Clinical characteristics, treatments, and prognosis of patients with multiple primary carcinoma of head and neck

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To the Editor: Multiple primary carcinoma (MPC) or secondary primary carcinoma refers to two or more malignant tumors occurring in the same organ or different organs of a patient. MPC is classified into synchronous MPC (time between diagnoses ≤6 months) and metachronous MPC (time between diagnoses >6 months). Clinically, MPC was easily misdiagnosed as the recurrence and metastasis of malignant tumor. In head and neck MPC patients, the correct diagnosis and active treatments are important.

Over a 10-year period (January 2008 to August 2018), 246 patients (145 males and 101 females) with MPC of head and neck were treated at the Chinese People’s Liberation Army General Hospital, including 66 patients of synchronous MPC and 180 patients of metachronous MPC. The mean patient age was 56.6 years (range, 19–93 years). According to the theory of regional cancer, MPC is classified into field cancerization of head and neck (FCHN) and non-field cancerization of head and neck (NFCHN). Inclusion and exclusion criteria (based on Warren and Gates’ diagnostic criteria of the MPC) are as follows: Inclusion criteria: (1) each tumor must be malignant; (2) each tumor must be solitary or tumor margin distance from normal tissue more than 2 cm; (3) in the same area, pathological types of tumors are different. Exclusion criteria: (1) the pathological diagnosis is non-malignant; (2) recurrence or metastasis of the primary tumors.

All patients received magnetic resonance imaging scan of the primary site, ultrasound examination of cervical and superior clavicle lymph node and abdominal organs, fibronasopharyngoscopy, esophageal barium meal angiography, chest computed tomography (CT), and bone scan examinations; 79 patients received the whole body positron emission tomography-CT examination. According to the treatment methods, patients could be divided into three groups: synchronous FCHN patient group (time between diagnoses ≤6 months): 34 patients were given the most sensitive treatment according to clinical staging; synchronous NFCHN patient group (time between diagnoses ≤6 months): 32 patients, for whom the life-threatening tumor sites with serious lesion were treated firstly; and metachronous patient group (time between diagnoses >6 months): 180 patients, for whom standard treatment plans were chosen according to the international guidelines or expert consensus. Follow-up was conducted mainly through out-patient review and telephone. The last follow-up was conducted in November 2018. Statistical analysis was performed with SPSS (ver. 22; IBM, Armonk, NY, USA). For categorical data, Chi-square test was used for comparison. Survival rates were assessed using the Kaplan-Meier method. The log-rank test and the Cox proportional hazards model were used to identify prognostic factors independently associated with survival.

The follow-up period was 3.0 to 127.0 months, with a median of 77.5 months. After follow-up, 60 patients died, 21 patients lost, and 165 patients survived. Among them, the synchronous MPC group had 19 deaths and three patients lost to follow-up; the metachronous MPC group had 41 deaths and 18 patients lost to follow-up. The 3-year and 5-year overall survivals (OSs) of the 246 patients were 89.91% and 83.82%, respectively; progression-free survivals (PFSs) were 78.71% and 66.9%, respectively. Among them, hypopharyngeal carcinoma associated with esophageal cancer was the most common; the 3-year and 5-year OS of them were the lowest (78.71% and 66.9%, respectively). The second most common was thyroid

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cancer associated with breast cancer, while patients with them had the highest OS (both 100%). The 3-year and 5-year OS of synchronous MPC patients were 71.71% and 63.36%, respectively, compared with 95.39% and 89.76% for metachronous MPC patients \( (P < 0.0001) \) [Figure 1A]. The 3-year and 5-year PFS of the synchronous MPC patients were 70.98% and 64.93%, respectively, compared with 92.57% and 84.38% for metachronous MPC patients \( (P = 0.0012) \) [Figure 1B]. The 3-year and 5-year OS of FCHN patients were 83.45% and 76.66%, respectively, compared with 93.55% and 89.73% of NFCHN patients \( (P = 0.0014) \) [Figure 1C]. Single factor analysis showed that gender, smoking, alcohol, interval time, and the site of the first primary cancer were all factors affecting the survival of patients with MPC of head and neck (all \( P < 0.05 \)). And log-rank test and Cox proportional hazards model analysis showed that interval length was an independent risk factor (odds ratio = 0.500, 95% confidence interval, 0.389–0.644; \( P < 0.05 \)).

For long-surviving patients with head and neck carcinoma, regular imaging and head and neck check-up are crucial for the early detection of metachronous MPC. For patients with hypopharyngeal or esophageal cancer, cross-screening is required. In addition, pathological biopsy is recommended for patients with head and neck tumors when other tumors are found outside the primary site. With improving of tumor diagnosis and treatments, the incidence of MPC is rising and has become a focus of clinical and basic research. Cancer patients should be regularly reviewed and screened for potential tumors of other pathological types in the predisposed sites.

**Declaration of patient consent**

We certify that we have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

**Conflicts of interest**

None.

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