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Concurrent chemoradiotherapy with adjuvant chemotherapy for high-risk nasopharyngeal carcinoma

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Abstract

Objectives: To evaluate the impact of invasion of the prevertebral or parapharyngeal spaces and large tumor volume on treatment outcomes in patients with nasopharyngeal carcinoma (NPC).
Methods: A total of 105 patients with newly diagnosed NPC were enrolled in this study. TNM stage and presence of invasion of the prevertebral or parapharyngeal spaces were recorded. All patients received a total dose of 70–75 Gy.
Results: After controlling for age, sex, and chemotherapy status, invasion of the prevertebral or parapharyngeal spaces and large primary tumor volume produced a significantly increased hazard ratio for distant metastasis and recurrence. We defined patients with two or more such prognostic factors as high-risk patients, in whom the 3-year metastasis-free survival rate, with and without adjuvant chemotherapy, was 100% and 69.6%, respectively ($P = 0.02$). Their 3-year recurrence-free survival rate, with and without adjuvant chemotherapy, was 93.3% and 70.2% ($P = 0.09$). This benefit was not observed in low-risk NPC patients.
Conclusion: NPC patients with any two or more of the factors, involvement of the prevertebral space, large primary tumor volume, or advanced parapharyngeal space invasion, had more recurrence and poor survival rates and benefited from concurrent chemoradiotherapy followed by adjuvant chemotherapy.

Keywords: Nasopharyngeal carcinoma; Prognostic factors; Prevertebral space; Primary tumor volume; Parapharyngeal space; Concurrent chemoradiotherapy; Adjuvant chemotherapy

1. Introduction

Taiwan is one of the areas with a high incidence of nasopharyngeal carcinoma (NPC): the annual incidence rate is 6.17 per 100,000 as compared with <1 per 100,000 in Western countries [1]. Treatment for patients with NPC has relied primarily on radiotherapy or concurrent chemoradiotherapy (CCRT), partly because of the inaccessibility of the anatomic site and the tumor's high sensitivity to radiotherapy and chemotherapy [2]. Numerous systems have been used to classify NPC in studies throughout the world. The most widely used systems are those of the American Joint Committee of Cancer (AJCC), the International Union Against Cancer (UICC), and Ho. For classifying and staging NPC, all of these systems are based on anatomic location and involvement of cranial nerves. Neel and Taylor [3] developed a working formulation that was able to stratify patients into groups with markedly different prognoses, but it may require prospective study in endemic areas.

Recently, three new prognostic factors, which were not included in the AJCC staging system, have been noted. Involvement of the prevertebral space in oropharyngeal or hypopharyngeal cancer determines whether the tumor is unresectable (T4b) or incurable [4]. However, the impact of invasion of the prevertebral space on the prognosis for NPC is poorly understood and controversial. Tumor volume is

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known to be a significant prognostic factor in the treatment of malignant tumors, and previous studies have revealed that primary tumor volume is closely related to the survival rates in patients with NPC [5–7]. A high incidence of parapharyngeal extension occurs early in the course of NPC. Parapharyngeal extension is regarded as a parameter of T-stage in the present AJCC staging system, but the radiologic definition of tumor infiltration lacks consensus [8]. We have conducted a retrospective study to elucidate the impacts of primary tumor volume and invasion of the prevertebral or parapharyngeal spaces on treatment outcomes in patients with NPC and have also analyzed how outcomes were affected by different therapeutic approaches.

2. Materials and methods

2.1. Subjects

Patients with a diagnosis of NPC were identified from the cancer registry of the Kaohsiung Veterans General Hospital from 2002 to 2006. One hundred and forty-five cases were identified and retrieved from the archives. Forty patients were not eligible for analysis because of the presence of distant metastasis at the time of presentation, loss of follow-up, or incomplete baseline magnetic resonance imaging (MRI) information. Patients were staged according to the AJCC stage classification modified in 1997. In addition to the TNM staging system, gross tumor volume of the primary tumor and retropharyngeal node, and presence of invasion of the prevertebral or parapharyngeal spaces were recorded.

2.2. Identification of invasion of the prevertebral space

Involvement of the prevertebral space was defined on the basis of MRI findings. Diagnosis of prevertebral space involvement was made if the prevertebral space was indistinguishable from the tumor, if the retropharyngeal fat between the tumor and prevertebral space was lost, or if there was asymmetric enlargement of the ipsilateral prevertebral space (Fig. 1A) [9,10].

2.3. Measurement of primary tumor volume

Measurement of gross volume of the primary tumor and involved retropharyngeal nodes was made using the image system in the hospital. The volume was calculated by multiplying the sum of all areas by the image reconstruction interval (summation of area technique). All images were evaluated by the first author (C.-C. L.). A radiologist who specialized in head and neck cancer participated when the outline of the tumor margin was unclear. We chose 15 ml as the cut-off index according to the tumor volume proposed by Sze et al. [7]. Their results revealed that NPC patients with primary tumor volume larger than 15 ml had more local failures.

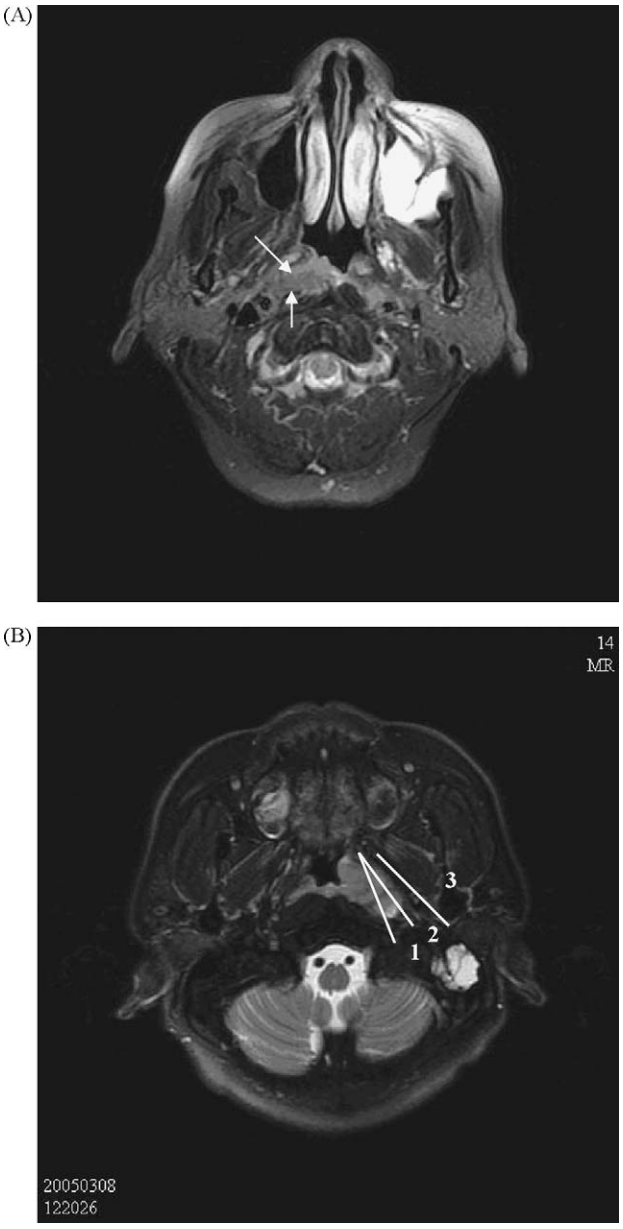

Fig. 1. Magnetic resonance imaging showing nasopharyngeal carcinoma (NPC) patients (A) with prevertebral space invasion on T2-weighted image with fat suppression (between arrows) and (B) with Grade 2 parapharyngeal space invasion on T2-weighted image with fat suppression.

2.4. Parapharyngeal space invasion

A grading system proposed by Sham and Choy [11] was used to assess the degree of parapharyngeal extension. A line extending from the medial pterygoid plate to the lateral border of the carotid artery formed the first boundary. The second boundary extended from the medial pterygoid plate to the styloid process, and the third boundary extended from the lateral pterygoid plate to the posterior border of the mandibular ramus. Grade 0 denoted tumor extension within the first boundary. Tumors extending into the parapharyngeal space beyond the first, second, and third boundaries were ranked as Grades 1, 2, and 3, respectively (Fig. 1B).