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Nasopharyngeal carcinoma

Patterns of lymph node metastasis from nasopharyngeal carcinoma based on the 2013 updated consensus guidelines for neck node levels ☆

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ABSTRACT

Purpose: To explore patterns of node distribution in nasopharyngeal carcinoma (NPC) based on the 2013 updated guidelines for neck node levels.

Methods and materials: We retrospectively reviewed the imaging documents of 3100 cases of newly diagnosed NPC between January 2010 and January 2013. All patients received an MRI scan. The scan range extended from 2 cm above the anterior clinoid process to the inferior margin of the sternal end of the clavicle. All MR images were evaluated by the multi-disciplinary treatment group of NPC.

Results: A total of 2679 (86.4%) cases had involved lymph nodes. The detailed distribution was: level Ia 0, level Ib 115 (4.3%), level IIa 1798 (67.1%), level IIb 2341 (87.4%), level III 1184 (44.2%), level IVa 350 (13.1%), level IVb 28 (1.0%), level Va,b 995 (37.1%), level Vc 49 (1.8%), level VI 0, level VIIa 2012 (75.1%), level VIIb 178 (6.6%), level VIII 53 (2.0%), level IX 2, level Xa 2, level Xb 3. Among patients with level VII involvement, only 6 (0.3%) were located at the medial group. Of the patients with level II disease, the upper borders of metastatic nodes in 25.9% cases were beyond the caudal edge of C1. Patients with level VIII, or IX, or X node metastasis were always with extensive ipsilateral lymphadenopathy, and the total number of involved nodes was $\geqslant$6. There were 35 cases of lymphadenopathy beyond the range of the updated guidelines, located inside the trapezius muscles, but posterior to level V.

Conclusions: This is the first description of nodal spread patterns based on the updated consensus guidelines. Involvement of the retropharyngeal nodes was mainly located at the lateral group, the medial group was rarely seen. The suggested upper border of level II cannot fully cover all the involved level II nodes. The posterior level V border is not enough to cover all level V lymphadenopathies for NPC.

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The successful implementation of intensity modulated radiation therapy (IMRT) for nasopharyngeal cancer (NPC) requires optimal selection and delineation of not only the gross tumor volume (GTV), but also the clinical target volume (CTV). Since NPC has the highest preponderance for regional lymph node metastasis among head and neck cancer (HNC), the bilateral neck lymphatic drainage area is always contoured as CTV in order to achieve far greater loco-regional control, regardless of the stage at diagnosis.

Recommendations for selection and delineation of the neck node CTV were published by several researchers in the past ten years [1–3]. However, some important discrepancies exist regarding the boundaries of the same node level, thus leading to inter-observer heterogeneity in contouring the neck CTV. A consensus was proposed in 2003 and accepted throughout the world [4]. But the consensus guidelines only apply to the node-negative neck. The patterns of nodal metastases from NPC have been described by several authors [5–9]. The actual distribution of enlarged nodes as described in terms of nodal levels differs between those studies, resulting in some discrepancies. Proposals for the delineation of the nodal CTV in the node-positive and the post-operative neck were published in 2006, adding the retrostyloid space and the supra-clavicular fossa [10]. Still, some nodal regions described in the TNM atlas were excluded. Therefore, experts in the field of radiation therapy for HNC reviewed the literature and updated the previously published guidelines on delineation of the neck CTV in 2013 [11]. In the new guidelines, 10 nodal groups were defined in accordance with the TNM atlas for cervical lymph nodes. However, there is a paucity of knowledge on patterns of nodal metastasis from NPC based on these new guidelines. In addition, there is no evidence on whether these guidelines fully

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cover the lymphatic drainage pathway of NPC. Therefore, we carried out this retrospective study to explore the patterns of nodal spread, in order to provide evidence for delineation of the neck CTV for NPC.

Methods and materials

Patients

We retrospectively reviewed the imaging documents of the newly diagnosed NPC between January 2010 and February 2013 in the Fudan University Shanghai Cancer Center. All patients were previously untreated and have received MRI scans of the nasopharynx and neck. Altogether, 3100 cases were included in the study. All patients had WHO type II or type III pathology. The median age was 52 years (from 11 to 82). The male to female ratio was 2.81 (2287 versus 813).

MR scanning protocol

All MR images were acquired with the same GE 1.5 Tesla unit using a head and neck coil. The examined area extended from the upper border of the orbit to the inferior margin of the sternal end of the clavicle. T1-weighted fast spin-echo (FSE) images in the axial and sagittal planes (repetition time [TR] 400–500 ms and echo time [TE] 10–15 ms), and T2-weighted FSE images in the axial plane (TR 4000–5000 ms and TE 80–100 ms) were obtained before injection of contrast material. After intravenous injection of gadolinium-complexed diethylene triamine pentaacetic acid at a dose of 0.1 mmol/kg of body weight, T1-weighted fast spoiled gradient echo (FSPGR) fat-suppressed axial and coronal sequences were acquired (TR 150–250 ms and TE 2–10 ms). Section thickness was 6 mm with a 1-mm interslice gap for the axial plane, and 4 mm without an interslice gap for the coronal and sagittal planes.

Image assessment

All MR images were evaluated by the multi-disciplinary treatment group of NPC, which included five radiation oncologists and two diagnostic radiologists. Radiologic criteria for diagnosis of lymph node metastasis were based on the literature. Retropharyngeal lymph node (RPLN) assessment included the medial and lateral chains.

Criteria of RPLN involvement include: (1) Minimal axial diameter of 5 mm or larger; (2) Any RPLN with central necrosis; (3) Any groups of two or more RPLNs; (4) Any visible medial group RPLN. Cervical nodes were considered metastatic in the presence of necrosis or extracapsular spread, or if their shortest axial diameter was $\geqslant$10 mm, or if there was a group of three or more nodes that were borderline in size [12–15]. Definition of central necrosis on MR images was a focal area of high signal intensity on T2-weighted images or a focal area of low signal intensity on T1-weighted images with or without a surrounding rim of enhancement [16]. The minimal axial diameter corresponded to the widest diameter of the node in the axial plane that was perpendicular to the maximal axial diameter.

The actual distribution of enlarged nodes was recorded in detail according to the consensus guidelines published in 2003 [4] and updated proposals in 2006 [10]. Nodes uncovered by those guidelines were recorded by the actual region as described in the TNM atlas. Data were kept in the computer by the research secretary.

The initial purpose of this work is to provide the distribution patterns of nodal involvement from NPC, aiming to find out a nodal classification guideline specific for NPC. However, an updated consensus guideline for neck node levels was published in 2013 [11]. We reviewed the data and rearranged the nodal distribution according to the 2013 updated guidelines.

Results

Incidence and distribution of nodal metastasis

A total of 2679 (86.4%) cases had involved lymph nodes, and 1398 (45.1%) cases had bilateral lymphadenopathy. The distribution is detailed in Table 1.

Level I: None had nodal disease at level Ia. There was no solitary metastasis to level I b. Of the 115 patients with level Ib node involvement, all were simultaneously accompanied with level II lymphadenopathy. In addition, 31 cases were also with oropharynx infiltration, 18 cases were with the primary cancer infiltrating more than one third of the posterior nasal cavity.

Level II: Of the 2341 patients with level IIb node involvement, the upper border of metastatic lymphadenopathies relative to the cervical vertebra was assessed visually by one oncologist. We found that the most superior edge in 607 (25.9%) cases was beyond the caudal edge of the lateral process of the first vertebra (C1), the suggested upper border of level II in the updated guidelines, with 492 (21.0%) cases reaching half of C1, and 115 (4.9%) cases reaching the skull base (Fig. 1). However, all the 1798 cases with level IIa lymphadenopathy were below the caudal edge of the lateral process of C1.

Level III: Of the 1184 cases with level III node involvement, 1151 cases (97.2%) were located laterally or posteriorly to the carotid sheath, only 33 (2.8%) cases were located anterior to the carotid sheath (Fig. 2).

Level IV: There were 350 cases (13.1%) with level IVa lymphadenopathy, all were located laterally or posteriorly to the carotid sheath. Of the 28 cases (1.0%) with level IVb node involvement, all were simultaneously accompanied with level IVa lymphadenopathy. There was no solitary metastasis to level IVb. The total number of involved nodes in patients with level IVb node involvement was always more than six.

Level V: 576 (21.5%) cases had nodal disease in level Va, 419 (15.6%) cases in level Vb, and 49 (1.8%) cases in level Vc. All patients with level Vc lymphadenopathy were simultaneously accompanied with nodal involvements in other levels, and the total number of metastatic nodes was always more than seven. 35 cases had lymphadenopathy beyond the suggested level V boundaries. They were limited laterally by the trapezius muscle, and medially by the levator scapulae, but posterior to level V (Fig. 3). Those 35

Table 1
Detailed distribution of the 2679 cases with involved nodes.

Level	Number of patients	Percentage (%)
Ia	0	0
Ib	115	4.3
IIa	1798	67.1
IIb	2341	87.4
III	1184	44.2
IVa	350	13.1
IVb	28	1.0
Va	576	21.5
Vb	419	15.6
Vc	49	1.8
VIa	0	0
VIb	0	0
VIIa	2012	75.1
VIIb	178	6.6
VIII	53	2.0
IX	2	0.07
Xa	2	0.07
Xb	10	0.4

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