 Non-enhanced T1-weighted MR image without fat saturation of a nasopharyngeal tumor extending posteriorly, infiltrating the clivus bone marrow (**a**, *arrowhead*), well identified on this sequence by signal loss within the normally hyperintense bone marrow. **b** On the enhanced T1-weighted image, the tumor is seen to extend laterally to the jugular foramen (*anterior arrow*) and the hypoglossal canal (XII) (*posterior arrow*)



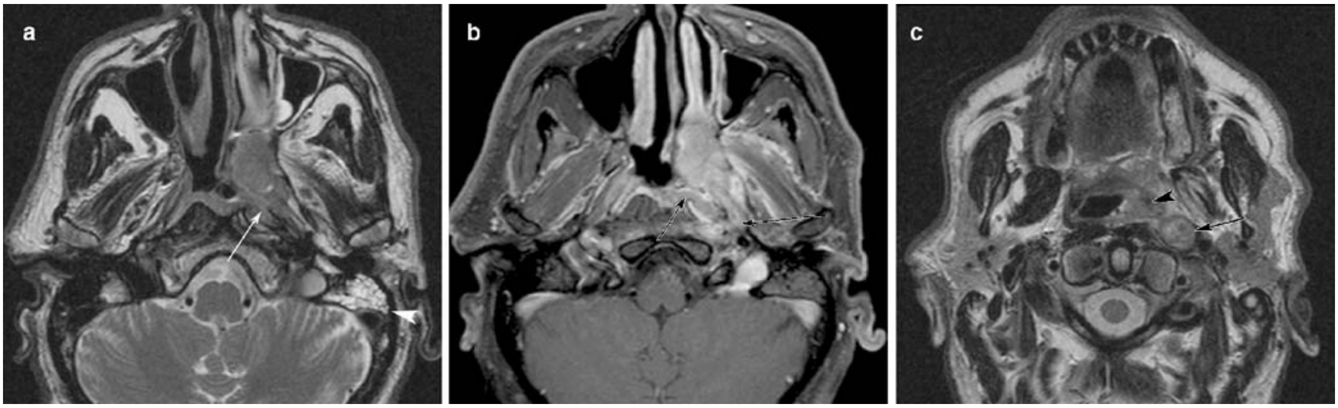


Fig. 11 Patient presenting with a nasopharyngeal tumor, clinically revealed by a serous otitis (**a**, *arrowhead*) without lateral extension but a posterior spread to the retropharyngeal space (*arrow*) and posterior parapharyngeal space (**b**, *arrow*). **c** A left retropharyngeal node (*arrow*). Note the inferior extension to the oropharynx (*arrowhead*)

Nodal metastasis

Cervical node metastasis is very common in nasopharyngeal tumors. It represents a usual initial presenting complaint.

The first nodes to be involved are the retropharyngeal nodes, and this is seen in 65% of nasopharyngeal tumors [2]. Lymphadenopathy at this location should be sought on imaging with attention (Fig. 11). It is interesting to note that involvement of retropharyngeal nodes does not appear in the TNM staging system as there is not sufficient evidence that these nodes affect the prognosis of the patient [12, 13].

In 75% of patients, enlarged cervical nodes are present, particularly high jugular nodes, sometimes without involvement of retropharyngeal nodes. For the N staging, the greatest dimension of the lymphadenopathy should be noticed, in particular in case of lymphadenothy greater than 6 cm (N3, stage IVB). Bilateral cervical lymphadenopathy may be seen in many patients. Supraclavicular fossa should be included in the analysis; in case of metastasis to lymph nodes in this location, the staging is IVB (Table 1) and the risk of distant metastasis is higher.

Distant metastasis

Nasopharyngeal tumors show a high frequency of distant metastases compared with other head and neck tumors, varying between 5% and 41% [2]. Patients with low cervical lymphadenopathy, especially in the supraclavicular fossa, and patients with important extension to the deep facial spaces, in particular the parapharyngeal space, have a significantly higher risk of distant metastases. The most common sites of metastases include bone (20%), lung (13%) and liver (9%) [14].

Diagnostic strategies

Two groups of patients require imaging:

– Patients presenting with clinical suspicion of nasopharyngeal tumor (serous otitis associated with cervical lymphadenopathy). Many studies have shown that MRI is superior to CT in demonstrating perineural extension and skull base marrow changes. It is also recommended to perform a CT scan on the skull base as discussed previously. Cervical node metastasis can either be evaluated on CT or MRI.
– Patients presenting with cervical lymphadenopathy without any known primary head and neck tumor. In this case, the entire aerodigestive tract should be analyzed carefully, including the nasopharynx, oropharynx, hypopharynx and larynx. Most teams prefer to obtain a contrast-enhanced CT scan from the skull

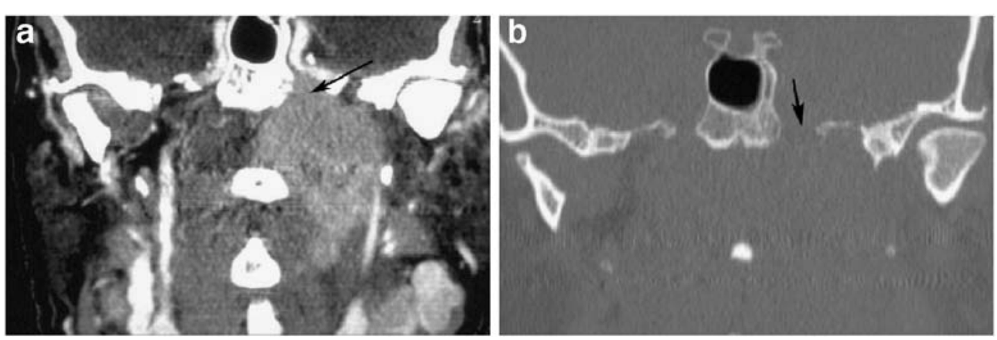


Fig. 12 **a** CT images illustrate a nasopharyngeal tumor extending to the foramen lacerum. **b** Note the enlargement of the foramen lacerum

base to the cervico-mediastinal orifice. If a nasopharyngeal tumor is suspected, a MRI should be performed in order to better demonstrate possible skull base extension.

A contrast-enhanced thoraco-abdominal CT scan, or PET-study, should be performed for T2b and/or N3 tumor to look for distant metastases. Most teams do this exam systematically [5].

Conclusion

Imaging is of particular interest in coming to a correct staging of the lesion. Extension of nasopharyngeal tumors, especially at the skull base and the deep facial spaces, is well illustrated on imaging. MRI best depicts perineural spread and bone marrow changes in the skull base, whereas CT is useful to detect early skull base erosion. Cervical node metastasis being very common in nasopharyngeal carcinomas, lymphadenopathy must be sought on imaging with attention.

A correct initial staging of the nasopharyngeal carcinoma is very important to perform the best treatment: small lesions (stage I and IIa) can be treated by radiotherapy alone, while larger lesions need heavier concomitant chemo-radiotherapy. The precise determination of the tumor borders is of great importance to determine the radiation portals.

References

1. Sigal R (1995) Tumeurs du nasopharynx. In: Bourjat P, Veillon F (eds) Imagerie Radiologique de la tête et du cou. Vigot, Paris, pp 375–389
2. Chong VFH (2006) Neoplasms of the nasopharynx. In: Hermans R (ed) Head and neck cancer imaging. Springer, Berlin Heidelberg New York, pp 129–142
3. Harnsberger HR (2004) Squamous cell carcinoma, Nasopharynx. In: Diagnostic imaging: head and neck, Part III. Amirsys, Salt Lake City, pp 1–16
4. Chong VF, Mukherji SK, Ng SH et al (1999) Nasopharyngeal carcinoma: review of how imaging affects staging. J Comput Assist Tomogr 23:984–993
5. Chong VF, Khoo JB, Fan YF (2004) Imaging of the nasopharynx and skull base. Neuroimaging Clin N Am 14:695–719, Nov
6. UICC, International Union Against Cancer (2002) TNM classification of malignant tumours, 6th edn. Wiley-Liss, New York, pp 27–29
7. Sobin LH, Wittekind C (eds) (2002) UICC TNM classification of malignant tumors, 6th edn. Wiley, New York
8. Chong VFH, Zhou JY, Khoo JBK, Huang J, Lim TK (2004) Nasopharyngeal carcinoma tumor volume measurement. Radiology 231:914–921
9. Mukherji SK, Schmalfuss IM, Castelijns J, Mancuso AA (2004) Clinical applications of tumor volume measurements for predicting outcome in patients with squamous cell carcinoma of the upper aerodigestive tract. AJNR Am J Neuroradiol 25:1425–1432
10. Lau KY et al (2004) Magnetic resonance for T-staging of nasopharyngeal carcinoma, the most informative pair of sequences. Jpn J Clin Oncol 34:171–175
11. Rohl JL, Sung MW, Kim KH, Choi BY, Oh SH, Rhee CS, Ha JW (2004) Nasopharyngeal carcinoma with skull base invasion: a necessity of staging subdivision. Am J Otolaryngol 25:26–32
12. Chong VF, Fan YF, Khoo JB (1995) Retropharyngeal lymphadenopathy in nasopharyngeal carcinoma. Eur J Radiol 21:100–105
13. Gross ND, Ellingson TW, Wax MK, Cohen JI, Andersen PE (2004) Impact of retropharyngeal lymph node metastasis in head and neck squamous cell carcinoma. Arch Otolaryngol Head Neck Surg 130:169–173
14. Sham JST, Cheung YK, Chan FL et al (1990) Nasopharyngeal carcinoma: pattern of skeletal metastases. Br J Radiol 63:202–205