The risk of the development of second primary malignancies is increased in patients with head and neck squamous cell carcinoma compared with the general population. Furthermore, this increased risk largely consists of aerodigestive tract malignancies, including head and neck cancer, lung cancer and oesophageal cancer. The World Health Organization classification defines two main categories of natural killer (NK) cell-derived neoplasms: extranodal NK/T-cell lymphoma (ENKTL), nasal type, and aggressive NK-cell leukaemia. Extranodal NK/T-cell lymphoma, nasal type, formerly called angiocentric lymphoma, is the most common cause of the syndrome known as “lethal midline granuloma”. Herein we aimed to report the development of ENKTL nasal type in a patient who received curativechemoradiotherapy for laryngeal epidermoid carcinoma and obtained complete remission.

Keywords: chemotherapy, extranodal natural killer/T-cell lymphoma, laryngeal cancer, radiotherapy.

Nasal type extranodal natural killer T-cell lymphoma in a laryngeal cancer survivor: the first case report

Dilek Unal, Arzu Tasdemir, Celalettin Eroglu, Neslihan Kurtul, Arzu Oguz, Banu Acma, Ali Unal

1Department of Radiation Oncology, Kayseri Education and Research Hospital, Kayseri, Turkey
2Department of Pathology, Kayseri Education and Research Hospital, Kayseri, Turkey
3Department of Radiation Oncology, Erciyes University Medical School, Kayseri, Turkey
4Department of Medical Oncology, Kayseri Education and Research Hospital, Kayseri, Turkey
5Department of Internal Medicine, Erciyes University Medical School, Kayseri, Turkey

Introduction

The risk of the development of second primary malignancies is increased in patients with head and neck squamous cell carcinoma compared with the age-matched general population. Furthermore, this increased risk largely consists of aerodigestive tract malignancies, including head and neck, lung and oesophageal cancers, and the risk remains relatively constant after the initial diagnosis of primary cancer [1, 2]. The World Health Organization (WHO) classification defines two main categories of natural killer (NK) cell-derived neoplasms: extranodal NK/T-cell lymphoma (ENKTL), nasal type, and aggressive NK-cell leukaemia [3, 4]. Natural killer/T-cell lymphomas have a distinctive geographical distribution with most cases being reported in Asia and Latin America. Clinically, it is useful to classify NK/T-cell malignancies into two categories: nasal NK/T-cell lymphomas, and non-nasal or extranasal NK/T-cell lymphomas, depending on the site of the lesions [5, 6]. Extranodal NK/T-cell lymphoma, nasal type, formerly called angiocentric lymphoma, is the most common cause of the syndrome known as “lethal midline granuloma” [7]. Herein we aimed to report the development of ENKTL nasal type in a patient who received curative chemoradiotherapy for laryngeal cancer.

Case report

A 56-year-old male patient presented with increasing hoarseness which started 5 months previously. He had a history of 60 pack-year smoking and no alcohol use. In October 2008 a submucosal mass on the left vocal cord, involving the anterior commissure extending to the arytenoid cartilages, was detected with direct laryngoscopy, and a biopsy from the mass was taken under local anaesthesia. Pathologic examination confirmed the diagnosis of laryngeal epidermoid carcinoma. Computed tomography (CT) did not reveal any pathologically enlarged lymph nodes in the neck region. Surgery or radiotherapy (RT) options were proposed to the patient, but he refused surgery. Radiotherapy was given to the primary field and bilateral neck region at a total dose of 70 Gy. Cisplatin at a dose of 50 mg/week was concomitantly administered with RT. After chemoradiotherapy, the imaging techniques revealed a complete response. While on follow-up, he presented with the complaint of nasal obstruction 28 months after the diagnosis of laryngeal cancer (January 2011). 18-Fuoro-deoxyglucose positron emission tomography (FDG-PET)/CT scanning revealed that a soft tissue mass measuring 60 mm × 50 mm × 40 mm filled the left ethmoid sinus, maxillary sinus, sphenoid sinus and nasal cav-
ties [the standardized uptake value (SUV) max: 20.3] (Fig. 1A). Also, a soft tissue mass measuring 66 mm × 63 mm in the head of pancreas (SUV max: 27.7) (Fig. 1B) and two soft tissue lesions measuring 24 mm × 20 mm in the right testis (SUV max: 19.3) (Fig. 1C) were observed. In addition, increased FDG uptake in the posterior part of the left testicular parenchyma was detected (SUV max: 8.0) (Fig. 1C). Intense FDG involvements in many parts of the musculoskeletal system were observed (SUV max: 15.2). Excisional biopsy was taken from the nasal cavity. Pathologic examination confirmed the diagnosis of NKTL, nasal type. Immunohistochemical analysis of biopsy specimens showed a positive immunohistochemical staining with CD56 (Fig. 2) and CD3 epsilon. According to the Ann Arbor staging system, the disease was found to be stage IV. Because of the presence of obstructive jaundice, a percutaneous biliary stent was introduced. Two cycles of chemotherapy consisting of etoposide, methylprednisolone, cisplatin and cytarabine (ESHAP) were given. Palliative RT was started for nasal mass because the patient complained of increasing shortness of breath. Radiotherapy could not be continued because the patient’s condition deteriorated on the 5th day of RT. While on best supportive care, the patient died in the third month after the diagnosis of ENKTL.

**Discussion**

Clinically, NK cell lymphomas can be divided into three categories: nasal, non-nasal and aggressive lymphoma/leukaemia subtypes [8]. Nasal NK/T-cell lymphomas occur in the nose and the upper aerodigestive tract. The nasal cavity, nasopharynx, paranasal sinuses, hypopharynx and larynx are the most common involvement sites [5, 6, 9]. The presenting symptoms are generally local, including facial swelling, nasal obstruction, bleeding, proptosis and impairment of extraocular movement. Downward extension of a nasal tumour may cause destruction of the hard palate, leading to the characteristic midline perforation [6]. Similarly, in our patient, clinical presentation of the lymphoma was nasal obstruction.

Non-nasal NK cell lymphomas may involve any anatomical site [10]. As its name implies, it occurs outside the typical nasal region [5]. The skin, gastrointestinal tract, salivary glands, spleen and testis are the common primary sites [5, 8]. Interestingly, primary involvement sites of non-nasal type are also sites to which nasal type most commonly disseminates [8]. On the other hand, distant metastasis in nasal type NK/T-cell lymphomas is unusual whereas distant dissemination occurs early in the clinical course of non-nasal NK/T-cell lymphomas [5]. Interestingly,
in our patient, distant dissemination was present at the time of diagnosis of nasal type NKTL. Peripheral blood cytopenias may be found in approximately 10–15% of patients with nasal and non-nasal NK cell lymphomas and are predominantly due to active haemophagocytosis in the bone marrow [8]. In the present patient, blood parameters, including haemoglobin concentration and white blood cell and platelet counts, were found to be normal.

Epstein-Barr virus (EBV) has been implicated in the development of a wide range of T cell lymphoproliferative disorders, including angioimmunoblastic T-cell lymphoma, nasal type ENKTL and other rare histological subtypes [11]. Epstein-Barr virus encodes a variety of products, interacting with or exhibiting homology to a wide variety of antiapoptotic molecules, cytokines and signal transducers, hence promoting immortalization and transformation [11]. However, in the present patient there was no history of EBV infection. On the other hand, EBV serology was not determined.

Natural killer/T-cell lymphoma shows an angiocentric and angiodestructive pattern of growth with associated regional necrosis and ulceration. Coagulation necrosis and apoptotic bodies are frequently present. The tumour cells are generally small or medium sized with occasional large and anaplastic forms. The immunophenotypes of NK lymphoma cells are classically CD2, CD56 and cytoplasmic CD3 epsilon positive [5]. In the present patient, immunohistochemical analysis of biopsy specimens showed a positive immunohistochemical staining with CD56 and CD3 epsilon.

There is not a clarified treatment plan for patients with NK/T-cell lymphomas and so they have poor survival rates [12]. Radiotherapy is an important treatment modality for stage I/II nasal NK-cell lymphomas. Non-nasal NK-cell lymphomas are usually at an advanced stage at presentation; if not, early-stage disease may disseminate rapidly. Therefore, RT is mostly used for complementary or palliative purposes [6]. The mainstay of treatment for stage III/IV nasal type ENKTL is chemotherapy [6]. Anthracycline-containing chemotherapeutic regimens such as CHOP (cyclophosphamide, doxorubicin, vincristine, prednisolone) or the non-anthracycline-containing regimens such as ESHAP can be used [6, 12]. In our patient, since the disease was stage IV at the time of diagnosis, chemotherapy, but not RT, was used as the primary treatment modality. On the other hand, palliative RT was started for nasal mass because of the patient’s complaint of progressive increase in shortness of breath.

In conclusion, nasal type ENKTL may develop as a second primary malignancy after complete response in laryngeal carcinoma patients and has an aggressive course.

References


Address for correspondence

Dr. Dilek Unal
Kayseri Eğitim ve Araştırma Hastanesi Radyasyon Onkoloji Kliniği
38010, Kayseri, Türkiye
Tel. 90-3522076666/1480
Fax 90-3524375807
e-mail: dilekunaldr@gmail.com

Submitted: 5.06.2013
Accepted: 7.08.2013