Case Report: Coexistence of Non-Keratinizing Squamous Cell Carcinoma and Follicular Lymphoma in Nasopharynx

Tao Xu[1,2], Weihong Wei[1,2], Zeli Huang[1,2] and Weihan Hu[3,*]

[1]*Department of Radiation Oncology, Cancer Center, First People's Hospital of Foshan, Foshan 528000, Guangdong Province, China*

[2]*Foshan Head and Neck Cancer Group, Foshan 528000, Guangdong Province, China*

[3]*Department of Radiation Oncology, Cancer Center, Sun Yat-sen University, Guangzhou 510060, Guangdong Province, China*

Abstract: We report a very rare case of coexistence of non-keratinizing nasopharyngeal carcinoma and follicular lymphoma in nasopharynx. A 52-year-old woman was admitted in our hospital because of painless enlarged bilateral cervical mass. Nasopharyngoscopy revealed a nasopharyngeal mass, and biopsy showed follicular lymphoma cells infiltrating non-keratinizing squamous carcinoma. The patient underwent combined treatment which targeted two tumors and was alive without any progression in one-year follow up.

Keywords: Nasopharyngeal carcinoma, follicular lymphoma.

INTRODUCTION

Nasopharyngeal carcinoma (NPC) is a disease with distinct ethnic and geographic distribution. This tumor represents a significant disease burden in Asia, particularly in the Cantonese population of China. The cervical metastatic rate in patients with NPC has been reported as high as 73%. Epstein-Barr virus (EBV) is closely associated with NPC carcinogenesis. In pathological subtype, undifferentiated non-keratinizing carcinoma (WHOIII) constitutes more than 95% of all NPC cases [1]. Follicular lymphoma is one of most common non-Hodgkin's lymphoma (NHL), followed diffuse large B-cell ymphoma, accounts for 20% ~ 25% in NHL [2]. However, coexistence of non-keratinizing nasopharyngeal carcinoma and follicular lymphoma in nasopharynx is extremely rare.

In this paper, we report a case of non-keratinizing nasopharyngeal carcinoma with synchronous follicular lymphoma and review the literature on the clinical and histopathological aspects of these malignancies.

CASE REPORT

A 52-year-old native Guangdong female patient with 2-month history of a painless enlarged bilateral cervical mass was referred to the Cancer Center of First People's Hospital of Foshan. Clinical examination revealed a mass about 5cm×5cm in the left level II to V, and another mass about 4cm×5cm in the right level II to V. On indirect nasopharyngoscopy, a mass was found in nasopharyngeal cavity. There was no neural lesion. Nasopharyngeal carcinoma was the initial impression. Chest X-ray, abdomen and pelvis ultrasound, total body bone scanning didn't detect any distant metastases. MR of head and neck showed a mass in pharyngeal recess and enlarged bilateral cervical nodes from level II to V (Figure **1**). She had no family history of NPC and lymphoma. Direct nasopharyngoscopy and punch biopsy were performed under anaesthesia, the pathological diagnosis was non-keratinizing squamous carcinoma by histological examination wtihout immunohistochemical examination initially. And serum LDH for this patient was 500 U/L, EBV DNA level by real-time PCR (RT-PCR) was 2.1×10^5 copies/mL. The tumor was diagnosed as nasopharyngeal carcinoma and staged as T2N3M0, IVb (UICC, 2002).

Considering the large cervical lymph nodes, the patient underwent one-cycle induction chemotherapy with PF regimen (cisplatin 80mg/m^2, d1; 5-Fu 1000mg/m^2, CIV, 48h). However, cervical nodes were not sensitive with PF regimen according to our experience. Then after a consultation, the patient received radical chemoradiotherapy, radiation was delivered by Intensity-modulated radiation therapy (Varian Trilogy™ system). A total planning dose of 70Gy in 31 fractions at 2.25Gy/fraction to the GTV-p, 66Gy in 31 fractions at 2.12Gy/fraction to the GTV-n, 60Gy in 31 fractions at 1.81Gy/fraction to the CTV-1 and 54Gy in 31 fractions at 1.74Gy/fraction to the CTV-2. Concurrent chemotherapy was delivered with cisplatin alone (40mg/m^2, weekly).

*Address correspondence to this author at the Department of Radiation Oncology; Cancer Center, Sun Yat-Sen University, Guangzhou 510600, Guangdong Province, China; Tel: +86-20-87343608;
E-mail: huweihan@163.com, asian.you@163.com

ISSN: 1929-2260 / E-ISSN: 1929-2279/14

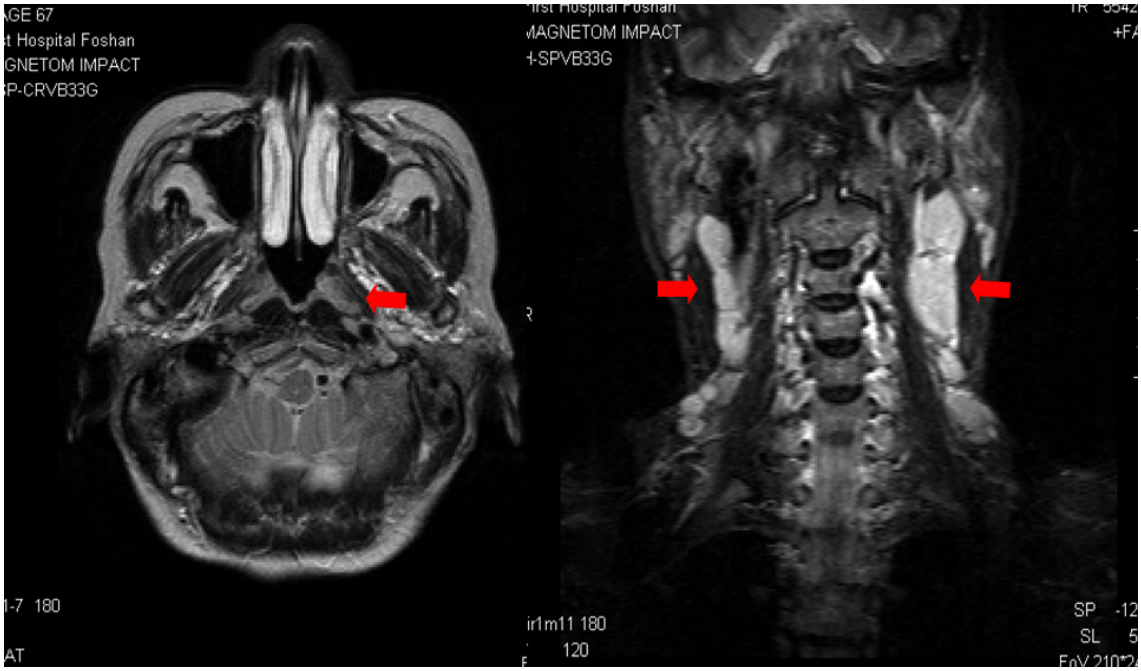

Figure 1: Head and neck MR showing a mass in nasopharyngeal cavity and enlarged cervical nodes bilaterally.

Eight days after the first day of radiotherapy, the cervical nodes distinctly shrunk, but the patient had a fever (>39℃) and was found enlarged axillary and inguinal lymph nodes suddenly (Figure **2**), and so biopsy was performed in enlarged axillary and inguinal lymph nodes and we considered to re-confirm the pathological result of nasopharyngeal mass. Surprisingly, on microscopic examination, apart from non-keratinizing squamous carcinoma cells were found in primary site, heterogeneous lymph cells were found (Figure **3**). An extensive immunohistochemical (IHC) panel was performed to evaluate the origin tumor, it found CK(+), EBERs(+), L26(+), CD79a(+), CD23 follicle (+), Bcl-2(+), CD3(-), UCHL1(-), Bcl-6(-), CD5(-), CD10(-) and Ki67(+,50%) in nasopharyngeal mass. Pathologists diagnosed coexistence of non-keratinizing nasopharyngeal carcinoma and follicular lymphoma in nasopharynx. The follicular lymphoma cells were found in axillary and inguinal lymph nodes. IHC revealed L26(+), CD79a(+),CK(-), CD23 follicle (+), Bcl-2(+), CD3(-), UCHL1(-), Bcl-6(-), CD5(-), CD10(-) and Ki67(+,45%).

Then we supplemented the diagnosis as follicular lymphoma, according to the Ann-Arbor staging system, the tumor was evaluated as stage III_{EB}. After the concurrent chmoradiotherapy, there was complete response in nasopharyngeal site and cervical nodes. According the guideline of NHL, patient was treated chemotherapy with six cycles CHOP protocol (cyclophosphamide, CTX, 750mg/m^2; adriamycin, ADM, 50mg/m^2; vincristine, VCR, 1.4mg/m^2; prednisolone, 60mg/m^2, d1-5) in combination with Rituximab (375 mg/m^2). She was referred for radiotherapy and a total dose of 34Gy/17 fractions administered to the involved field of axillary and inguinal lymph nodes. After treatment, whole body CT

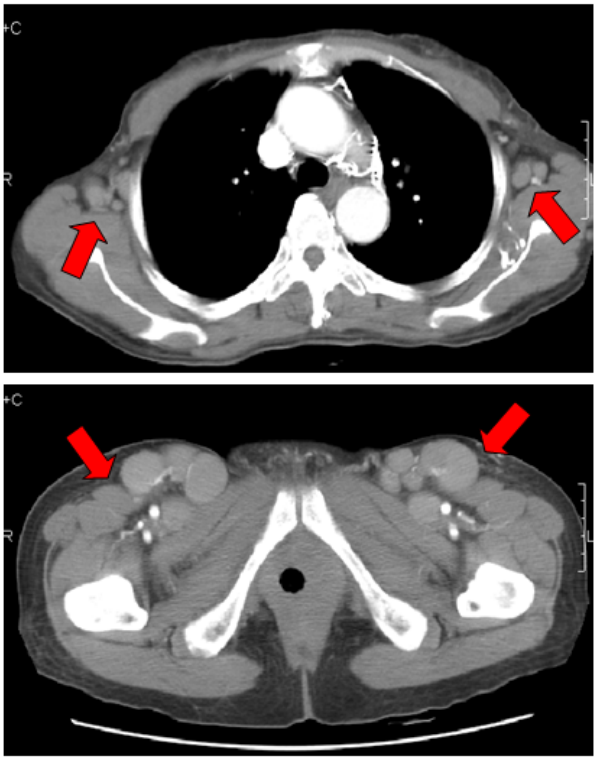

Figure 2: Images of CT scan showing enlarged axillary and inguinal lymph nodes during the treatment.

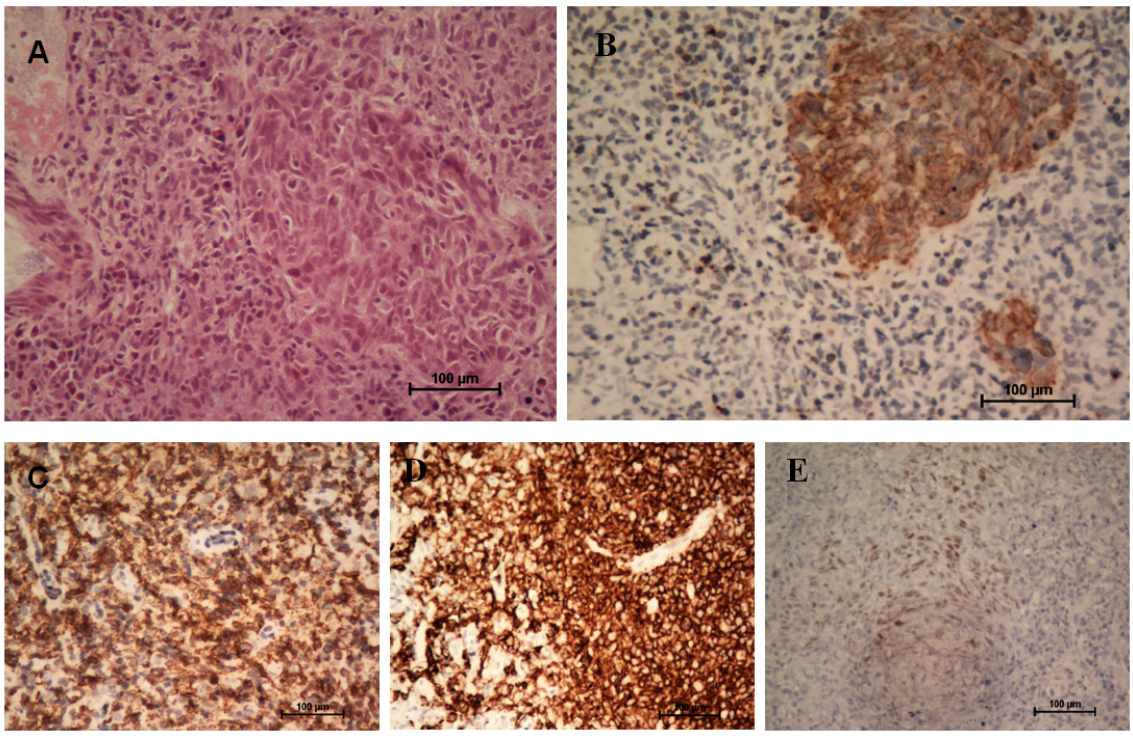

Figure 3: Hematoxylin-eosin staining section of tumor at medium power (×400) showing follicular lymphoma cells surrounding with nasopharyngeal carcinoma cells (**A**) and CK+ (**B**), CD79A+ (**C**), L26+ (**D**), EBERS+ (**E**) in IHC (×400).

scan showed no mass existed. In the one-year following up, we didn't find any recurrence.

DISCUSSION

NPC is the most common tumor in southern China, especially in Guangdong province, and the incidence was about 25 per 100,000 [1]. This neoplasm is frequently seen at Rosenmüller's fossa, undifferentiated non-keratinizing carcinoma (WHOIII) is the most common pathologic type of NPC in endemic region. NHL of head and neck is one of the most involved in extranodal site. In Asian, the most common sites include nasal cavity and nasopharynx, and nasopharyngeal lymphoma is part of Waldeyer ring's lymphoma. In pathologic type, extranodal nasal-type natural killer (NK) cell lymphoma is more common in nasal cavity but B-cell neoplasm is more common in nasopharynx [3]. More importantly, it is difficult to distinguish the non-keratinizing carcinoma and NHL. Zong *et al*. [4] found that infiltrating lymphoid elements were seen commonly in NPC tissue. So the appropriate immunohistochemical examination is needed. However, undifferentiated non-keratinizing carcinoma coexisting with lymphoma in nasopharynx is very rare, and to our knowledge, our report is the first case.

There have been limited reports concerning squamous head and neck cancer coexisting with lymphoma. In the case reported by Hisashi *et al*. [5], though MALT-type lymphoma and squamous cell carcinoma of the larynx was coexisting, it was not synchronously, a squamous cell carcinoma found in the larynx was later than lymphoma. Tezer *et al*. [6] reported a rare case coexistence of both tumor, but biopsy sample was from different site, squamous cell carcinoma in larynx and B-cell lymphoma in neck and nasophrynx. We should point out in our case, coexist both tumors were form nasophynx. The true synchronous both tumors case was only reported by Hadjileontis *et al*. [7], the patient was diagnosed with situ squamous cell carcinoma coexisting with intravascular lymphoma of T-cell origin. Interestingly, NPC and NHL are the malignant diseases which have closely associated relationship with EBV. EBERs and EBV DNA level (2.1×10^5copies/mL) were detected in our case. Rey *et al*. [8] reported a NPC patient developed Hodgkin lymphoma (HL) after eight years of the initial treatment, they detected the LMP-1 gene sequence by polymerase chain reaction, and deduced that EBV might increase risk of developing subsequent HL.

Treatment guideline of coexistence of more than one tumor in same patient is lacking, the appropriate management should synthetically consider histopathology, tumor stage and patient's performance.

It was a coincidence that radiotherapy with or without chemotherapy is main treatment not only for NPC but also NHL. Both NPC and HNL are very sensitive to radiation, the difference are target volume and total dose delivered. As to chemotherapy, PF protocol is the first choice for NPC, but not for NHL, CHOP protocol is appropriate. So we didn't observe any response after induction chemotherapy with PF protocol, but the cervical mass completely disappeared after radiotherapy. Rituximab, an anti-CD20 monoclonal target drug, was approved by the FDA to treat B-cell non-Hodgkin lymphomas in 1997, and was formally approved by the European Commission for treatment of follicular lymphoma in 2010. We treated the patient with R-CHOP protocol and radiotherapy successfully, no recurrence and metastasis was observed in following-up.

In conclusion, this is a case synchronous coexistence of non-keratinizing nasopharyngeal carcinoma and follicular lymphoma. The correct diagnosis of two tumors is important, based on careful review of the specimen and immunohistochemical examination is useful. The systemic treatment must be target to the both tumors.

FINANCIAL DISCLOSURE

This work was supported by a grant from the Science and Technology Project of Guangdong, P. R. China, (To: WHH, No. 2010B031600086) and the Natural Science Foundation of Guangdong Province, P. R. China, (To: WHH, No. 9151008901000223).

CONFLICTS OF INTEREST

The authors indicated no actual or potential conflicts of interest exist.

REFERENCES

[1] Jemal A, Bray F, Center MM, *et al*. Global cancer statistics. CA Cancer J Clin 2011; 61(2): 69-90. http://dx.doi.org/10.3322/caac.20107

[2] Heinzelmann F, Ottinger H, Engelhard M, *et al*. Advanced-stage III/VI follicular lymphoma: treatment strategies for individual patients. Strahlenther Onkol 2010; 186(5): 247-54. http://dx.doi.org/10.1007/s00066-010-2091-8

[3] Lei KI, Suen JJ, Hui P, Tong M, Li W, Yau SH. Primary nasal and nasopharyngeal lymphomas: a comparative study of clinical presentation and treatment outcome. Clin Oncol (R Coll Radiol) 1999; 11: 379-87. http://dx.doi.org/10.1053/clon.1999.9088

[4] Zong YS, Lin H, Choy DT, *et al*. Nasopharyngeal carcinoma and lymphoinfiltration. Oncology 1991; 48: 290-6. http://dx.doi.org/10.1159/000226945

[5] Hisashi K, Komune S, Inoue H, Komiyama S, Sugimoto T, Miyoshi M. Coexistence of MALT-type lymphoma and squamous cell carcinoma of the larynx. J Laryngol Otol 1994; 108: 995-7. http://dx.doi.org/10.1017/S0022215100128725

[6] Tezer MS, Tuncel U, Uzlugedik S, Coexistence of laryngeal squamous cell carcinoma and non-Hodgkin's lymphoma with nasopharyngeal involvement. J Laryngol Otol 2006; 120: e2. http://dx.doi.org/10.1017/S0022215105000782

[7] Hadjileontis CG, Kostopoulos IS, Kaloutsi VD, Nikolaou AC, Kotoula VA, Papadimitriou CS. An extremely rare case of synchronous occurrence in the larynx of intravascular lymphoma and in situ squamous cell carcinoma. Leuk Lymphoma 2003; 44: 1053-7. http://dx.doi.org/10.1080/1042819031000063426

[8] Rey J, Xerri L, Bouabdallah R, Keuppens M, Brousset P, Meggetto F. Detection of different clonal EBV strains in Hodgkin lymphoma and nasopharyngeal carcinoma tissues from the same patient. Br J Haematol 2008; 142: 79-81. http://dx.doi.org/10.1111/j.1365-2141.2008.07162.x

Received on 07-04-2014 Accepted on 18-04-2014 Published on 08-05-2014

DOI: http://dx.doi.org/10.6000/1929-2279.2014.03.02.2