Current Trends in
Clinical & Medical Imaging
ISSN: 2573-2609

Juniper Publishers
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Research Article
Volume 3 Issue 3 - June 2019
DOI: 10.19080/CTCMI.2019.03.555612

Curr Trends Clin Med Imaging

Pre- and Post Treatment Computed Tomography Finding of Nasopharyngeal Carcinoma

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Received date: May 23, 2019; **Published date:** June 13, 2019

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Abstract

Background: Nasopharyngeal carcinoma, the most common neoplasm to arise in the nasopharynx, is a locally aggressive tumor with a high incidence of cervical nodal metastases. This study aimed to investigate the role of computed tomography in the evaluation of nasopharyngeal carcinoma before and after treatment.

Methods: 338 patients with an initial diagnosis of nasopharyngeal carcinoma before and after neoadjuvant chemotherapy were enrolled. All patients were undergone pre- and post-treatment CT scan.

Results: The 338 patients included in this analysis comprised 92 men and 246 women with a median age at diagnosis of 49 years (range, 10–89 years). WHO histopathologic type of non-keratinizing undifferentiated carcinoma was acounted 281/338 (83.1%), non-keratinizing differentiated carcinoma was 15.1%, and keratinizing squamous cell carcinoma was 1.8%. With CT scan staging, the proportions of T1, T2, T3 and T4 were 8.9% (30/338), 17.7% (60/338), 32.8% (111/338) and 40.5% (137/338), respectively; the proportions of N0, N1, N2 and N3 were 12.7% (43/338), 31.9% (108/338), 45.0% (152/338), and 10.4% (35/338), respectively. After treatment, a persistence of the disease was found in 14% of patients, while a recurrence of the cancer was diagnosed in 5% and distant metastasis developed in 11% of the patients.

Conclusion: Computed tomography is essential for detection of early NPC, staging of the primary tumor, and follow-up.

Keywords: Computed Tomography; Nasopharyngeal Carcinoma; Radiotherapy; Chemotherapy

Abbreviation: NPC: Nasopharyngeal Carcinoma; CT: Computed Tomography; HCMC: Ho Chi Minh City; NKUC: Non-keratinizing Undifferentiated Carcinoma; NKDC: Non-keratinizing Differentiated Carcinoma; KSCC: Keratinizing Squamous Cell Carcinoma; 18F-FDG. PET/CT: [18F] Fluoro-D-glucose Positron-Emission Tomography

Introduction

Nasopharyngeal carcinoma (NPC), the most common neoplasm to arise in the nasopharynx, is a locally aggressive tumor with a high incidence of cervical nodal metastases. The tumor has a propensity towards extensive invasion into adjacent tissues, particularly laterally into the parapharyngeal space and superiorly into the skull base. However, spread to the palate, nasal cavity, and oropharynx have also commonly reported. Distant metastases can arise within bone, lung, the mediastinum and, more rarely, the liver [1-3]. Although NPC is rare in North America and Europe with an incidence of 0.5-2 per 100,000, intermediate incidence rates are seen in Southeast Asia, the Mediterranean Basin, and the Arctic ranging from 0.5 to 31.5 per 100,000 person-years in males and 0.1 to 11.8 person-years in females [4-6]. In southern China, NPC is endemic with overall NPC incidence rates reaching 20-30 per 100,000 person-years and 15-20 per 100,000 person-years amongst males and females, respectively, in the province of Guangdong [7,8]. NPC has a male to-female ratio of 2-3:1 [9,10], and is most common among patients 40–60 years old with bimodal age peaks in the second and sixth decades of life [11,12].

Early detection, early diagnosis, accurate staging and evaluation after treatment had been the key to improve the efficacy of treatment and prolong survival period [13]. CT has been the most reliable and well-established imaging technique for staging and assessing the extent of nasopharyngeal carcinoma. The biggest advantage of CT imaging is that the surrounding bony destruction by NPC can be clearly visualized on CT image [13]. Zheng et al. [14] found that radiologists should pay attention to bony structures invaded by nasopharyngeal carcinoma on CT images. In addition, CT scan is very quick and abundant information can be achieved, it is also relatively cheaper and therefore is still an effective imaging method for

diagnosis and follow-up of nasopharyngeal carcinoma [15,16]. This study aims to investigate the role of computed tomography in the evaluation of nasopharyngeal carcinoma before and after treatment.

Material and Methods

From July 2015 to April 2019, a total of 338 consecutive patients with NPC visited HCMC Oncology Hospital, Vietnam. All patients with histologically proven NPC newly diagnosed were enrolled in this study. They completed a pre- and post-treatment evaluation that included physical examination, nasopharyngeal fiberoptic endoscopy, CT scan of the nasopharynx and neck, chest radiography, abdominal sonography.

The CT scans were obtained with a GE Optima CT660, in axial plane and coronal, sagittal recontruction after the injection of contrast medium (Ultravist 370, Schering, Berlin, Germany) using 3 mm section thickness; 50 mL of Ultravist was administered by intravenous.

All the images were reviewed and assessed by two of the authors independently. Cases with variable interpretation or disagreement in staging between the observers were reevaluated side by side, and the differences were confirmed to reach a final consensus. Medical records and imaging studies were analyzed, and all patients were restaged according to the 8th edition of the Union for International Cancer Control/American Joint Committee on Cancer staging system [17] relies on evaluation of the primary tumor (T category), the draining nodal groups (N category). Histopathologic evaluation was according to the 2003 World Health Organization classification: non-keratinizing undifferentiated carcinoma (NKUC), non-keratinizing differentiated carcinoma (NKDC), keratinizing squamous cell carcinoma (KSCC).

SPSS version 20.0 (IBM, Armonk, NY) was used for all statistical analyses.

Results

The 338 patients included in this analysis comprised 92 men and 246 women with a median age at diagnosis of 49 years (range, 10–89 years). WHO histopathologic type of NKUC was acounted 281/338 (83.1%), NKDC was 15.1%, KSCC was 1.8%. According to the eighth edition UICC/AJCC staging standards, the proportions of T1, T2, T3 and T4 were 8.9% (30/338), 17.7% (60/338), 32.8% (111/338) and 40.5% (137/338), respectively; the proportions of N0, N1, N2 and N3 were 12.7% (43/338), 31.9% (108/338), 45.0% (152/338), and 10.4% (35/338), respectively (Table 1). After treatment, a persistence of the disease was found in 14% of patients, while a recurrence of the cancer was diagnosed in 5% and distant metastasis developed in 11% of the patients. (Figures 1–4) are the enhanced CT images of patients before and after treatment.

Table 1: Clinical features and pre-treatment CT scan finding of the study patients.

Variables	Number	%
Age (year)		
<50	176	52.1
≥50	162	47.9
Sex		
Male	92	27.2
Female	246	72.8
WHO Histopathologic Type		
NKUC	281	83.1
NKDC	51	15.1
KSCC	6	1.8
T stage		
T1	30	8.9
T2	60	17.7
T3	111	32.8
T4	137	40.5
N stage		
N0	43	12.7
N1	108	31.9
N2	152	45
N3	35	10.4

Discussion

Nasopharyngeal carcinoma is a unique disease with clinical behavior, epidemiology, and histopathology that is different from that of squamous cell carcinomas of the head and neck. NPC accounts for 0.25% of all malignancies in the United States and 15–18% of malignancies in southern China. It also accounts

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for 10–20% of childhood malignancies in Africa. The male to-female ratio is 3:1. It is most common among patients 40–60 years old, and bimodal age peaks occur in the second and sixth decades of life [18-22]. NPC is caused by the interaction of genetic susceptibility, environmental factors (e.g., exposure to chemical carcinogens), and infection with Epstein-Barr virus. High antibody titers to Epstein-Barr virus antigens are useful diagnostic markers, and there are many tests to detect both IgG and IgA titers. In China, dietary factors for NPC include nitrosamine-rich salted food [19-22]. Patients often present with local symptoms, such as epistaxis and a blocked nose, but may also present with hearing loss, otalgia, headache, or cranial nerve involvement. However, the nasopharynx is a relatively clinically silent area; therefore, the first presentation may be with cervical nodal or distant metastasis [19-23]. Our results of patient demographics were consistent with the findings of previous researches with the median age at diagnosis of 49 years (range, 10–89 years) and male/femal ratio was 1/2.67.

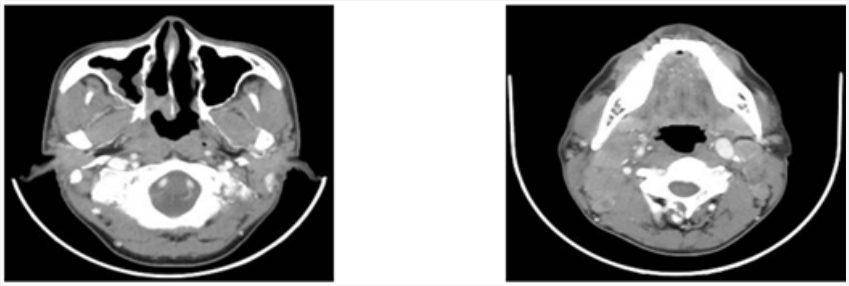

Figure 1: Pre-treatment enhanced CT image: (a) nasopharyngeal carcinoma with posterior nasal cavity and right cavernous sinus infiltration; (b) both side lympho node metastasis at level II, III, IV.

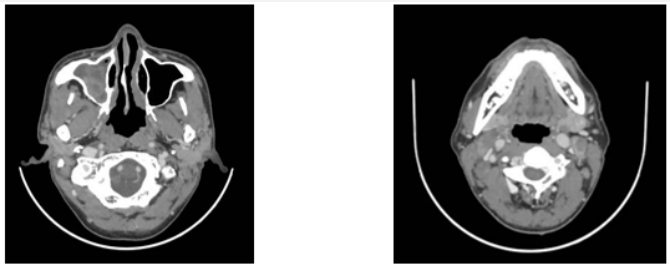

Figure 2: Post-treatment enhanced CT image: (a) The tumor was not seen. (b) Nodals were not changed after treatment.

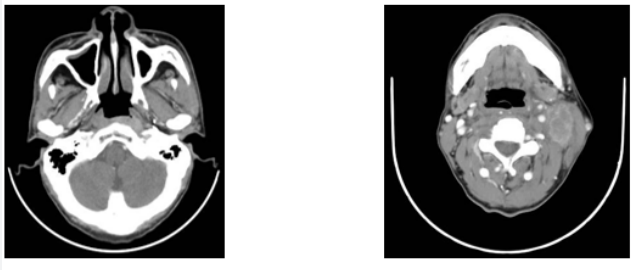

Figure 3: Pre-treatment enhanced CT image of NPC (a); and lymph node metastasis at level II, III with inside necrosis (b).

The World Health Organization classification of NPC recognizes three histologic types. Keratinizing squamous cell carcinoma (type 1) is found more often in nonendemic areas and has the worst prognosis. It is analogous to squamous cell carcinoma elsewhere in the pharynx and is associated with cigarette and alcohol use. Nonkeratinizing carcinoma (type 2) behaves in a fashion similar to type 3. Both types are radiosensitive and have a much better prognosis. Undifferentiated carcinoma (type 3) was previously called B lymphoepithelioma because of the mix of undifferentiated epithelial and nonmalignant T lymphocytes. In North America, around 25% of patients with NPC have type 1, 12% have type 2, and 63% have type 3. The histologic distribution in southern China is 2%, 3%, and 95%, respectively [20-23]. In our study, NKUC was counted for 281/338 (83.1%), NKDC was 15.1%, KSCC was 1.8%.

CT has long been used for staging NPC, especially for the detection of skull base tumor involvement with lytic or sclerotic lesions [23,24], but it has now largely been replaced by MRI

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for primary and nodal staging. However, CT is still used for radiotherapy planning and, in some centers, is used together with PET using 18F-FDG. PET/CT has been shown to be of value in NPC staging, where the main advantage is for the detection of distant metastasis [25]. It is also used for monitoring patients after therapy and detecting NPC recurrence.

Staging of NPC according to the seventh edition of the American Joint Committee on Cancer's TNM staging system [17] relies on evaluation of the primary tumor (T category), the draining nodal groups (N category), and evidence or absence of metastatic disease (M category). NPC is considered as a radiosensitive tumor and, therefore, radiotherapy is the main treatment in almost all the cases. The local control rates in patients treated by radiotherapy remains generally acceptable with good results (80%-90%) in T1 and T2 stages, whereas worse outcomes are observed in locally advanced diseases with a higher risk of local recurrence and metastasis [26]. At a 5 year follow up, the authors reported various results with regard to the rate of relapse noted especially in locally extensive tumors [26-28].

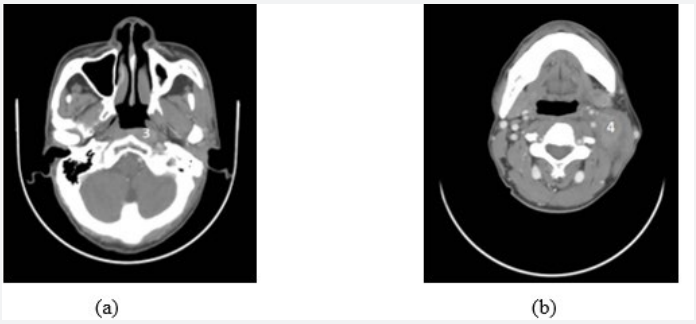

Figure 4: Post-treatment enhanced CT image of NPC: (a) lesion with intense enhancement (showed at number 3); (b) lymph node metastasis at level II.

When it comes to acute radiotoxicity, oral mucositis is the most frequent complication, followed by dermatitis and alterations in taste. The most frequent late toxicities are hyposialosis, xerostomia and dental complications which may be prevented by oral hygiene measures and fluoride use [29]. Regional recurrences and distant metastasis are not uncommon with NPC, even after completing the therapeutic approach [30]. Thus, a long-term follow-up is mandatory for many years after treatment.

In case of recurrent and metastatic NPC, different protocols of chemotherapy have been used. The most active chemotherapeutic agents include Cisplatin, Bleomycin, Doxorubicin and 5-Fu [31]. Chemotherapy can be neoadjuvant, adjuvant or concomitant to radiotherapy [32]. In our study, most of our patients were treated by concomitant chemo radiotherapy. This approach mainly aims to provide a much better control of the disease [33].

Bone and pulmonary metastases from nasopharyngeal carcinoma are the most common type of distant metastasis and represent the main etiology of fatal outcome in these patients [34]. A second radiation therapy is often indicated in case of local relapse [32]. However, second-line chemotherapy with Cisplatin seems to be the most effective protocol to treat the NPC metastatic lesions even if this therapy doesn't improve significantly the long-term mortality [35]. New drugs are actually in trial stage for treating recurring and metastatic nasopharyngeal carcinoma: gemcitabine, capecitabine and paclitaxel. A chinese study has shown that a monotherapy with capecitabine (Xeloda) has shown a significantly better survival rate [36].

NPC is a particular type of head and neck cancer characterized by a specific therapeutic approach and outcome. The most important issue with this tumor remains the high risk of relapse and/or distant metastasis especially in advanced stages of NPC. A long-term follow-up is mandatory to detect early these complications.

Conclusion

In conclusion, computed tomography is essential for detection of early NPC, staging of the primary tumor, and evaluation of associated local lymphadenopathy. A careful follow-up of patients by CT scan is necessary to detect and manage any iatrogenic complication, locoregional recurrence or metastasis of the disease.

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