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PICTORIAL ESSAY

Local and Regional Staging of Nasopharyngeal Carcinoma Using Magnetic Resonance Imaging

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BACKGROUND

Nasopharyngeal carcinoma is the most common cancer originating from the nasopharynx. The tumour accounts for up to 70% of all primary malignant lesions arising from the nasopharynx.[1,2] Most cases are seen in adults with the disease rare in the paediatric population. The peak incidence occurs between age 40 and 60 years. The disease is prevalent in southern China, with most cases located in Guangdong, Guangxi, and Fujian provinces.[3] The disease is relatively rare in Western populations. The disease is more prevalent among men than women, with the incidence in men up to 3 times that of women,[4] regardless of geographic location.

Multiple aetiologies have been postulated in the development of nasopharyngeal carcinoma. The first is viral: the Epstein-Barr virus shows a strong association in some cases of nasopharyngeal carcinoma.[5] A positive correlation for level of antibodies to Epstein-Barr virus (EBV) with size of tumour has been demonstrated, with the former used to monitor disease status and response to therapy. Recently, human papilloma virus has been shown to have an association with non-endemic EBV negative cases of nasopharyngeal carcinoma. These cases demonstrate a worse outcome than EBV positive cases.[6] A second aetiology is related to environmental factors. Chinese-style salted fish and other preserved foods contain high levels of volatile nitrosamine, a carcinogen that contributes to the development of many cases of nasopharyngeal carcinoma. Other environmental factors include smoking and cooking. Genetics also play a role in the development of nasopharyngeal carcinoma: multiple human leukocyte antigens have been shown to have a causative effect.[7]

Similar to many other squamous cell carcinomas in the head and neck region, the TNM staging system is applied in nasopharyngeal carcinoma.[8,9] This pictorial essay focuses on different stages of nasopharyngeal carcinoma according to the latest guideline from the American Joint Committee on Cancer (AJCC) 8th edition, that has been recommended and implemented since 1 January 2018.[8,9] Comment is made about revisions made since the 7th edition. A series of nasopharyngeal carcinoma cases of various stages was retrieved from the reporting system of the Department of Radiology at Tuen Mun Hospital.

IMAGING FINDINGS

The typical appearance of nasopharyngeal carcinoma is that of a T1 isointense and T2 isointense/mildly hyperintense lesion with reference to the adjacent muscles. It usually shows heterogeneous contrast

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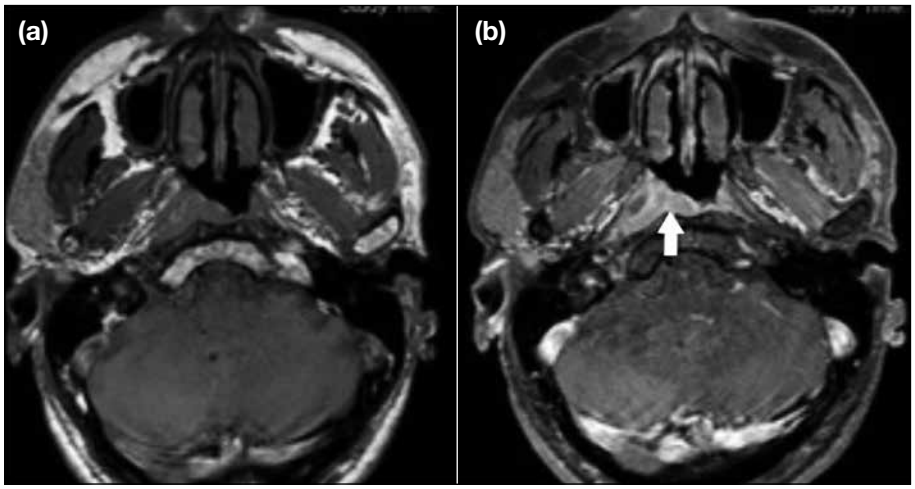

Figure 1. (a) Axial T1 non-contrast and (b) axial T1 post-contrast fat saturation images. Right fossa of Rosenmüller is obliterated. The enhancing lesion is confined to only the mucosal space without invasion of adjacent longus colli muscle (arrow).

enhancement following injection of gadolinium contrast, particularly useful when evaluating perineural spread of the disease. For both T1 post-contrast and T2-weighted sequences, a fat saturation technique is usually employed to improve visualisation of the tumour.[10]

T STAGE

Detailed descriptions of the local staging of tumours can be found in the AJCC Cancer Staging Manual.[9]

TX or T0

TX indicates that the primary tumour is too small or inconspicuous to be visualised on imaging. T0 is a new addition to the AJCC 8th edition, and describes no conspicuous primary tumour detected despite positive EBV involvement of cervical lymph nodes.[11] It is relatively uncommon among different T stages owing to the high sensitivity of magnetic resonance imaging.[12]

T1 Disease

T1 disease indicates that the tumour is confined to the nasopharynx, or has extended to the oropharynx and/or nasal cavity without parapharyngeal involvement.[9] The nasopharynx is defined as the most superior part of the pharynx. Inferiorly, it continues as the oropharynx and anteriorly as the nasal cavity through the choana. On its superior aspect, it is bound by the basisphenoid and basiocciput that form the roof of the nasopharynx. On the bilateral lateral aspects of the nasopharynx, there is focal insinuation of mucosa to form an indentation called the fossa of Rosenmüller, a.k.a. lateral recess. It is the most common site of origin for nasopharyngeal carcinoma.[13] The fossa of Rosenmüller lies posterior to the opening of the eustachian tube, and torus tubarius, an elevation at the base of the cartilaginous portion of the eustachian tube. There is no involvement of adjacent prevertebral muscle or parapharyngeal space in T1 disease (Figure 1).

Nasopharyngeal carcinoma tends to spread upwards rather than inferiorly to the oropharynx,[12,14] although involvement of the oropharynx is still denoted as T1 disease (Figure 2). The boundary of the nasopharynx

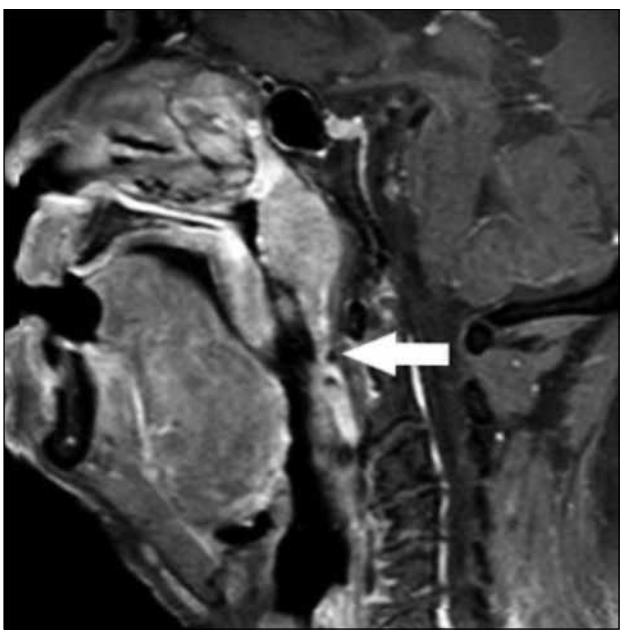

Figure 2. Sagittal T1 post-contrast fat saturation image showing tumour extension down to the level of the oropharynx (arrow). This is still regarded as T1 disease.

and oropharynx is defined according to the level of the soft palate. Solitary involvement of the oropharynx is uncommon as the tumour tends to spread upwards and laterally to the parapharyngeal space.[12,14] Nasopharyngeal tumour extending to the nasal cavity or oropharynx but not the parapharyngeal space has no significantly worse outcome than tumours confined to the nasopharynx. As such they are both categorised as T1 disease.

If the tumour extends beyond the choana, it enters the nasal cavity. Usually there is only minimal extension through the choana (Figure 3) and bulky tumour growth within the nasal cavity is relatively uncommon.[12] Expansion of the nasal cavity may be noted without definite invasion of underlying osseous structure as evidenced by the preserved T1 fatty signal.[10]

The criteria for T1 disease in the AJCC 8th edition are unchanged from the 7th edition.

T2 Disease

T2 disease is defined as tumour with extension into the parapharyngeal space, and/or adjacent soft tissue involvement including medial pterygoid (Figure 4), lateral pterygoid and prevertebral muscle (Figure 5).[9] In the AJCC 7th edition, involvement of the pterygoid muscles was denoted as T4 disease.[11] The medial aspect of the parapharyngeal space is bound by the levator veli

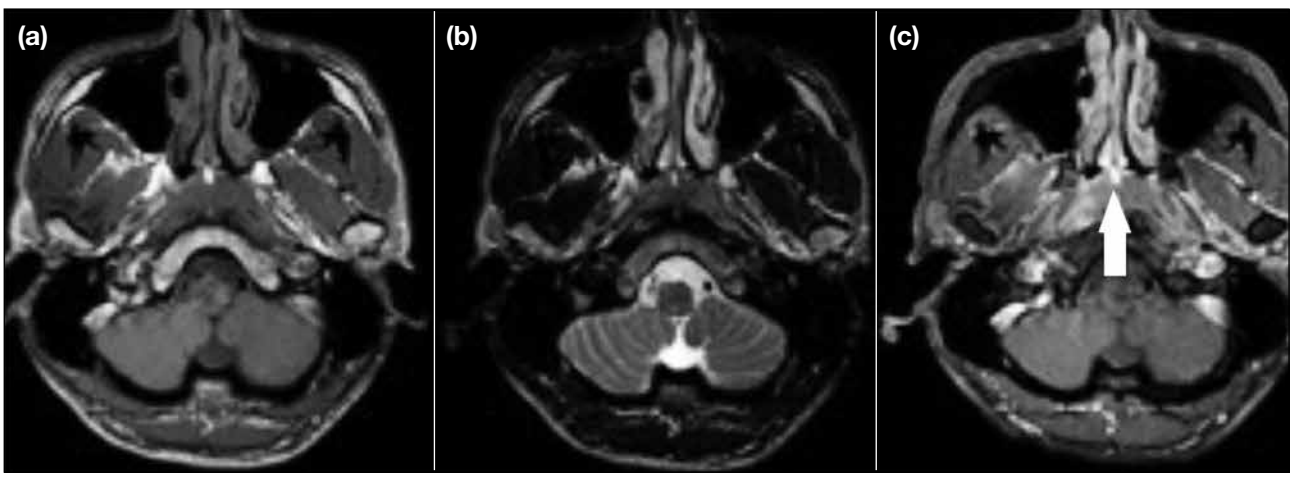

Figure 3. (a) Axial T1 non-contrast, (b) axial T2 and (c) axial T1 post-contrast fat saturation images. Enhancing tumour extending into the choana beyond the posterior aspect of the nasal septum. T1 high bone marrow signal of the nasal septum is still preserved (arrow).

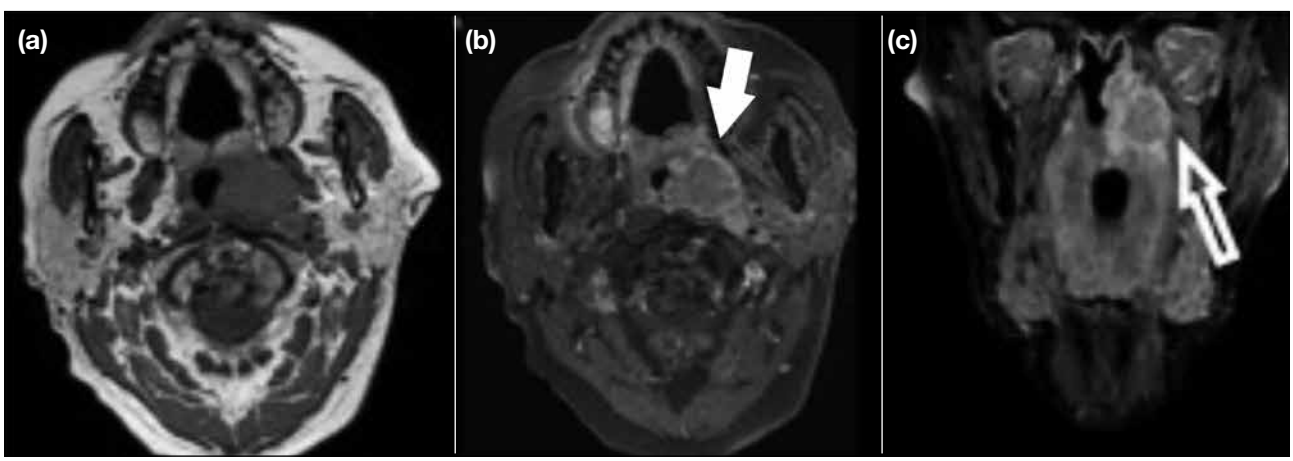

Figure 4. (a) Axial T1 non-contrast, (b) axial T1 post-contrast fat saturation and (c) coronal T1 post-contrast fat saturation images. Left medial pterygoid muscle is invaded by the tumour (solid arrow). There is no clearly delineated plane between the tumour and left medial pterygoid muscle (open arrow). The tumour stands out vividly in post-contrast fat saturation sequence. Magnetic resonance imaging has a high level of soft tissue contrast and enables delineation between the primary tumour and the left retropharyngeal lymph node.

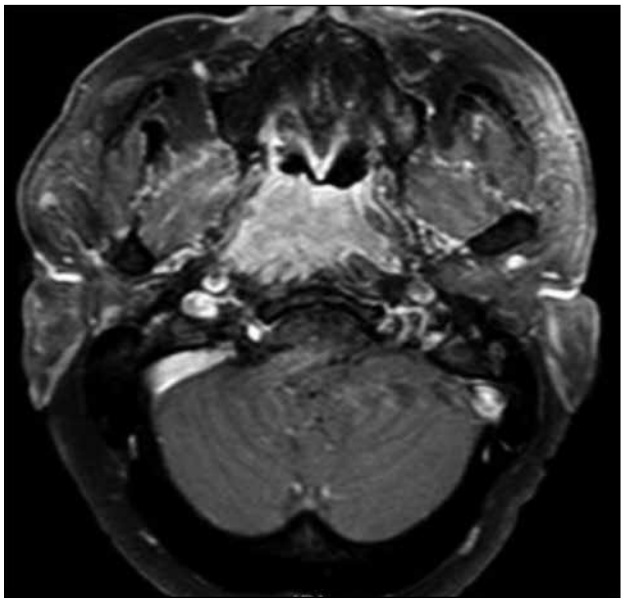

Figure 5. Axial T1 post-contrast fat saturation image showing right longus colli muscle is invaded by the tumour at T2 disease. The boundary of the right longus colli is not intact in this case.

palatini muscle that is an elevator muscle of the soft palate. When the tumour invades through this muscle laterally and the pharyngobasilar fascia (the submucosal layer between mucosa and muscular layer) into the fatty parapharyngeal space, it is categorised as T2 disease (Figure 6). When the tumour invades the parapharyngeal space, structures such as the ascending pharyngeal artery, lymph nodes, part of pterygoid venous plexus and branches of the trigeminal nerve may be affected.[15]

With T2 disease, the tumour is usually quite sizable and often compresses the Eustachian tube with consequent complications such as mastoid effusion (Figure 7).

Adjacent soft tissue involvement including the medial pterygoid, lateral pterygoid or prevertebral muscles have been added to T2 classification in addition to parapharyngeal involvement in the AJCC 8th edition.

T3 Disease

T3 disease is defined as tumour with infiltration of bony structures at the skull base, cervical vertebra, pterygoid structures, and/or paranasal sinuses.[9] The most common bony structures involved include the clivus (Figure 8), the pterygoid bones, petrous apices and body of sphenoid. Bony invasion can be readily confirmed through evaluation of any loss of T1 fatty marrow signal and comparison of bilateral bony structures.[9]

A couple of skull base foramina and canal are also evaluated, including the foramen lacerum, foramen ovale, foramen spinosum, foramen rotundum, carotid canal, jugular foramen, and hypoglossal canal. As most of these skull base foramina enable passage of neurovascular structures craniocaudally, optimal evaluation uses the coronal plane that has the added benefit of enabling bilateral structural comparison. Involvement of the pterygopalatine fossa is commonly denoted as T3 and evaluation of this structure is of utmost importance in staging nasopharyngeal carcinoma as this structure is cross-roads in head and neck imaging (Figure 9). Medially it communicates with the nasal cavity via the sphenopalatine foramen. Laterally it communicates with the masticator space via the pterygomaxillary fissure.

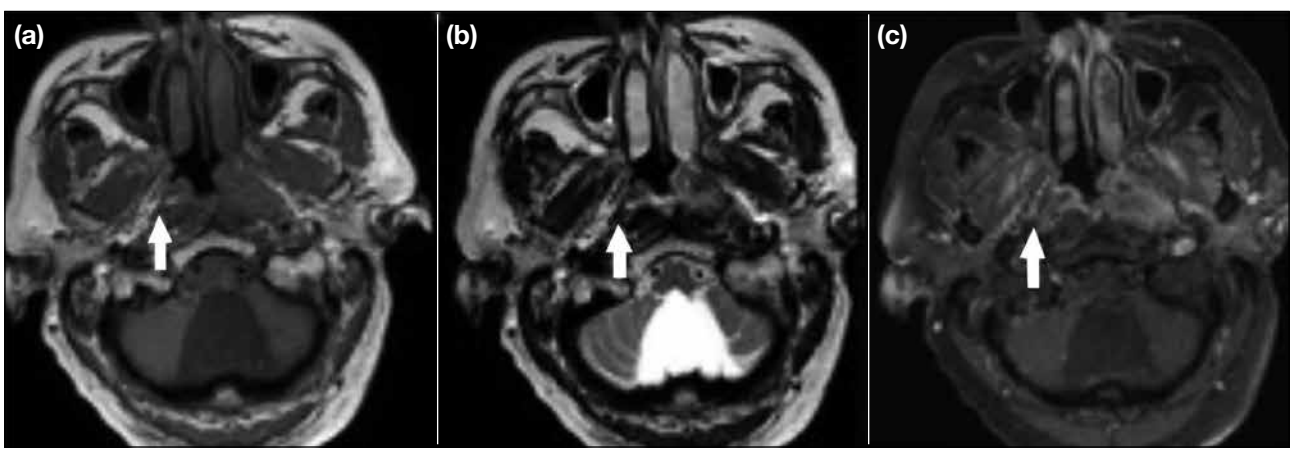

Figure 6. (a) Axial T1 non-contrast, (b) axial T2 and (c) axial T1 post-contrast fat saturation images. Tumour at the left nasopharynx has invaded through the left levator veli palatini muscle into the left parapharyngeal fat space. The right levator veli palatini muscle is intact (arrows), signifying uninvolved right parapharyngeal space.

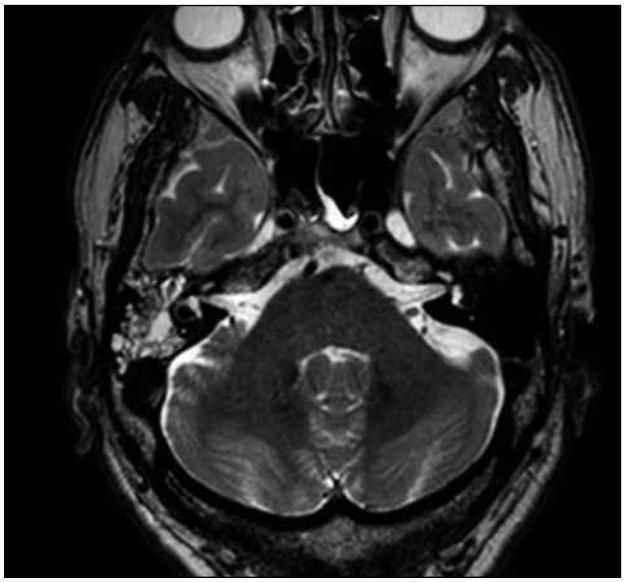

Figure 7. Axial T2 images showing in T2 disease, the tumour is usually quite large. Thus, compression of Eustachian tube and occurrence of mastoid effusion may be seen. The side of mastoid effusion usually correlates with the side of tumour occurrence. In this case the tumour is situated at the right side of the nasopharynx.

Anteriorly it continues into the orbit through the inferior orbital fissure (Figure 10). Posteriorly and superiorly, it communicates with the cavernous sinuses of the middle cranial fossa through the foramen rotundum (Figure 10). Posteriorly and inferiorly, another passage into the middle cranial fossa is through the vidian canal (Figure 11). Posteriorly and medially, it communicates with the nasal cavity via the palatovaginal canal. Inferiorly, it continues into the palate via the greater and lesser palatine canals.

When the tumour invades the paranasal sinuses, the disease is quite advanced (Figure 12). Continuity between a mass at the nasopharynx and paranasal sinus disease involvement is often observed. Absence of metastasis to the paranasal sinuses is rare.[9,12] When a solitary paranasal sinus tumour is seen, another primary with differential diagnoses including sinonasal squamous cell carcinoma or sinonasal undifferentiated carcinoma should be considered.[16]

In T3 disease, further specification of bony structure involvement including the skull base, cervical vertebra and pterygoid structures has been added to the AJCC 8th edition.

T4 Disease

T4 disease includes tumour with intracranial extension, involvement of cranial nerves, hypopharynx, orbit, parotid gland (Figure 13), and/or extensive soft tissue infiltration beyond the lateral surface of the lateral pterygoid muscle.[9] Involvement of the hypopharynx is rare and associated with a much poorer outcome. The disease is thus upgraded from T1 to T4 when the tumour extends through the oropharynx to the hypopharynx. When the cavernous sinus is invaded (Figure 14), symptoms include those affected by cranial nerve III, IV, V1, V2 and VI function. It is usually the site of involvement when disease spread is from the pterygopalatine fossa through the foramen rotundum before further disease involvement of the cerebrum. In involvement of the posterior cranial fossa, the most common route of invasion is through the longus colli muscle and clivus, with extension to the prepontine cistern

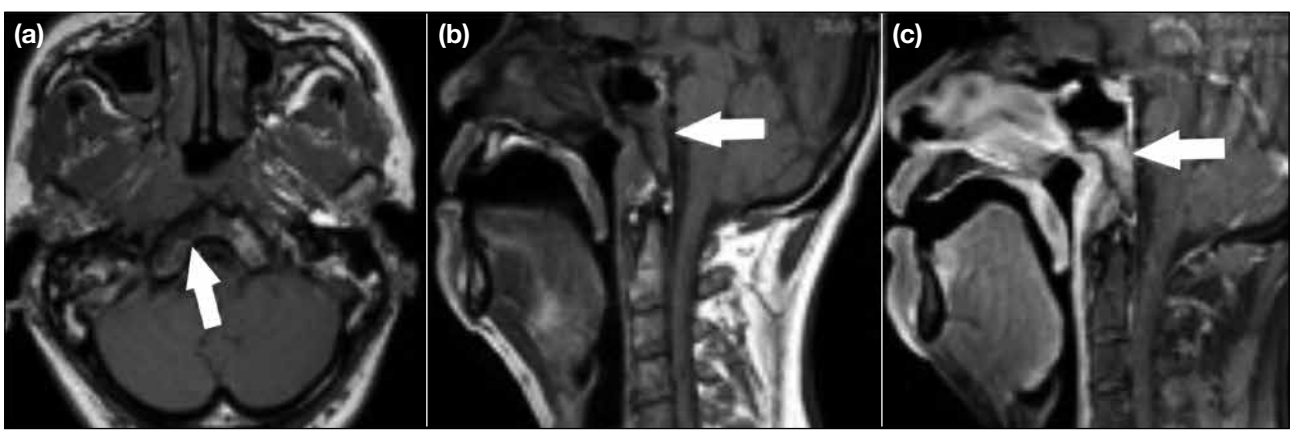

Figure 8. (a) Axial T1-weighted non-contrast magnetic resonance images showing decreased T1 marrow signal at the right side of clivus (arrow). (b) Sagittal T1 non-contrast image. (c) The sagittal post-contrast magnetic resonance image shows contrast enhancement of the clivus (arrows), suggestive of tumour invasion and hence T3 disease.

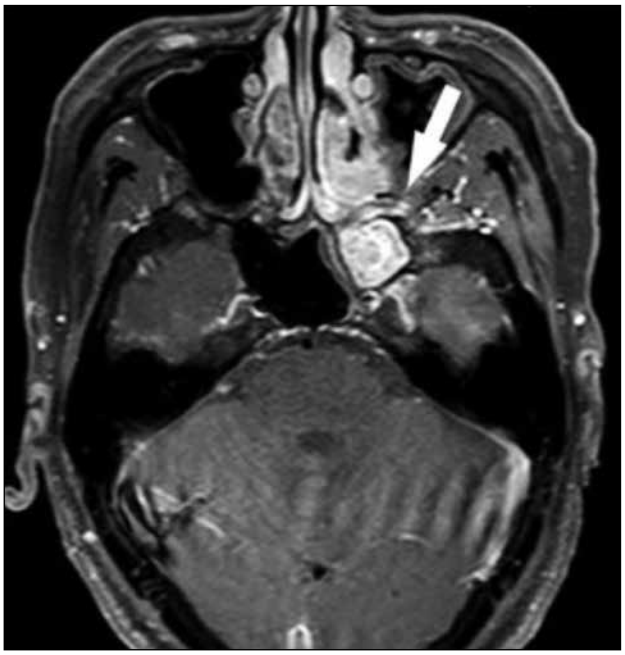

Figure 9. Axial post-contrast T1-weighted magnetic resonance image showing tumour involvement of the left pterygopalatine fossa (PPF, indicated by the arrow). The tumour has not invaded the left temporalis muscle through the left pterygomaxillary fissure. Notice that fat suppression is seen at the right PPF, signifying that the right PPF is still fat-filled and not invaded by tumour. The left PPF appears expanded apart from showing contrast enhancement.

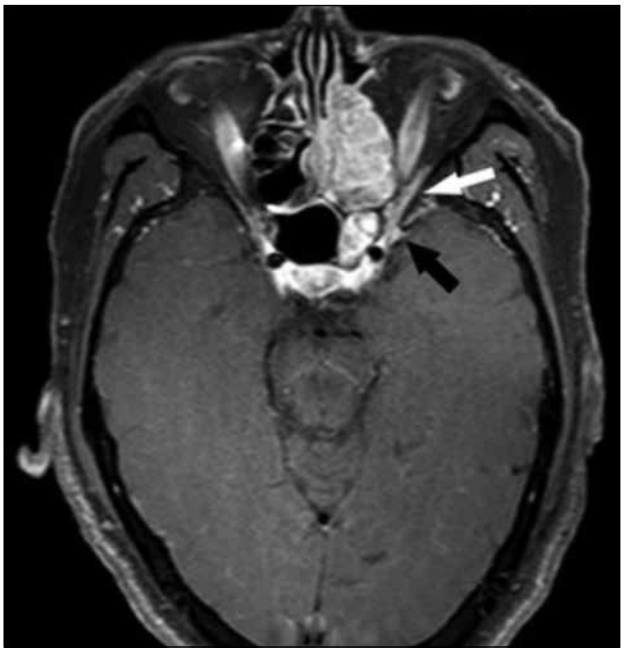

Figure 10. Axial T1 post-contrast fat saturation image showing enhancing tumour extends to the left inferior orbital fissure (white arrow) and left foramen rotundum (black arrow) that connect to the left orbit and left middle cranial fossa, respectively. Once the tumour reaches the pterygopalatine fossa, extensive involvement in different head and neck regions may follow. The left ethmoid and sphenoid sinuses are also invaded in this patient.

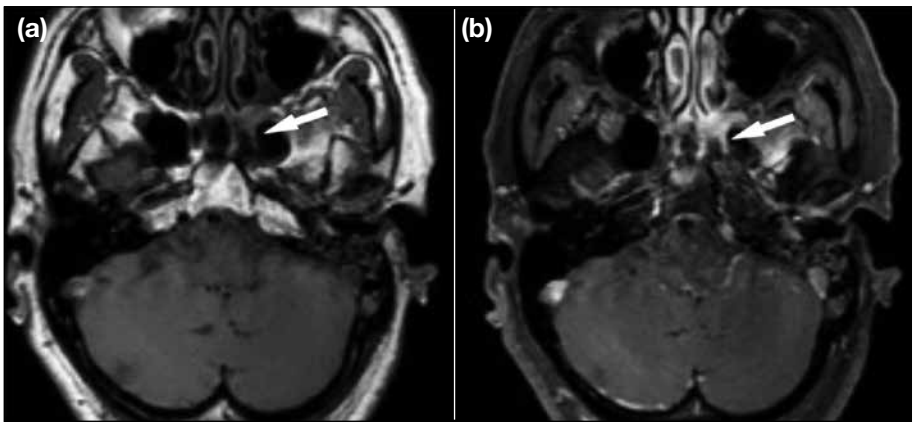

Figure 11. (a) Axial T1 non-contrast and (b) axial T1 post-contrast fat saturation images. Left pterygopalatine fossa (PPF) involvement. A tract extending backwards from the left PPF at the level of the petrous segment of the internal carotid artery is seen with contrast enhancement (arrows), suggestive of invasion of the left vidian canal and involvement of the left vidian nerve.

(Figure 15).[12] In severe cases, invasion of tumour from the pterygopalatine fossa into the orbit through the inferior orbital fissure can be seen.[14] Proptosis may be noted due to mass effect of the tumour.

In T4 disease, "extension to parotid gland and/or extensive soft tissue infiltration beyond the lateral surface of lateral pterygoid muscle" in the AJCC 8th edition replaces "extension to infratemporal fossa/masticator space" in the AJCC 7th edition. Other contents such as intracranial extension, involvement of cranial nerves, hypopharynx, and/or orbit are unchanged.

N STAGE

Detailed descriptions of staging of regional lymph nodes can be found in the AJCC Cancer Staging Manual.[9]

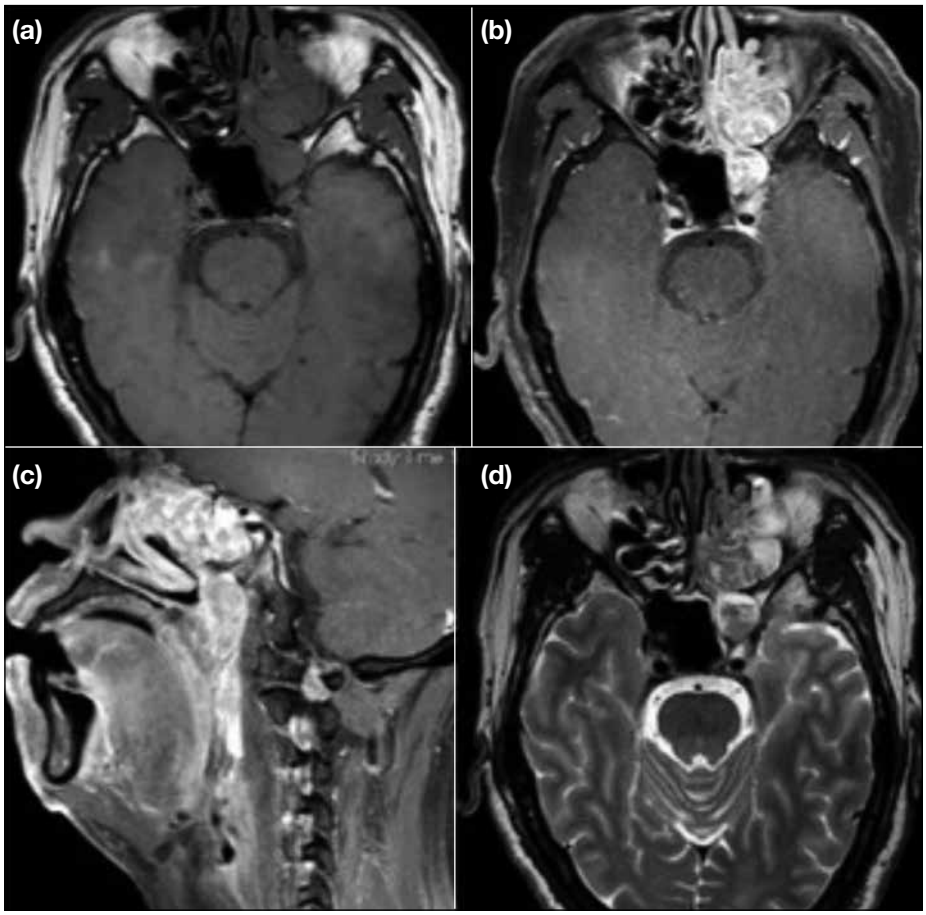

Figure 12. (a) Axial T1 non-contrast, (b) axial T1 post-contrast fat saturation, (c) sagittal T1 post-contrast fat saturation, and (c) axial T2 images. Extensive tumour involvement of the left ethmoid, maxillary and sphenoid sinuses, nasopharynx, and oropharynx is evident. This is T3 disease and no evidence of intracranial extension is seen.

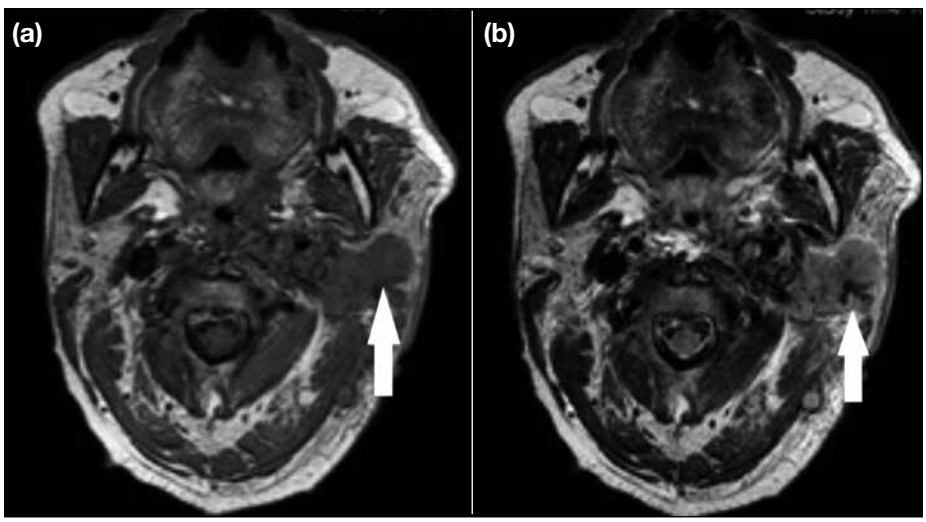

Figure 13. (a) Axial T1 non-contrast and (b) axial T1 post-contrast images showing tumour extends beyond the left parapharyngeal space to the left parotid space (arrows), signifying T4 disease.

NX or N0

NX signifies that regional lymph nodes cannot be assessed while N0 indicates that no regional lymph node metastasis is noted.

N1 Disease

N1 denotes unilateral metastasis in cervical lymph nodes and/or unilateral or bilateral metastasis in retropharyngeal lymph nodes, ≤6 cm at their largest dimension, above

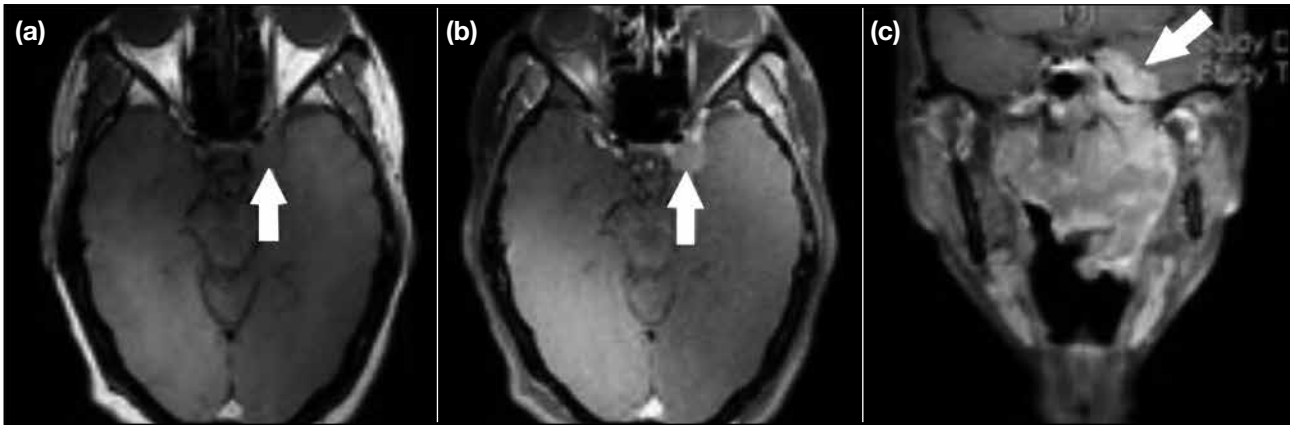

Figure 14. (a) Axial T1 non-contrast, (b). axial T1 post-contrast fat saturation, and (c) coronal T1 post-contrast fat saturation images. Extensive tumour at the nasopharyngeal region is noted, with invasion through the left foramen lacerum (coronal view) to the left cavernous sinus (arrows). The left internal carotid artery is engulfed.

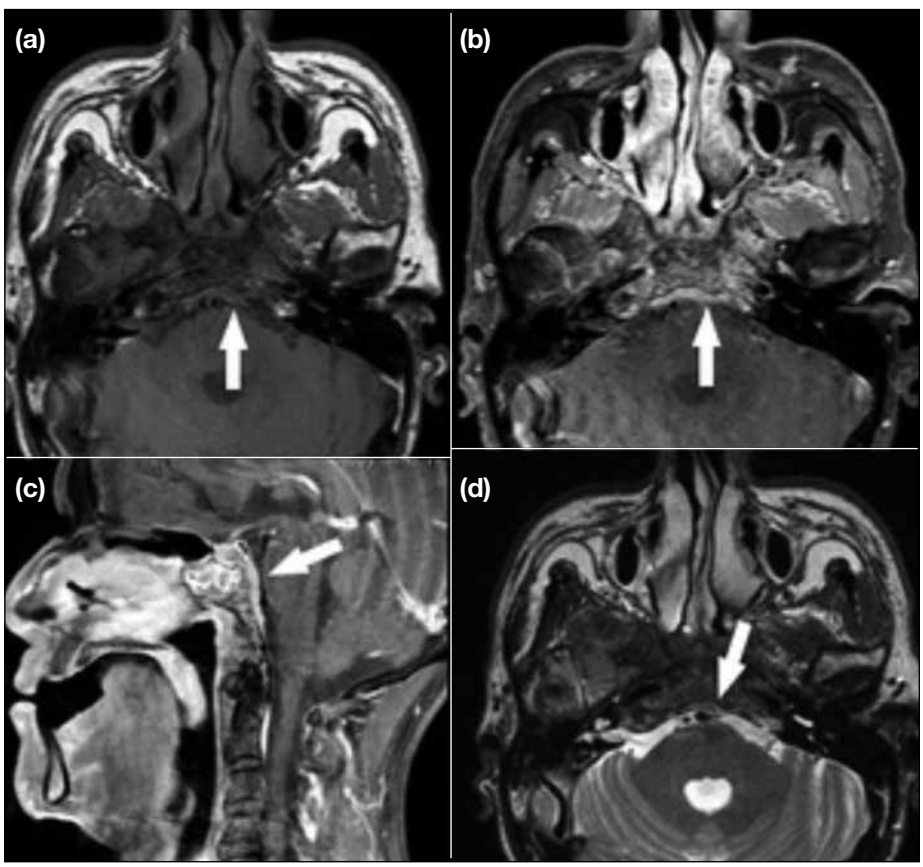

Figure 15. (a) Axial T1 non-contrast, (b) axial T1 post-contrast fat saturation, (c) sagittal T1 post-contrast fat saturation, and (d) axial T2 images. Another route of intracranial invasion is by direct invasion through prevertebral muscles and clivus to posterior cranial fossa. Retroclival epidural space and prepontine cistern is involved (arrows). This is T4 disease.

the caudal border of the cricoid cartilage.[9] In addition to T2 and T1 post-contrast images for primary tumour and nodal metastasis, diffusion-weighted imaging is also valuable for assessment of nodal metastasis.[17] The most important lymph node to evaluate is the retropharyngeal lymph node, a node located at the retropharyngeal space usually lateral to prevertebral muscle (Figure 16). It is the most common and earliest node to be involved in nasopharyngeal carcinoma. The lymphatic involvement of cervical lymph nodes usually follows a specific pattern with first involvement of the retropharyngeal lymph nodes, then spreading from upper to lower cervical

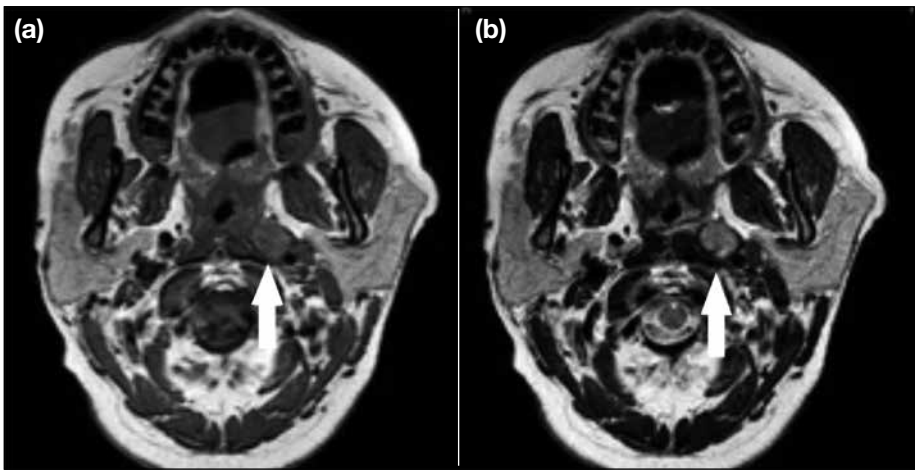

Figure 16. (a) Axial T1 non-contrast and (b) axial T1 post-contrast images showing the retropharyngeal lymph node is usually located lateral to the longus colli muscle at the retropharyngeal space. In this case, a pathological left retropharyngeal lymph node evident (arrows).

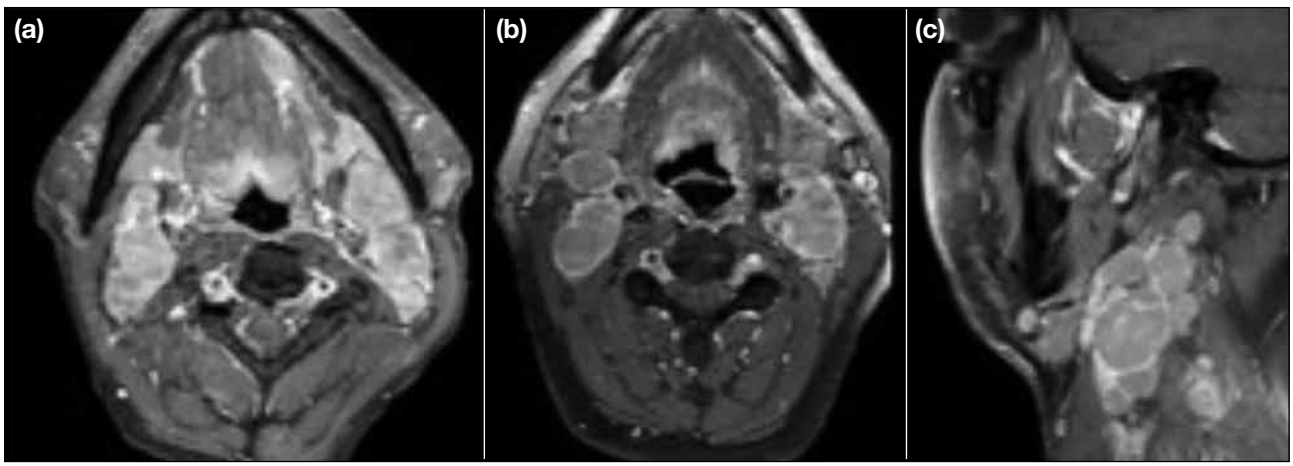

Figure 17. (a, b) Axial T1 post-contrast fat saturation and (c) sagittal T1 post-contrast fat saturation images. Enhancing pathological lymph nodes <6 cm at their greatest dimension at bilateral level II. All pathological lymph nodes are still above the inferior border of the cricoid cartilage when correlating with sagittal image. This is N2 disease instead of N3 disease.

nodes.[18] Skip metastases are not common but can still happen with cases that show involvement of cervical nodes without involvement of the retropharyngeal lymph node.[9,18]

For N1 disease, "above the caudal border of cricoid cartilage" has replaced "above supraclavicular fossa" in the AJCC 8th edition.

N2 Disease

N2 disease is diagnosed when there are bilateral metastases in cervical lymph nodes, ≤6 cm at the largest dimension and above the caudal border of cricoid cartilage (Figure 17).[9] It denotes bilateral lymph node involvement at level IIa, IIb, III and Va. Level IIa and IIb lymph nodes are the most commonly involved non-retropharyngeal lymph nodes. Lymph nodes from level IIa are the higher internal jugular group, above the hyoid bone and in contact with the internal jugular vein. Level IIb lymph nodes are also above the hyoid bone but posterior to and separated from the internal jugular vein although still anterior to the posterior border of the sternocleidomastoid (SCM) muscle. Level III nodes are between the level of the inferior border of the hyoid bone and the inferior border of the cricoid cartilage and beneath the SCM muscle. Level Va are any nodes posterior to the posterior border of the SCM muscle and above the inferior border of the cricoid cartilage. Involvement of submental (level Ia) and submandibular (level Ib) lymph nodes is uncommon but should be excluded.

For N2 disease, "above the caudal border of cricoid cartilage" has replaced "above supraclavicular fossa" in the AJCC 8th edition.

N3 Disease

N3 disease is said to be present when any cervical lymph nodes exceed 6 cm at their largest dimension and/or with extension below the caudal border of the cricoid cartilage, regardless of laterality of lymph node involvement.[9] It refers to any pathological lymph nodes at level IV or Vb. Involvement of these nodes carries the worst prognosis as they are the most distant cervical lymph nodes to be involved.[9]

For N3 disease, "below the caudal border of cricoid cartilage" has replaced "in supraclavicular fossa" in the AJCC 8th edition.

For AJCC criteria, the nodal staging is based on maximum dimension, laterality, and site of lymph nodes. Any lymph nodes along the midline are considered ipsilateral nodes. Nonetheless identification of nodal metastases relies on a short axis of lymph nodes and morphological features including central necrosis and extranodal extension (Figure 18).[19] In general, most cervical lymph nodes normally should be <10 mm in their short axis. In particular, normal retropharyngeal lymph nodes should not exceed 5 mm in the short axis.[20] If positron emission tomography–computed tomography is performed, any marked hypermetabolism of lymph nodes along the expected nodal path of disease spread should raise a suspicion of lymph node metastases, regardless of size of lymph nodes.[21] One more point to note is that the size of the primary tumour does not correlate with the extent of nodal metastases.[12]

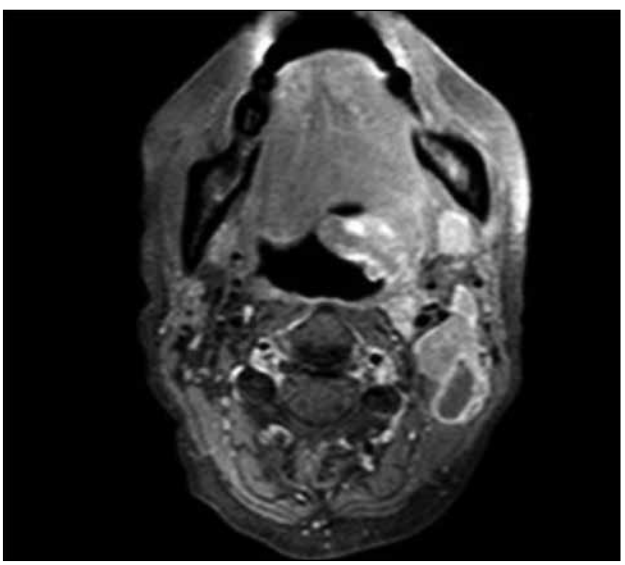

Figure 18. Axial T1 post-contrast fat saturation image showing the left level II lymph node measures 3.8 cm at its greatest dimension. Central necrosis is seen in this lymph node, suggestive of a metastatic lymph node. Since there is only unilateral lymph node involvement, it is staged as N1 disease.

CONCLUSION

Nasopharyngeal carcinoma staging is important to guide treatment and determine disease prognosis. Head and neck magnetic resonance imaging adds high value in achieving this goal. Its multiplanar capability, high soft tissue contrast, and immense anatomical detail makes it a powerful imaging modality. The staging method in this article is based on AJCC 8th edition. Major changes from the AJCC 7th edition include incorporation of involvement of medial pterygoid, lateral pterygoid or prevertebral muscles into T2 disease, further specification of bony structure involvement including skull base, cervical vertebra and pterygoid structures in T3 disease, and discarding of terms such as infratemporal fossa/masticator space in T4 disease and replacement with "soft tissue infiltration beyond the lateral surface of lateral pterygoid muscle". Nodal staging is now classified using the anatomical boundary of the caudal border of the cricoid cartilage instead of supraclavicular fossa. Continuous update on disease staging will be necessary in the future with advancement of imaging modality and treatment options.

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