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Relationship between the growth pattern of nasopharyngeal cancer and the cervical lymph nodes based on MRI findings: can the cervical radiation field be reduced in patients with nasopharyngeal cancer?

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ABSTRACT. To identify patients with nasopharyngeal cancer in whom the cervical radiation field can be reduced, we classified the growth patterns of nasopharyngeal cancer based on MRI findings into 4 types and performed an evaluation. Based on MRI findings, we classified the growth patterns of primary cancer in 94 patients with nasopharyngeal cancer into Type 1 (superficial type), Type 2 (lateral invasive type), Type 3 (upward invasive type), and Type 4 (anterior extension type), and further classified Type 2, based upon nasopharyngoscopic findings, into Type 2a (unilateral invasive type) and Type 2b (bilateral invasive type). The cervical lymph node metastasis areas were evaluated according to these types. Type 2 showed a significantly higher incidence of cervical lymph node metastasis only on the ipsilateral side than the other types ($p=0.0024$). In particular, all patients with Type 2a had cervical lymph node metastasis only on the ipsilateral side ($p=0.0212$). This study suggests that the distribution of metastasised cervical lymph nodes depends on the pattern of tumour extent of the primary site.

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Cervical lymph node metastasis often occurs in patients with nasopharyngeal cancer (NPC). It has been reported that 60–87% of patients demonstrated cervical lymphadenopathy at the time of diagnosis [1–5]. Previous articles [6–8] have attributed bilateral cervical lymphadenopathy to the abundance of lymphatic tissues in the posterior wall of the nasopharynx and the presence of abundant lymphatic anastomoses crossing the midline. Therefore, bilateral cervical lymph nodes have always been included in the target volume on radical radiotherapy (RT) [6, 7]. As a result, the radiation fields were wide and complications such as the xerostomia secondary to parotid irradiation have been experienced [9–14].

Recently, MRI has been used to evaluate NPC [15–22]. Multiplanar imaging can show tumour extension in all planes, and there is improved tumour delineation and identification of the spread of the tumour to adjacent areas as a result of the better soft tissue contrast in comparison with CT.

We previously evaluated the relationship between tumour growth patterns and lymph node metastasis based on MRI images in 32 patients with nasopharyngeal cancer. We showed a high incidence of cervical lymph node metastasis only on the ipsilateral side in patients with tumour invasion only to the lateral nasopharynx (lateral invasive type), and the cervical radiation field can be reduced in such patients [23].

In this study, to identify patients in whom the cervical radiation field can be reduced, the relationship between the growth pattern of nasopharyngeal cancer and lymph node metastasis on MR images was evaluated in detail in 94 patients, obtained by adding 62 patients to the above 32 patients.

Methods and materials

Patients

Between April 1990 and August 2004, 94 patients (70 males and 24 females) were retrospectively reviewed. The patient age ranged from 14 years to 80 years (median 51 years). Histology revealed that 17 cases of nasopharyngeal cancer were WHO type I, 15 were type II, and 62 were type III. According to the 1997 TNM classification, the tumour stage was classified as stage I in 3 patients, stage II A in 1 patient, stage II B in 31 patients, stage III in

22 patients, stage IV A in 11 patients, stage IV B in 20 patients and stage IV C in 6 patients.

As a basic treatment method, patients aged ≤ 70 years were treated with alternating chemoradiotherapy, in which chemotherapy (CDDP, 5FU) is alternated with radiotherapy [24], and those aged ⩾ 71 years were treated by radiotherapy alone.

Evaluation items

The evaluation items were the possible relationships between the growth pattern as well as the size of nasopharyngeal tumour and cervical lymph node metastasis, between the degree of histological differentiation and cervical lymph node metastasis, and between the tumour growth pattern and the degree of histological differentiation.

Differences were analysed by the log-linear model without interaction terms using the contingency table data [25].

MRI techniques

MR studies were performed with a 1.5 T unit (Signa; General Electric Medical Systems, Milwaukee, WI). Images were obtained with 5 mm thick contiguous sections in two or three planes (axial, coronal, sagittal) depending on the extent of the tumour. All patients underwent both plain and contrast-enhanced MRI. A spin-echo (SE) multisection imaging technique was used in all examinations. A SE 600/25 image and a SE 2000/80 image were considered to be T_1 weighted and T_2 weighted, respectively.

Classifications of MR image

To determine the pattern of tumour extent at the primary site and existence of metastasised cervical lymph nodes, MR images were evaluated by three experienced radiologists specializing in head and neck cancers working together as a team. When they did not reach consensus after an initial reading regarding the primary tumour and the cervical lymphadenopathy, the final decision was made by majority rule.

The 94 patients were classified into 4 types with 2 subtypes (Figures 1–4) according to the tumour extent at the primary site demonstrated on MR images before the treatment. Type 1 (superficial type) tumours were limited to the nasopharyngeal mucosal space. Tumour locations could not be judged on MRI, but were assessed by nasopharyngoscopy from the appearance of slightly irregular surface of nasopharyngeal mucosa. Type 2 (lateral invasive type) tumours could be detected on the lateral pharyngeal wall with involvement of the parapharyngeal space laterally. This invasive type was divided into two subtypes. Type 2a (unilateral invasive type) tumours were those that remained on either side of the midline by MRI and did not extend the midline of the posterior wall of nasopharynx assessed by nasopharyngoscopy. Type 2b (bilateral invasive type) tumours were those that extended a cross the midline by MRI and/or nasopharyngoscopy. Type 3 (upward invasive type) were tumours that mainly invaded cranially toward the skull base. Type 4 (anterior extension type) tumours extended anteriorly toward the nasal cavity, but did not invade the adjacent normal structures. Tumours that could not be classified into the above 4 types were considered to be unclassifiable.

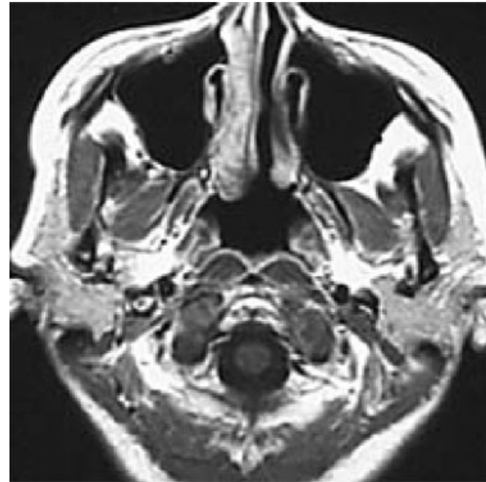


Figure 1. A 31-year-old woman presenting with Type 1 (superficial type) spread. Axial T_1 weighted MR image, Gd-DTPA enhanced, shows no abnormal findings in the nasopharyngeal mucosal space.

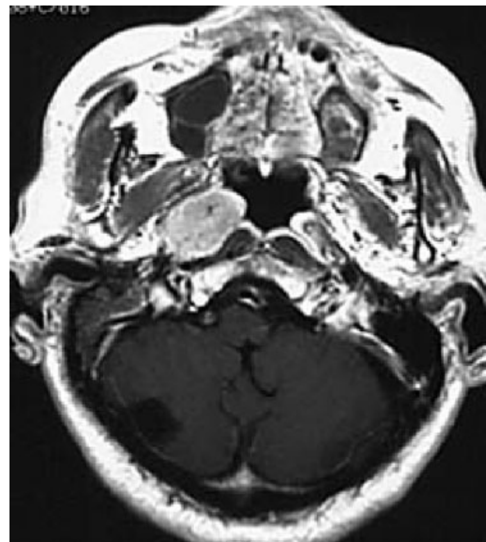


Figure 2. A 64-year-old man presenting with Type 2a (unilateral invasive type) spread. Axial T_1 weighted MR image, Gd-DTPA enhanced, shows a right nasopharyngeal tumour infiltrating the right parapharyngeal space.

Classification of tumour size

All 94 patients were classified into three groups according to the maximal tumour diameter of axial imaging: small (S≤2 cm), medium (2 cm<M<4 cm) and large (4 cm ≤L) tumours. Type 1 tumours that cannot be measured on MRI images were classified as small.

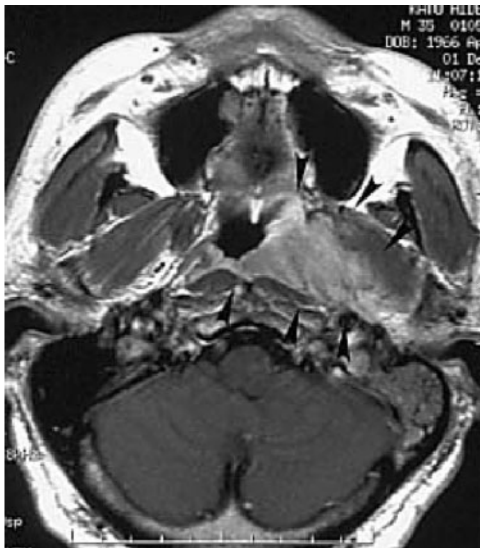


Figure 3. A 35-year-old man presenting with Type 2b (bilateral invasive type) spread. Axial T_1 weighted MR image, Gd-DTPA enhanced, shows a left a nasopharyngeal tumour (arrowheads) invading across the midline to the opposite side.

Classification of pathology

The 94 patients were divided into two groups according to the degree of tumour differentiation, those with lymphoepithelioma, undifferentiated carcinoma and poorly differentiated squamous cell carcinoma as Group 1, and those with moderately and well differentiated squamous cell carcinoma as Group 2.

Definition of metastatic lymph nodes

Metastatic cervical lymph nodes were defined as nodes with a minimal axial diameter of 10 mm in a previous study [26]. In this study, in addition to lymph nodes fulfilling this criterion, the following lymph nodes were also regarded as metastasis even when the minimal axis diameter was $\leq$ 10 mm: necrotic lymph nodes with a visualized capsule and lymph nodes showing a definite decrease in size on MR images after treatment.

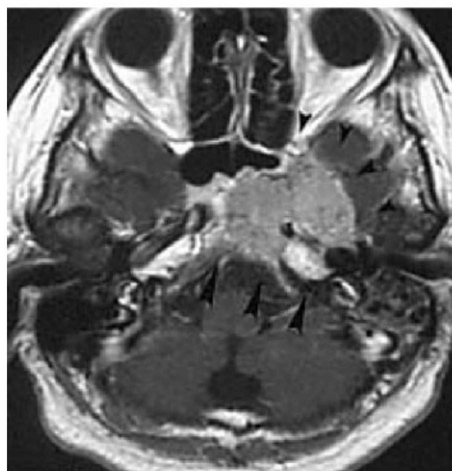
Results

Of the 94 patients, 19 (20%) had type 1, 12 (13%) had type 2a, 18 (19%) had type 2b, 14 (15%) had type 3, 29 (31%) had type 4 and 2 (2%) were unclassified. 82 (87%) out of 94 patients demonstrated unilateral and/or bilateral cervical lymphadenopathy. 41 (50%) out of 82 patients presented bilateral cervical and/or contralateral cervical lymphadenopathy.

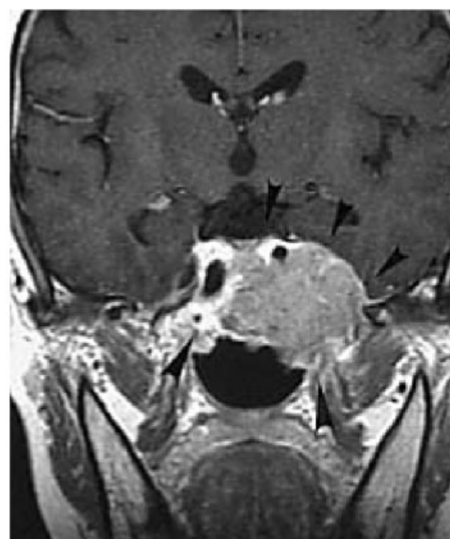
The relationship between the pattern of tumour extent at the primary site and the cervical lymph node metastasis is shown in Table 1. The incidence of ipsilateral cervical lymph node metastasis was significantly higher for Type 2 than for the other types (p=0.0024). In particular, all patients with Type 2a had cervical lymph node metastasis only on the ipsilateral side (p=0.0148). The incidence of bilateral cervical lymph node metastases was high for Types 1 (p=0.0393) and 4 (p=0.0482).

Table 2 shows the size of nasopharyngeal tumour and areas of cervical lymph node metastasis. No differences were observed in areas of cervical lymph node metastasis among these groups, but the incidence of lymph node metastasis was lower in large tumour groups (p=0.0435).

Table 3 shows areas and incidences of cervical lymph node metastasis according to the degrees of histological differentiation. No differences were observed in areas of cervical lymph node metastasis between Group 1 (differentiated type) and Group 2 (poorly differentiated type), but the incidence of lymph node metastasis was lower in Group 1 (p=0.0008).



(a)



(b)

Figure 4. (a) A 60-year-old man presenting with Type 3 (upward invasive type) spread. Axial T_1 weighted MR image, Gd-DTPA enhanced, shows a nasopharyngeal tumour (arrowheads) which is invading toward the left skull. (b) Coronal T_1 weighted MR image, Gd-DTPA enhanced, shows a nasopharyngeal tumour (arrowheads) which is invading mainly toward the left skull base.

Table 1. Relationship between the pattern of tumour extent at the primary site and areas of cervical lymph node metastasis

	Type 1 n=19	Type 2a n=12	Type 2b n=18	Type 3 n=14	Type 4 n=29
No lymph node metastasis (N0)	2	1	2	3	3
Ipsilateral lymph node metastasis	5	11	11	5	9
Bilateral and/or contralateral lymph node metastasis	12	0	5	6 (1)	17

Unclassified type (2 cases) was excluded from Table 1.
( ): Number of contralateral neck lymph node metastasis.

Table 2. Relationship between the size of nasopharyngeal tumour and areas of cervical lymph node metastasis

	Small n=19 (S≤2 cm)	Middle n=41 (2 cm<M<4 cm)	Large n=34 (4 cm≤L)
No lymph node metastasis	2	3	7 (1)
Ipsilateral lymph node metastasis	5	22	14
Bilateral and/or contralateral lymph node metastasis	12	16	13

( ): Number of contralateral neck lymph node metastasis.

Table 3. Relationship between the degrees of histological differentiation and of cervical lymph node metastasis

	Group 1 n=18	Group 2 n=76
No lymph node metastasis	7	5
Ipsilateral lymph node metastasis	8	33
Bilateral and/or contralateral lymph node metastasis	3	38 (1)

Group 1: differentiated squamous cell carcinoma.
Group 2: undifferentiated carcinoma, poorly differentiated squamous cell carcinoma.
( ): Number of contralateral neck lymph node metastasis.

Table 4 shows the degree of histological differentiation and the growth pattern of nasopharyngeal tumour. No association was observed between Type 1 or 2 and the degree of histological differentiation. However, patients with Type 3 (upward invasive type) were frequently included in Group 1 (p=0.0034), and all patients with Type 4 tumours were included in Group 2 (p=0.0383).

Discussion

In the 32 patients in our previous study, tumour growth patterns were classified into 3 major types (Type 1, superficial type: Type 2, invasive type; and Type 3, anterior extension type), and Type 2 was further classified into 3 subtypes (Type 2a, unilateral invasive type; Type 2b, bilateral invasive type; and Type 2c, upward invasive type) [23]. In the previous study, the lymph node metastasis pattern was similar between Types 2a and 2b, but Type 2c showed a different pattern. Therefore, in this study, Type 2 was defined as the lateral invasive type and classified into Type 2a (unilateral invasive type) and Type 2b (bilateral invasive type), while Type 2c was separated from Type 2 and changed to Type 3 (upward invasive type). In the previous study, Type 2a was differentiated from Type 2b based only on MRI findings. However, in this study, nasopharyngoscopic findings were also used, and Type 2a was defined as tumour extension not passing the midline of the nasopharynx.

As Table 1 shows, the incidence of cervical lymph node metastasis only on the ipsilateral side was significantly higher for Type 2 than for the other types (p=0.0024). In particular, all patients with Type 2a showed cervical lymph node metastasis only on the ipsilateral side, which suggested that the cervical radiation field can be reduced for this type. Types 1 (superficial type) and 4 (anterior extension type) showed similar lymph node metastasis patterns and higher incidences of bilateral cervical lymph node metastasis than the other types, which suggested that a reduction in the radiation field is difficult for these types.

No significant association was observed between tumour size and cervical lymph node metastasis. However, bilateral cervical lymph node metastasis was frequently observed in patients with small tumours (S≤2 cm) rather than patients with large tumours (p=0.0272).

Concerning the degree of histological differentiation and cervical lymph node metastasis, the percentage of patients with no lymph node metastasis (N0) was significantly higher in Group 1 (differentiated type) than in Group 2 (poorly differentiated or undifferentiated type) (p=0.0008). In Group 1, N0 was observed in 7 patients, of whom 3 showed Type 3 on MRI images. As Table 4 shows, the patients with Type 3 included 7 patients with the differentiated type. Of the 7 patients, 3 had no cervical lymph node metastasis, suggesting that the incidence of cervical lymph node metastasis is low in patients with Type 3 and the differentiated type, compared with those with the other types.

Table 4. Relationship between the pattern of tumour extent at the primary site and the degrees of histological differentiation

	Type1 n=19	Type 2a n=12	Type 2b n=18	Type 3 n=14	Type 4 n=29
Group 1	4	2	4	7	0
Group 2	15	10	14	7	29

Group 1: differentiated squamous cell carcinoma.
Group 2: undifferentiated carcinoma, poorly differentiated squamous cell carcinoma.
Unclassified type (2 cases) was excluded from Table 4.

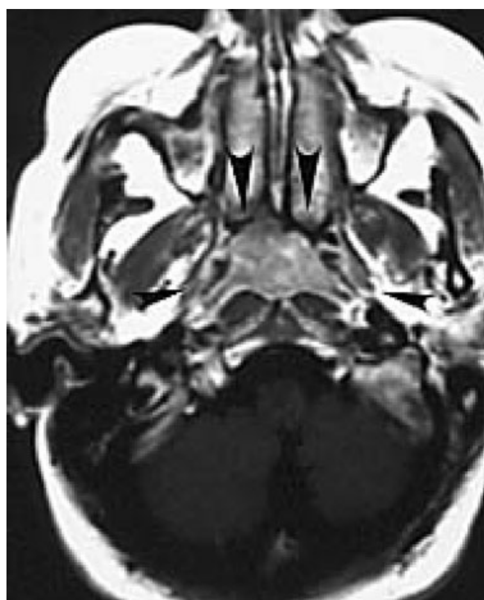


Figure 5. A 40-year-old woman presenting with Type 4 (anterior extension type) spread. Axial T_1 weighted MR image, Gd-DTPA enhanced, shows a nasopharyngeal tumour (arrowheads) extending anteriorly without invasion to adjacent areas.

When the growth pattern of nasopharyngeal cancer was classified and its association with cervical lymph node metastasis was evaluated, the incidence of bilateral cervical lymph node metastasis was high for Types 1 and 4, that of ipsilateral metastasis was high for Type 2, and intermediate findings were obtained for Type 3. The incidence of cervical lymph node metastasis was significantly low in patients with differentiated tumours.

These results suggest that the radiation field and dose of the neck for nasopharyngeal cancer can be individualized. The radiation field and dose of the neck may be reduced especially for patients with Type 2a. This hypothesis will be confirmed by prospective study.

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