IMAGING DIAGNOSIS OF NASOPHARYNGEAL TUMORS*

Ilka Yamashiro[1], Ricardo Pires de Souza[2]

Abstract **The nasopharynx is located in the upper aerodigestive tract. Its roof is formed by the basisphenoid, basiocciput and the anterior aspect of the first two cervical vertebrae, in front of the clivus. The lateral walls are formed by the margins of the superior constrictor muscle and the pharyngobasilar fascia, pharyngeal recess, torus tubarius and pharyngeal opening of auditory tube. The inferior margin of the nasopharynx is a horizontal plane passing through the hard palate and palatopharyngeal muscle. Anteriorly, it is in direct continuity with the nasal cavity through the posterior choanae. It is approximately 2.0 cm in anteroposterior diameter and about 4.0 cm in craniocaudal extent. Squamous cell carcinoma accounts for about 70% to 98% of nasopharyngeal malignant lesions found in adults. This tumor presents a high incidence in Asians, most frequently in men, and is the third most frequent cancer in women. The clinical presentation of this disease depends on the size and site of the lesion, with small-sized lesions being asymptomatic. Computed tomography and magnetic resonance imaging play essential and complementary roles in the staging and treatment of patients with nasopharyngeal cancer.**

Keywords: Computed tomography; Nasopharynx; Tumor; Carcinoma.

Resumo *Diagnóstico por imagem dos tumores da nasofaringe.*

A nasofaringe é a parte mais superior das vias aéreas superiores. Seu limite superior é a base do osso esfenóide e occipital, situa-se anteriormente às duas primeiras vértebras cervicais e à frente do clivo. Seus limites laterais são formados pelas margens do músculo constritor superior da faringe e pela fáscia faringobasilar, recessos faríngeos, toro tubário e tuba auditiva. O limite inferior é um plano horizontal que passa pelo palato duro e pelo músculo palatofaríngeo. Anteriormente, comunica-se com a cavidade nasal via coana posterior. Mede cerca de 2,0 cm de diâmetro ântero-posterior e cerca de 4,0 cm de extensão crânio-caudal. O carcinoma de células escamosas compreende aproximadamente 70% a 98% de todas as neoplasias malignas da nasofaringe em adultos. Este tipo de tumor apresenta alta incidência na população asiática, sendo mais comum entre os homens e o terceiro mais comum entre as mulheres. A manifestação clínica do carcinoma da nasofaringe depende do tamanho da lesão e da sua localização, sendo que as lesões de pequenas dimensões são geralmente assintomáticas. A tomografia computadorizada e a ressonância magnética desempenham papel essencial e complementar no estadiamento e no tratamento dos pacientes portadores de câncer da nasofaringe.

Unitermos: Tomografia computadorizada; Nasofaringe; Tumor; Carcinoma.

ANATOMICAL SUBSTRATE

The nasopharynx is the upper part of the superior aerial tract, and corresponds to the superior end of the pharynx. It contains the lateral pharyngeal recess, the torus tubarius and the pharyngeal tonsil.

The nasopharynx is situated at the center of the skull base. The anatomical relations of the nasopharynx include the clivus posteriorly, the posterior nasal cavity anteriorly, and the carotid spaces laterally. The inferior margin of the nasopharynx is a horizontal plane passing through the hard palate and palatopharyngeal muscle. Laterally, it is limited by the margins of the superior constrictor muscle, the pharyngobasilar fascia and by the parapharyngeal space[1]. Its wall is formed by three layers: a mucous lining, a muscular layer and a fibrous membrane denominated pharyngobasilar fascia.

It is approximately 2.0 cm in anteroposterior diameter and about 4.0 cm in craniocaudal extent[2].

The middle layer of the deep cervical fascia or buccopharyngeal fascia is characterized by a condensation of cellular tissue surrounding the lateral and posterior portions of the nasopharynx, providing it with a fascial limit as an interface with the neighboring structures. It is a tender, subtle membrane, and does not represent a significant barrier to neoplastic or infectious dissemination from the nasopharynx into adjacent spaces[3,4]. Laterally, it covers the pharynx, superiorly inserting into the skull base through the pharyngeal tubercle, with the superior constrictor muscle, pharyngobasilar fascia, and in the posterior margin of the medial pterygoid plate.

The structural protrusion and the tissues of the pharyngeal wall give shape to the mucosal lining of the nasopharynx, determining anatomical landmarks utilized in clinical evaluations and interpretation of computed tomography (CT) and magnetic resonance imaging (MRI) cross-sectional slices, as follows: a) torus tubarius – is the most prominent of these structures, corresponding to a projection of the cartilaginous portion of the auditory tube. It is visualized as a protrusion projecting into the

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lateral wall of the nasopharyngeal cavity, both on CT and MRI; b) pharyngeal ostium of auditory tube – localized antero-inferiorly to the torus tubarius[5]. On CT and MRI axial slices, it is observed as a small recess in the nasopharynx lateral wall; c) The salpingopharyngeal fold, a mucosal protrusion determined by the submucosal tract of the salpingopharyngeal muscle forming the anterior limit of the lateral pharyngeal recess; d) the lateral pharyngeal recess, posteriorly located, and extending superiorly to the salpingopharyngeal fold and torus tubarius (Figures 1 and 2). It is the most frequent site of origin for nasopharyngeal squamous cell carcinoma[6]. It originates in a subtle mucosal herniation through the Morgagni sinus, a region on the pharyngeal wall where muscular fibers are absent. The degree of distensibility is highly variable. It tends towards being symmetrical, although subtle asymmetries are not uncommon to be found at MRI and CT[7]. In youngsters, it presents with less amplitude because of the presence of retropharyngeal lymphoid tissue[8].

The nasopharynx is formed by:

a) A muscular layer formed by the upper, middle and lower pharyngeal constrictor muscles, pharyngeal levator muscles (palatopharyngeal, stylopharyngeal and salpingopharyngeal), palatoglossus, tensor palati and levator palati, and the palatopharyngeal muscle;

b) a fibrous structure or pharyngobasilar fascia situated between the muscular tunica and mucosa, extending uninterruptedly from the upper to the lower end of the pharynx, absent in the anterior portion, except in the attachment to the larynx where it is circular[1]. Cranially, where its external surface is not covered by a muscular layer (between the skull base and the inferolateral portion of the auditory tube cartilage), there is a lateral space denominated Morgagni sinus. It is through this space that the auditory tube and the levator palati penetrate into the nasopharynx internal portion. The Morgagni sinus, because of its anatomical characteristic, is an important route for the carcinoma dissemination from the nasopharynx towards adjacent spaces like the parapharyngeal space;

c) a mucosal membrane or internal tunica lining internally the pharyngobasilar fascia, continuing with the mucosal lining of the nasal cavity and oropharynx. It is formed by ciliated pseudo-stratified epithelium and chorium with a plenty of muciparous glands and lymphoid follicles[9]. Abundant lymphoid tissue in the chorium forms a part of the pharyngeal lymphatic ring, a probable site for development of non-Hodgkin lymphoma, the most frequent malignant nasopharyngeal neoplasm[2,10]. Smaller salivary glands are present in the sub-mucosa surrounding the auditory tubes, and might be a focus for benign or malignant nasopharyngeal lesions.

The knowledge of anatomical variations of this region is important to avoid confusion between normal alterations and disease.

Asymmetry of mucosal landmarks, especially the pharyngeal recess asymmetry, is a frequent variation. A decrease in depth of the pharyngeal recess, or even its collapse as a normal finding should be differentiated from disease. The analysis of adjacent, deep planes showing their integrity or symmetry suggests normality (Figure 3). Also, the acquisition of CT images during modified Valsalva maneuver or wide opening of the mouth might be useful. The modified Valsalva maneuver results in a maximum distention of the auditory tube ostium and pharyngeal recess. The wide opening of the mouth distends the pharyngeal recess and increases the auditory tube ostium depth[7].

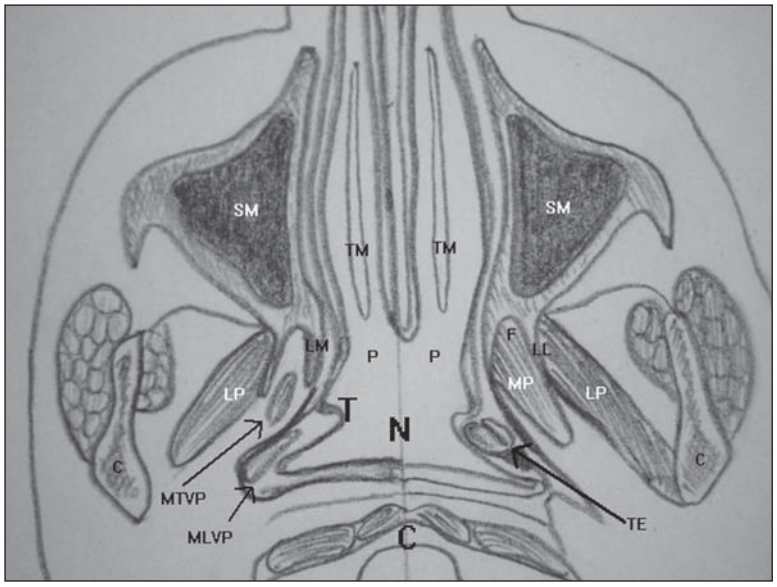

Figure 1. Scheme of axial view, in slightly different planes: SM, maxillary sinus; TM, middle turbinate; P, posterior choana; N, nasopharynx; LM, medial pterygoid lamina; F, pterygoid fossa; LL, lateral pterygoid lamina; LP, lateral pterygoid muscle; MP, medial pterygoid muscle; TE, auditory tube (Eustachian tube); T, torus tubarius; FR, pharyngeal recess (Rosenmuller's fossa); CL, clivus; C, mandibular condyle; MTVP, tensor palati; MLVP, levator palati.

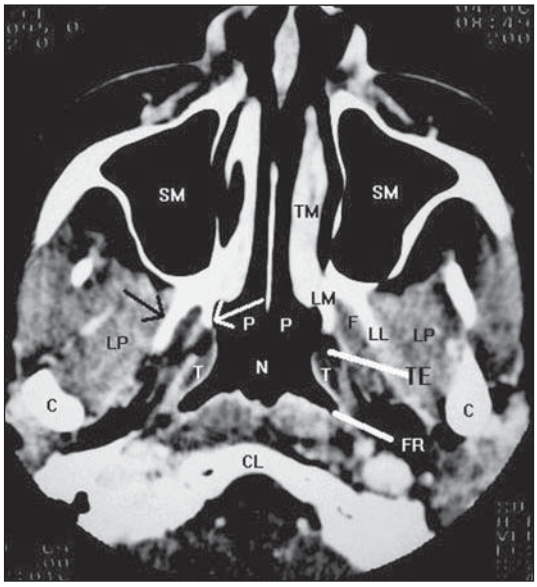

Figure 2. Contrast-enhanced CT axial view: normal anatomy. SM, maxillary sinus; TM, middle turbinate; P, posterior choana; N, nasopharynx; LM, medial pterygoid lamina (white arrow); F, pterygoid fossa; LL, lateral pterygoid lamina (black arrow); LP, lateral pterygoid muscle; TE, auditory tube (Eustachian tube); T, torus tubarius; FR, pharyngeal recess (Rosenmuller's fossa); CL, clivus; C, mandibular condyle.

Sometimes, the nasopharyngeal lymphoid tissue may appear like a tumor process. Taking into consideration that its normal limit is the mucosa and sub-mucosa, the extension to deep planes should be considered as an evidence of malignant lesion or an aggressive inflammatory process[11,12].

With the ageing process, there is a decrease in the volume of lymphoid tissues, levator and tensor palati, and constrictor muscles, and an increase of fat tissue. These changes are known as nasopharyngeal atrophy. On the radiological evaluation, an increase in size of the lateral pharyngeal recess is observed, with a larger prominence of the torus tubarius and auditory tube ostium.

It is important to note that, if the asymmetry found on axial slices is not fully clarified, coronal slices become mandatory, especially in case of alterations in the upper end of the lateral recess[13] (Figure 4).

LOCAL STAGING OF NASOPHARYNGEAL CARCINOMAS

Squamous cell carcinoma accounts for approximately 70% to 98% of all malignant nasopharyngeal neoplasms. Lymphomas account for about 20% of cases, and the remaining 10% result from an array of lesions, including adenocarcinomas, cystic adenoid carcinomas, rhabdomyosarcomas, etc. Nasopharyngeal squamous cell carcinoma is a relatively rare type of cancer, accounting for 0.25% of malignant neoplasms in the North America, however presents a high incidence among Asians, particularly in the Southeast Asia, accounting for up to 18% of all malignancies in China[2]. It tends to affect younger age groups than other lesions of the upper respiratory-digestive tract, with higher prevalence in men than in women[14].

Risk factors for development of nasopharyngeal carcinoma include those for oropharinx carcinoma, like nitrosamine (present in food seasonings) and polycyclic hydrocarbons consumption, chronic tobacco and alcohol consumption, precarious conditions of life, repeated sinonasal infections. Additionally, there is a strong association with Epstein-Barr virus, particularly in Southeast Asia, where the affected population usually is younger when compared with the Caucasian population[2].

The World Health Organization has updated the histological classification of nasopharyngeal carcinomas, dividing them into two large subtypes: 1 – squamous cell carcinoma, and 2 – non-keratinized carcinoma.

The non-keratinized carcinoma subtype is still subdivided into: subtype I – differentiated (2a) and II – undifferentiated (2b). The term lymphoepithelioma also is utilized to designate these two subtypes of tumors. These new nomenclatures 2a and 2b correspond, respectively, to 2 and 3 types in the former classification[2]. The latest one, undifferentiated subtype of non-keratinized, seems to be more closely related to the presence of Epstein-Barr virus, resulting in the development of cancer in younger patients, by a still unknown mechanism[15–17]. Yet, the presence of the viral genome (Epstein-Barr virus) in metastatic lymph nodes might suggest a nasopharyngeal carcinoma as primary site[18].

The site of origin varies. Most common sites are the lateral nasopharyngeal walls, most frequently the lateral pharyngeal recess. Frequently the torus tubarius is involved[14,19,20] (Figures 5A and 5B).

The nasopharyngeal carcinoma clinical manifestation depends on the size, localization and tumor dissemination route. Usually, small lesions are asymptomatic, but serous otitis media, headache, nasal obstruction, epistaxis, "throat ache", trismus, and proptosis may be present, depending on the degree of involvement of neighbor structures and the size of the lesion[2]. Other less frequent symptoms may be present: hemo-

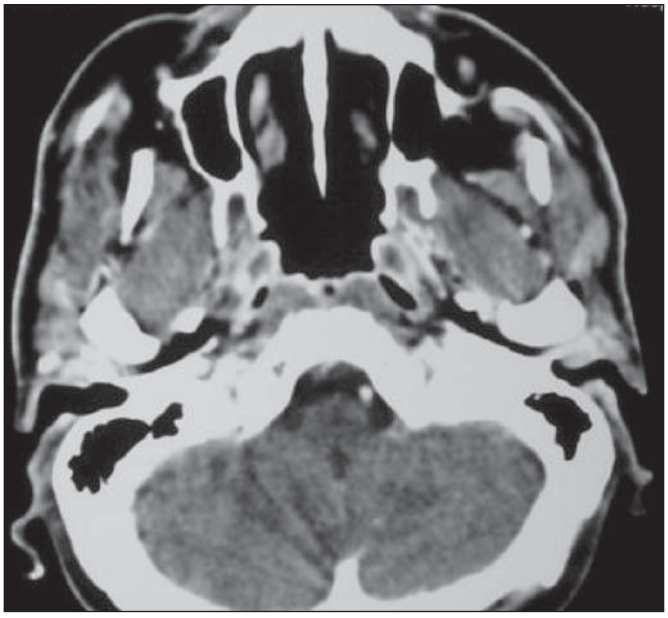

Figure 3. Contrast-enhanced CT axial view: normal asymmetry of the pharyngeal recess. Note that the recess at right is less evident than at left, but adjacent tissues present with no alteration.

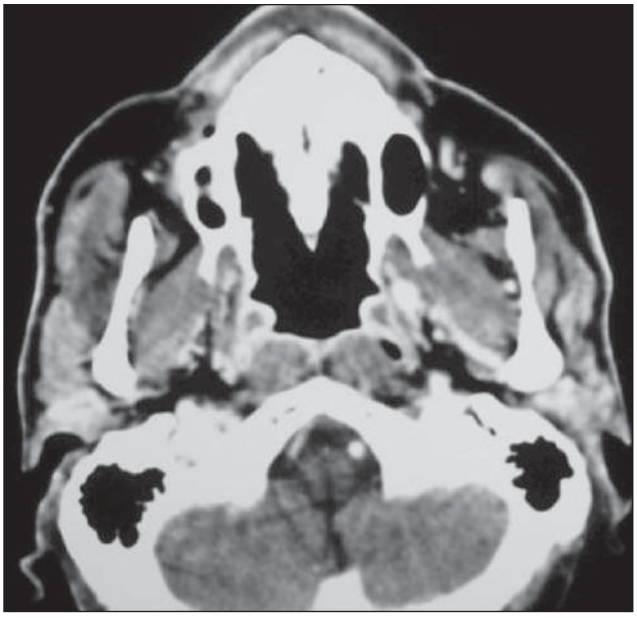

Figure 4. Contrast-enhanced CT axial view: normal asymmetry of pharyngeal recess. Note that the recess at right presents obliterated, with no abnormality of adjacent tissues.

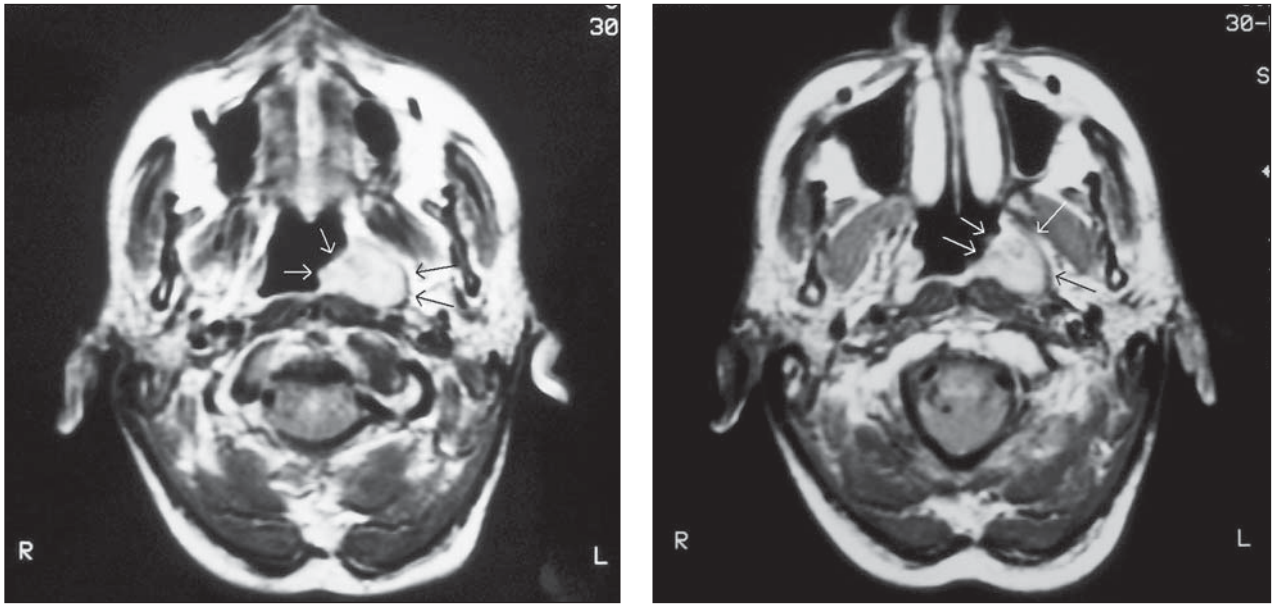

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Figure 5(A,B). MRI axial T2-weighted (TR 2.500/TE 25) image. Asymmetry with pharyngeal recess obliteration at left, evidenced by the presence of well-defined lesion with hypersignal in this sequence (arrows).

tympanum, periauricular mass, plugged ear sensation, barotrauma, polyp inside the inner ear, and sudden, neurosensorial hearing loss[21].

Specific anatomical routes through which the tumor disseminates to the skull base or intracranial regions, as well as the lymph node or distant metastatic dissemination are found on CT and MRI images.

Nasopharyngeal carcinoma is one of few head and neck tumors which do not present any relationship between the tumor size and the presence of lymph node metastasis, and this is due to the wide drainage plexus present in the region. About 90% of cases present with lymph node metastasis at the moment of diagnosis, and 50% of them already present bilateral disease[17].

The primary drainage site is to retropharyngeal lymph nodes, but, since in the adulthood these lymph nodes may present obliteration by inflammatory/infectious processes occurred in the childhood, they may not be involved. Other preferential drainage sites are the II, III, and, occasionally, V levels[2].

Distant metastasis may affect the lungs, sketeleton, liver, and, occasionally, the choroid plexus[17].

Usually, nasopharyngeal carcinomas disseminate through the mucosa and submucosa alongside muscular clusters, and in their origins and insertions, adjacent to fat planes surrounding the muscles, along the vascular/nervous bundles, and through the foramens created for the normal passage of these structures. Some structures, like the auditory tube cartilaginous portion and pharyngobasilar fascia, demonstrate higher resistance against the tumor invasion[2,19,22,23].

The perineural dissemination is the most insidious form of tumor dissemination, and its presence is extremely important for the prognosis and therapeutical planning. The nerve of the pterygoid canal represents the main nasopharyngeal carcinoma perineural dissemination route. Perineural dissemination should be suspected in case of abnormal enlargement or enhancement of the nerve with obliteration of fat planes[24].

The nasopharyngeal carcinoma frequently originates in the lateral pharyngeal recess region. On CT images, asymmetry, blurring or obliterations are usually seen, and may be associated with an increase of the levator palati[6,19,25].

When the tumor surpasses the pharyngobasilar fascia, it invades the parapharyngeal space; according to Hoe, this occurs in 65% of nasopharyngeal carcinomas[14,25]. Sham and Choy have found 85% involvement of this region[26]. From the parapharyngeal space, the tumor may extend superiorly, anteriorly, laterally or posteriorly.

The superior extension of the nasopharyngeal carcinoma is the most frequent route of direct dissemination (48%)[19,25]. Intracranial extension may occur by direct destruction of the skull base or by extension towards the sinus cavernosum via the foramen lacerum or foramen ovale. The superior extension of the tumor is visualized as an infiltration of sphenoid sinus with opacification or presence of fluid and bone destruction. Most usually, areas of bone destruction in the skull base are the clivus, the foramen lacerum and the middle cranial fossa, around the sphenoid sinus floor and foramen jugularis (Figure 6).

The tumor dissemination via foramen lacerum occurs perivascularly, through the carotid artery, resulting in erosion of the carotid canal (Figure 7). The dissemination via foramen ovale is perineural, resulting in erosion of the sphenoid base. A less common dissemination route towards the middle cranial fossa is the perineural route, via foramen rotundum[14,27]. It is important to note that the invasion of the skull base occurs irrespective of the size of the tumor, ranging from subtle erosion to extensive bone destruction. Other concomitant findings in cranial invasion include predomi-

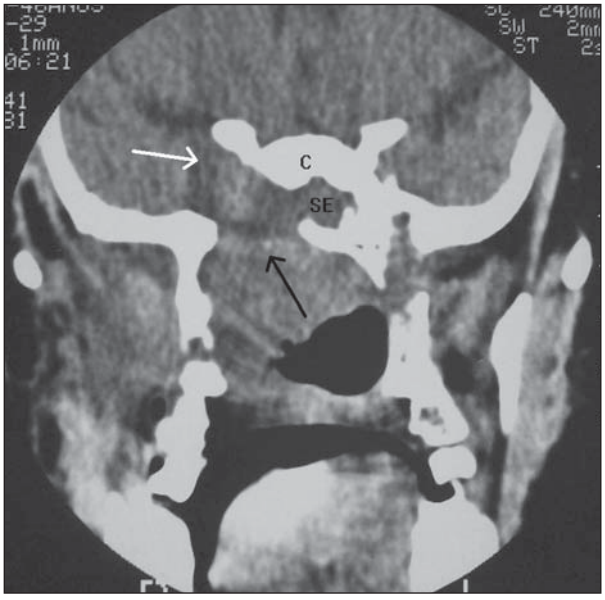

Figure 6. Pre-contrast CT coronal view demonstrating extensive lesion with density of soft tissues of the nasopharynx at right, invading the skull base through the sphenoid bone (black arrow), destructing the clivus (C) and affecting the ipsilateral sinus cavernosus (white arrow).

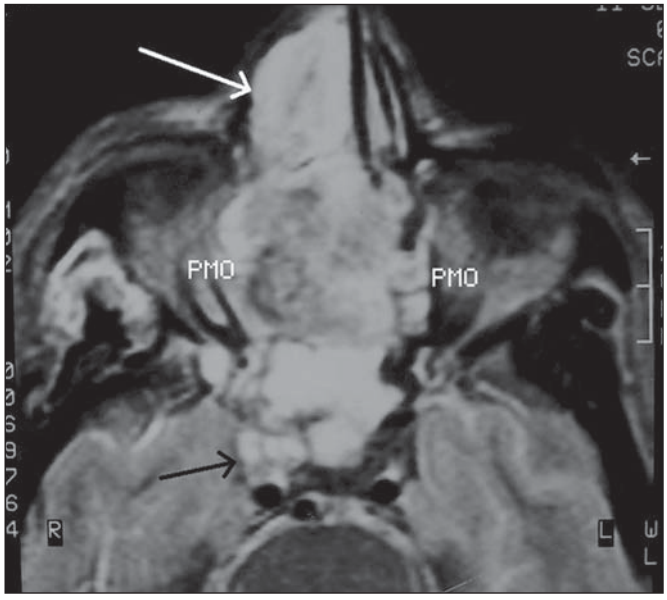

Figure 7. MRI axial, T2-weighted (TR 2.500/TE 80) image evidencing extensive, heterogeneous lesion, with an expansive aspect, predominantly hyperintense in this sequence, with bilateral, bulged medial orbital walls, extending anteriorly to the nasal fossa (white arrow), and superiorly reaching the sinus cavernosus at right (black arrow). Note the contact of the lesion with the right inner carotid.

nant involvement of base cisterns, of sinus cavernosum, associated with palsy of the affected cranial pairs[2,17].

Low et al. have reported the involvement of the cerebellopontine angles by these carcinomas, highlighting both the diagnostic and therapeutic difficulties of this disease, since the evaluated patients presented with advanced disease or a previously treated tumor recurrence[28].

Disease recurrence should be suspected if the patient presents apparently inexplicable neurological symptoms like neurosensorial hearing loss, sonitus or facial palsy[28].

The posterior extension is the second most frequent direct dissemination route (40%)[14]. A mass anterior to the prevertebral muscles is observed in cases where a tumor extends towards the retropharyngeal space. In this localization, there are retropharyngeal lymph nodes e it may be difficult to differentiate lymph node involvement from direct extension by the tumor. The prevertebral space infiltration is identified as a mass posterior to prevertebral muscles, and occurs in 14% of cases (Figure 8).

In cases with anterolateral extension, an invasion of the masticator space, including the infratemporal fossa, may occur (14%).

Inferiorly, carcinomas invade the oropharynx through the lateral walls of the pharynx, anterior and posterior tonsillar pillars. Since this type of dissemination is usually submucosal, it may be clinically occult. In such cases, CT and MRI might be useful for detecting this type of dissemination or identifying suspect areas, indicating the biopsy of the region.

As already mentioned, these tumors may be small and infiltrative, causing, or not, a mass effect; in these cases, fat planes obliteration and loss of definition of muscular margins constitute extremely useful diagnostic findings, and contrast-enhanced (gadolinium) MRI with fat suppression has shown to be superior to CT in soft tissues evaluation, both in deep and superficial na-

Figure 8. MRI sagittal, T1-weighted (TR 520/TE 20) image showing extensive, heterogeneous lesions affecting the posterosuperior nasopharyngeal wall, limited by the clivus (black arrow), and anteriorly invading the nasal fossa (white arrow).

sopharyngeal regions, besides being able to clearly differentiate lymphoid tissue from musculature[17,19]. This is a very important aspect, since the most relevant prognostic factor in nasopharyngeal carcinoma is the depth and degree of infiltration into neighboring structures, and not the tumor size[29]. On the other hand, CT is superior to MRI in demonstrating subtle involvement of bone structures in the skull base[6,30].

Both methods play an essential and complementary role in the staging and treatment of patients with nasopharyngeal cancers. PET - positron emission tomographic scanning, however, is a more appropriate method to assess recurrent tumors and very small lymph node metastasis[2,17].

Considering that imaging methods do not allow the definition of the histological type of the lesion — a significant aspect, since the prognosis is different for the distinct cellular types —, the only alternative, for the radiologist is precisely mapping the invaded sites, helping the clinician/surgeon in the correct staging of the lesion (Table 1) (Figure 9).

Typically, squamous cell carcinomas present an attenuation coefficient similar to that of muscles, and do not show significant enhancement after intravenous contrast agent administration at CT. At MRI, these tumors present a signal of intermediary intensity in all the sequences. Tumor/tissue interfaces are better demonstrated by MRI, while a subtle bone destruction is better demonstrated by CT. Neoplastic extension through the foramens lacerum and ovale is better evaluated by MRI. The utilization of intravenous paramagnetic contrast agents (gadolinium) is advantageous in MRI studies, since the intense tumor enhancement allows a better lesion definition, avoiding extent underestimation, a frequent phenomenon in non-contrast enhanced margins as a function of the presence of edema and perilesional inflammatory process[31,32] (Figures 10A and 10B).

For a complete staging, it is also necessary to study the lymph node involvement present in approximately 90% of patients at the moment of the diagnosis. Retropharyngeal lymph nodes usually are firstly affected, but may present normal features, in case of obliteration by previous inflammatory processes. The following are those of levels II and III, and, occasionally, those in levels I and V may be involved[2] (Table 2).

Generally, the therapy of choice for nasopharyngeal carcinomas is radiotherapy. For this reason, imaging methods are so significant for the tumor mapping with the purpose of radiotherapy planning[33].

However, the post-therapy evaluation, both by CT and MRI, presents a low sensitivity — about 45% to 67% for CT, and 56% for MRI —, and low specificity — about 64% to 70% for CT, and 78 to 83% for MRI[34].

Table 1 TNM staging of nasopharyngeal epithelial tumors.

*Primary tumor**
T1 – tumor confined to the nasopharynx
T2 – tumor extending to oropharyngeal and/or nasal fossa tissues
T2a – without extension to the parapharyngeal space
T2b – with extension to the parapharyngeal space
T3 – tumor destructing bone structures and/or invading paranasal sinuses
T4 – tumor presenting intracranial extension and/or affecting cranial nerves, infratemporal fossa, hypopharynx or orbit
Lymph nodes
Nx – regional lymph nodes are not clinically accessed
N0 – there is no clinically positive lymph node
N1 – single, homolateral, positive lymph node, < 6 cm in the largest diameter, above the clavicular fossa†
N2 – bilateral, positive lymph nodes, < 6 cm in the largest diameter, above the clavicular fossa
N3 – lymph node metastases
N3a – > 6 cm in the largest diameter
N3b – lymph node extension to the supraclavicular fossa
Metastases
M0 – there is no evidence of metastasis
M1 – present distant metastases

* Reproduced from: Mukerji SK. Pharynx. In: Som PM, Curtin HD, editors. Head and neck imaging. 4th ed. St. Louis: Mosby, 2003;1478.

† The supraclavicular fossa is delimited by the Ho triangle, a plane defined by the upper margin of the sternum, clavicle lateral margins, and the posterior region where the neck meets the shoulder.

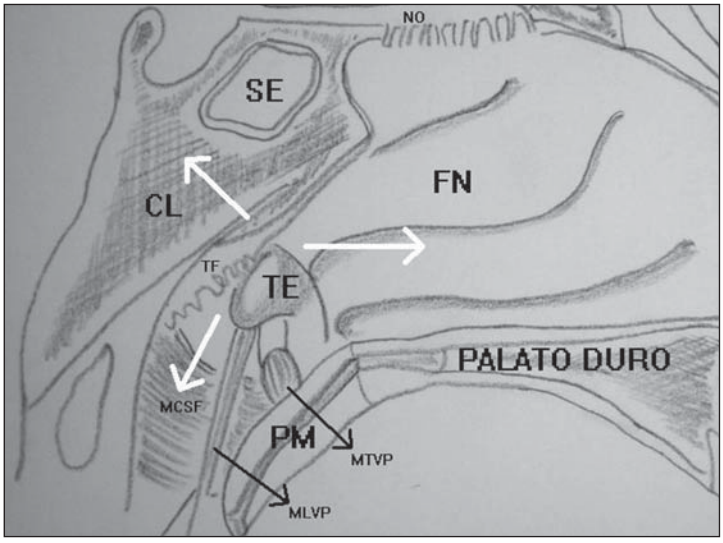

Figure 9. Scheme of sagittal view: NO, olfactory nerve; SE, sphenoid sinus; FN, nasal fossa; CL, clivus; TF, pharyngeal tonsil (adenoid); TE, auditory tube (Eustachian); MTVP, tensor palati; MLVP, levator palati; PM, soft palate. White arrows: potential subsites of nasopharyngeal carcinomas dissemination.

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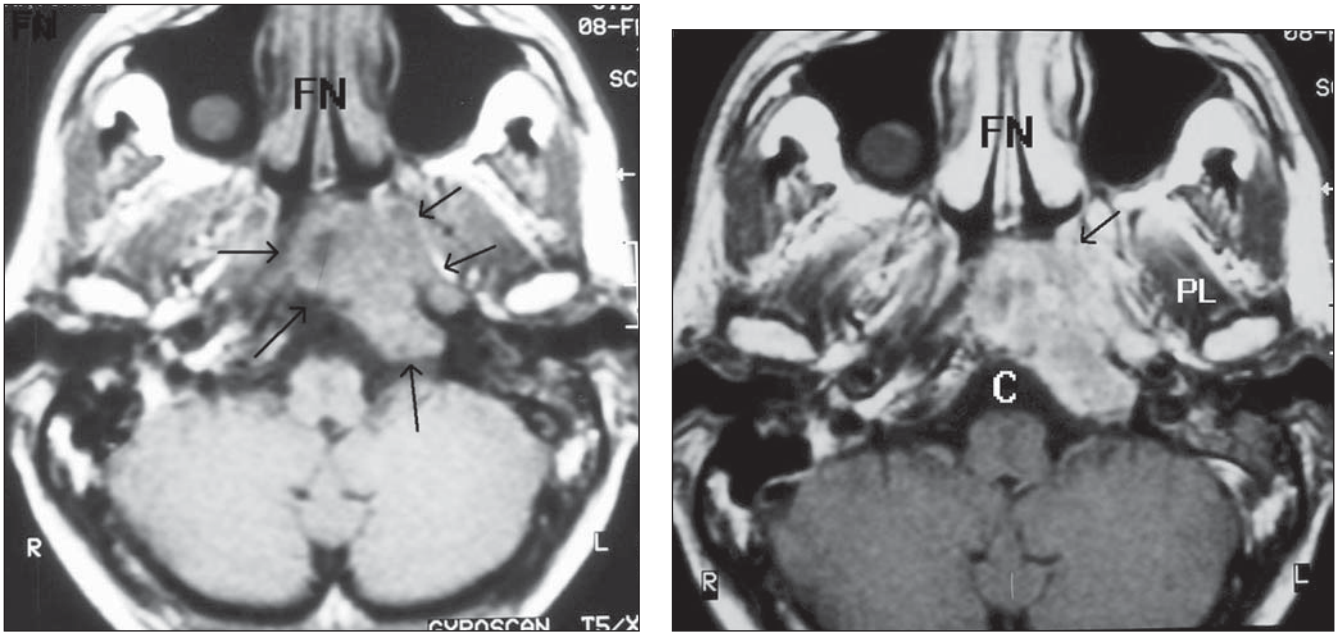

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Figure 10(A,B). A: MRI, axial, T1-weighted (TR 520/TE 20) image showing lesion with intermediary intensity affecting the left nasopharyngeal posterolateral wall (arrows), almost obliterating the whole lumen, reaching anteriorly the nasal fossa (FN) without invading it. **B:** After gadolinium injection, an intense, heterogeneous enhancement is observed, delimitating the lesion affecting the medial pterygoid lamina, the pterygoid fossa (black arrow), the medial pterygoid muscle, the auditory tube, the torus tubarius, the pharyngeal recess, and the adenoid tissue (posteriorly), limited by the clivus (CL), nasal fossa (FN), lateral pterygoid muscle (PL).

Table 2 Lymphnodal classification of nasopharyngeal carcinomas according to the American Joint Committee on Cancer*.

Nx – regional lymph nodes are not clinically accessed
N0 – there is no clinically positive lymph node
N1 – single, homolateral, positive lymph node, < 6 cm in the largest diameter, above the clavicular fossa†
N2 – bilateral, positive lymph nodes, < 6 cm in the largest diameter, above the clavicular fossa
N3 – lymph node metastases
N3a – > 6 cm in the largest diameter
N3b – lymph node extension to the supraclavicular fossa

* Reproduced from: Som PM, Brandwein MS. Lymph nodes. In: Som PM, Curtin HD, editors. Head and neck imaging. 4th ed. St. Louis: Mosby, 2003;1882.

† The supraclavicular fossa is delimited by the Ho triangle, a plane defined by the upper margin of the sternum, clavicle lateral margins, and the posterior region where the neck meets the shoulder.

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