

A Case Study on Double Primary Cancer of Non-Hodgkin's Lymphoma Together with Lung Squamous Cell Carcinoma

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ABSTRACT

Multiple primary cancer (MPC) is a type of repetitive cancer with two or more primary malignant tumors occurring simultaneously or successively in a single organ or multiple organs of the same host. At present, multiple primary cancers still need confirming by the following diagnostic criteria once proposed by Warren and Gates [1] in 1932: (1) Each of suspicious tumor requires proving as malignant one by histocytological analysis; (2) Each tumor shows different pathological tissue types; (3) Tumors occur in different body parts or organs, and each tumor has its unique way of metastasis, which excludes the possibility of mutual metastasis or recurrence. According to the diagnosis interval, MPC can also be divided into simultaneous cancer (diagnostic interval of two cancers is within 6 months and less than 6 months) and metachronous cancer (diagnostic interval of two cancers is more than 6 months) [2]. The incidence of multiple primary cancers is more common in double cancer, and less in triple cancer and above. In recent years, with the unceasing advancement of diagnosis and treatment technology, and the prolonged survival period of patients with malignant tumors, the incidence of multiple primary cancers shows a tendency of increasing [3-5], but the current incidence rates are different from each country, from 0.73% to 11.70% abroad [6], and about 2.67% in China [7]. Due to rich lymphoid tissues, the neck is believed as a common pathogenic site of non-Hodgkin's lymphoma (NHL), and the incidence rate has shown an obvious increase in recent years. This thesis demonstrates a rare case of double primary cancer of non-Hodgkin's lymphoma together with lung squamous cell carcinoma and to improve the understanding of this disease.

Keywords: Non-Hodgkin's Lymphoma; Lung Squamous Cell Carcinoma; Double Primary Cancer

Case Information

A 67-year-old male patient with 50 years of smoking history was found a mass with medium hardness and poor mobility in the left submandibular and oropharyngeal region in the early March, 2020. His Physical Examination shown as follows: left tonsil enlargement (III⁰) with less diaphanous on the surface; Lymph node progressive enlargement in the left jaw and neck, merging with the tumor; pain and difficulty in swallowing. Due to the outbreak of COVID-19, the patient didn't receive any treatment. Till Oct. 19, 2020, the patient got treatment in our hospital. Chest enhanced contrast CT scan shows a space-occupying lesion in the inferior lobe of right lung. Nasopharynx perfusion enhanced contrast MRI and left neck soft tissue MRI shows tumorous lesion in the left pharynx wall and parapharyngeal region, together with left neck lymph node enlargement (Figures 1 and 2). Pathology of right lung space-occupying lesion indicates non-keratinizing squamous cell carcinoma. On Nov. 13, the patient underwent neck tumor resection and biopsy under general anesthesia. Its pathology shows (neck tumor tissue) non-Hodgkin's Lymphoma (invasion type, non-germinal center type) which is considered as diffuse large-B cell lymphoma (Figure 3). Because the Synchronous pulmonary lymphoma and carcinoma is relatively rare. So there are currently no standards or guidelines for tumor grading, staging, treatment, and prognostic information. The treatment of our case to address his diet and pain, we preempted lymphoma treatment with R-CHOP chemotherapy. Because the sideeffect of chemotherapy patients has IV degree myelosuppression, the subsequent treatment was palliative treatment.

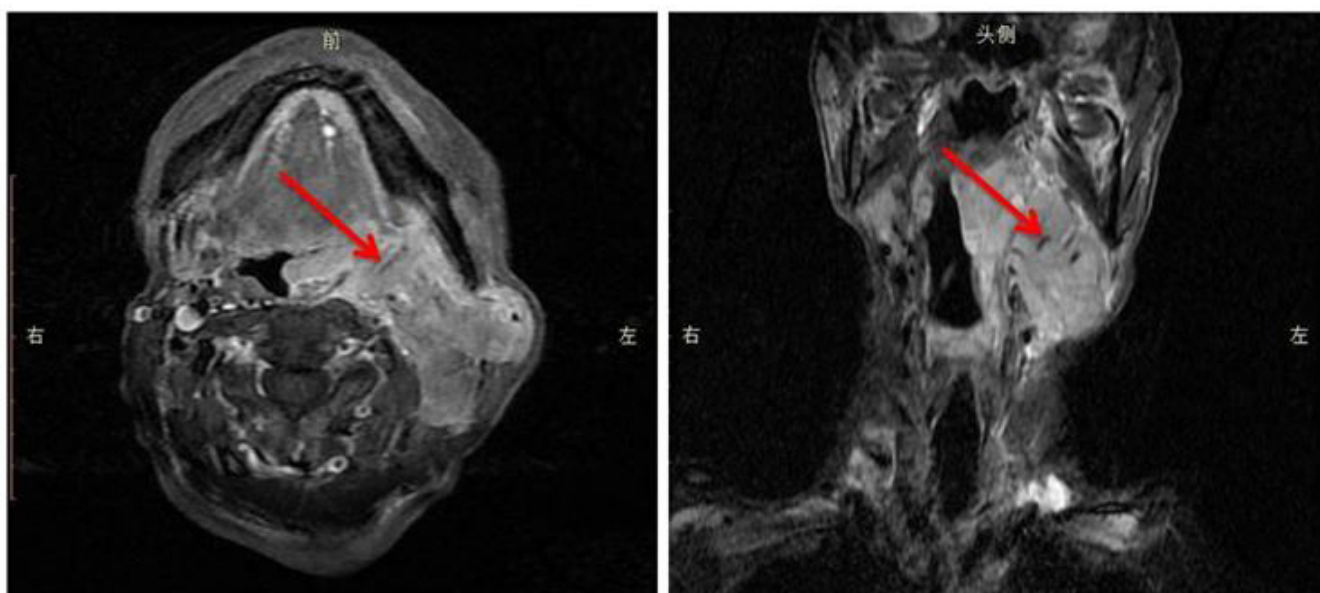


Figure 1: An irregular poorly-defined tumor with soft tissue signal protruding to the pharyngeal cavity is seen in the left pharynx wall of oropharyngeal region. Left eustachian tube is narrowed. An irregular soft tissue tumor is seen in the left parapharyngeal region. Perfusion enhanced contrast scan: uneven enhancement is detected in the tumor of left pharynx and parapharyngeal region. Moderate ring-shaped enhancement is detected in neck lymph node

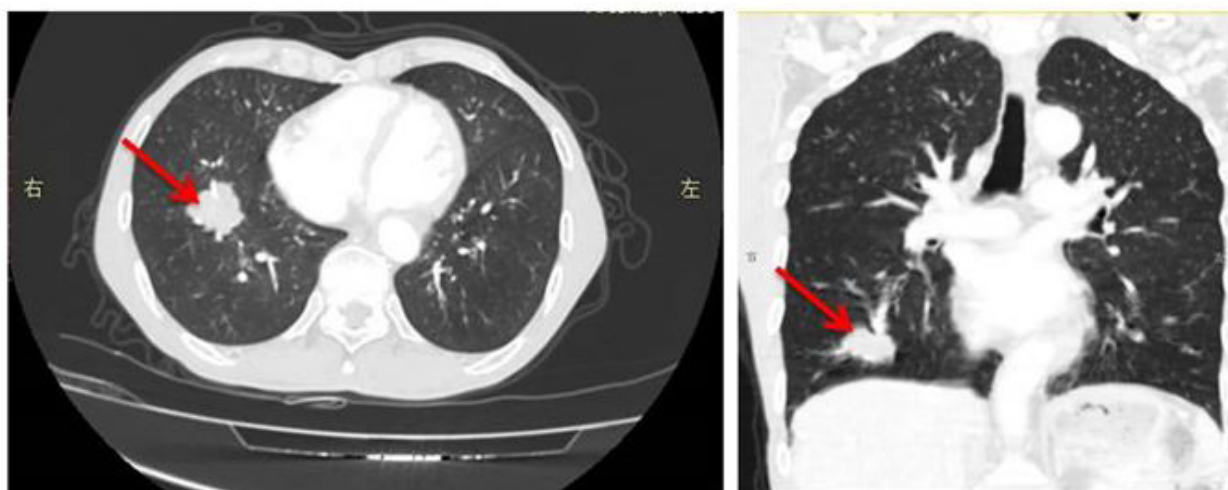


Figure 2: Chest enhanced contrast CT scan shows a lobulated tumor measuring 35mm*31mm in the inferior lobe of right lung

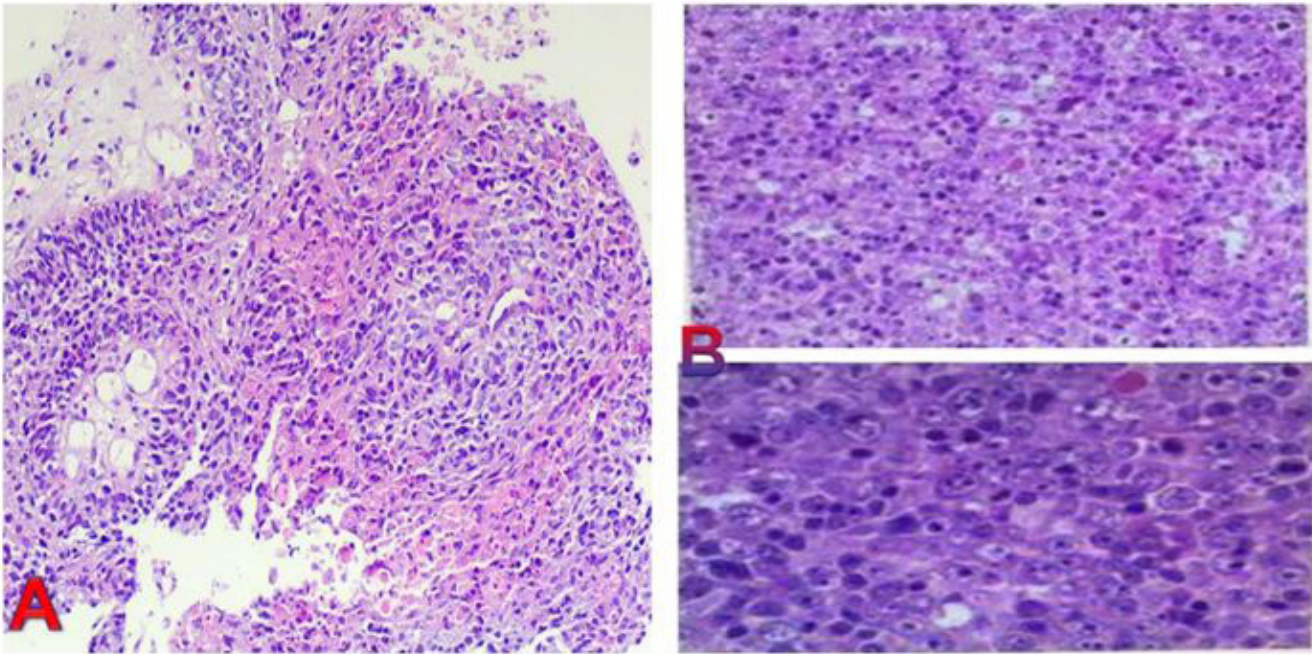


Figure 3: (A) Pathology of right lung space-occupying lesion: non-keratinizing squamous cell carcinoma. Immunohistochemistry: P40(+), CK5/6(+), CK7(-), TTF-1(-), Syn(-), CD56(-), P53(mutant type), Ki67(+, around 25%); (B) pathology of neck tumor resection and biopsy: (neck tumor tissue) non-Hodgkin's lymphoma (invasion-type, non-germinal center) which is considered as diffuse large-B cell lymphoma. Immunohistochemistry: tumorous cell CD20 (+, positive control+), CD19(+), CD22(+), BCL2(about 100%+), BCL6(about 5%+), CD23(+), C-MYC(about 60%+), MUM(about 90%+), CD43(+), P53(+, mutant type), CD3(-), CD5(-), CD10(-), CyclinD1(-), CD21(-), CD30(-,positive control+), PCK(-), P40(-), CK5/6(-), TTF-1(-), NapsinA(-), ALK(D5F3)(-,positive control+,negative control-),Ki-67 LI; around 80%. Molecular pathology:EBERCISH(-,positive control+)

Discussion

In recent years, multiple primary cancers have shown a continuous increase in clinical cases. Among the people with confirmed malignant tumors, the incidence of multiple primary cancers is between 2.4% and 8.0%. The longer the follow-up period after diagnosis is, the more likely it is to discover the second malignant tumor. The incidence rate can reach as high as 17% within 20 years of follow-up [8,9]. The onset of multiple primary cancers is a process involving multiple factors, multiple genes, and multiple steps. At present, experts at home and abroad have basically reached a consensus that the causes of multiple primary cancers mainly include multiple risk factors like genetic factors (immune deficiency and escape of cancer cells, accumulation of gene mutations, abnormal gene expression, etc.), iatrogenic factors (radiotherapy, chemotherapy, immunotherapy, etc.), living environment factors (smoking, alcoholism, obesity, etc.), [10]. The most famous "regional cancerization" theory and a number of related studies of MPC have shown that after tumors occurring in cancerous areas, the risk of new tumor recurrence is higher than that of non-tumor populations [11]. Besides that, there is evidence that unhealthy lifestyle, age, some anti-cancer treatments can also increase the risk of multiple primary cancers. Diffuse large B-cell lymphoma is the most common pathological type of non-Hodgkin's lymphoma. The head and neck are the second most likely position of lymphoma occurrence, of which diffuse large B-cell lymphoma of the head and neck (HN-DLBCL) is the most common invasive malignant B-cell lymphoma. As shown in the results of TAKANO's research [12,13]: HN-DLBCL generally occurs in non-reproductive ages, with higher proportion of male than that of female. The most common site of HN-DLBCL occurrence is oropharynx, followed by the cervical lymph nodes. The most common pathological type of lung cancer is lung squamous cell carcinoma, with higher occurrence rate of male than that of female, especially relating to smoking history. The patient in the case above was diagnosed with right lung squamous cell carcinoma and neck non-hodgkin's lymphoma in the same month. The two cancers are simultaneous multiple primary cancer. Studies have shown that the prognosis of metachronous multiple primary cancers is better than that of simultaneous multiple primary cancers, and the shorter the interval between the occurrence of two tumors is, the worse the prognosis gets. Summarized the published cases of synchronous pulmonary lymphoma and carcinoma. There were 17 cases (male: 10; female: 7) including our case, Most patients were middle-aged and elderly with the median age was 64 years. All the 17 cases had no specific symptoms. Eight patients (male: 5; female: 3) had a history of smoking, most patients with synchronous pulmonary lymphoma and carcinoma are middle-aged

and elderly, and it is more common in men than women. The most frequent type of PPL is B-NHL, especially MALT lymphoma, and the lung cancer is predominantly adenocarcinoma [14]. Multiple primary cancers have different clinical manifestations due to different types of tumor, and it is easy to overlook another primary lesion during the diagnosis process, resulting in missed diagnosis. At present, there is no uniform standard of the treatment plan for MPC, but whether it is a patient with simultaneous MPC or metachronous MPC, simultaneous surgery, or complete excision of each lesion one by one is believed as the first choice of treatment. Due to the individualized characteristics, MPC patients often adopt multidisciplinary discussions and treatment plans that can maximize their survival benefits. At present, many literatures highly recommend the radical treatment methods mainly including surgery, radiotherapy and chemotherapy on the basis of tumor pathology type, tumor position, and general conditions of patients with MPC. The distance between the two tumors also has a great impact on the selection of treatment plan. In MPC cases, if the two tumors are far apart, the patient can receive the treatments such as surgery or radiotherapy and chemotherapy for one primary tumor, which may have less effect on the second primary tumor; if the two tumors occurs close to each other, considering the potential postoperative adhesions and anatomical changes caused by the surgical treatment of a single tumor, as well as the influence of radiotherapy and chemotherapy on the tissue structure and blood supply, conservative treatments such as radiotherapy or chemotherapy are often adopted to treat the second tumor. When surgery cannot be selected during treatment, it is generally considered that the lesion with the greatest physiological impact and the most prominent symptoms are the main symptoms, and active anti-cancer treatment can be carried out to prolong the survival of patients. This case study aims that from the in-depth learning of multiple primary cancers, we should not only be satisfied with the first diagnosis, but also need endeavour to know patient's medical history in details, do thorough physical examination, adhere to follow-up results, and perfect all aspects of examination to minimize the rate of missed diagnosis clinically.

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