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Mediastinal Neuroendocrine Carcinoma of Unknown Origin Presenting with Superior Vena Cava Syndrome (SVCS): A Case Report

Mahnaz Amini[1], Elham Ghalenavi[2]*, Mansore Sobhani [3], Hadi Mohamaddoust[4]

[1] *Pulmonologist, Lung Disease Research Center, Faculty of Medicine Mashhad University of Medicine Sciences, Mashhad, Iran*
[2] *Internist, Lung Disease Research Center, Faculty of Medicine Mashhad University of Medicine Sciences, Mashhad, Iran*
[3] *Internal Medicine Resident, Faculty of Medicine Mashhad University of Medicine Sciences, Mashhad, Iran*
[4] *Pulmonologist, Internal Medicine Department, Bojnurd. North khorasan Medical University, Bojnurd, Iran*

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ABSTRACT

Primary neuroendocrine carcinoma (NEC) of the mediastinum is a rare type of carcinoma. According to the literature, only five cases of this condition have been reported so far. In this paper, we present a rare case of mediastinal NEC of unknown primary site. The patient was a 34-year-old man with mediastinal NEC, who presented with chronic dry cough and a right-sided mediastinal mass one year prior to hospital admission (winter 1391). His condition was confirmed by cervical lymph node biopsy. The patient refused to undergo chemotherapy treatment. During the hospital admission, the patient presented with severe dyspnea and signs of superior vena cava syndrome. Contrast-enhanced CT scan of the chest revealed a large heterogeneous mass extended from the right superior mediastinum to the right lung base with the encasement of the superior vena cava. After radiotherapy, the patient's symptoms subsided and he underwent etoposide and cisplatin chemotherapy. After a 20-month patient follow-up, the subject remained alive and symptom-free.

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Case report

A 34-year-old man with mediastinal neuroendocrine carcinoma (NEC) presented with severe dyspnea and cervical edema. During the physical examinations, the patient was unable to lie down. Jugular vein engorgement and collateral superficial veins were seen on the upper chest.

The disease started one year ago (winter 1391) manifesting with dry cough for six months. Physical examinations revealed bilateral, multiple, non-tender cervical and supraclavicular lymph nodes. In addition, the patient's chest X-ray showed a right-sided mediastinal mass (Figure 1). Contrast-enhanced CT (CECT) scan of the chest revealed a large heterogeneous mass extended from the right superior mediastinum to the right lung base next to the diaphragm with vessel encasement (Figure 2). No pulmonary parenchymal abnormalities of vascular origin were observed and the abdominal CECT was normal.

The excisional biopsy of cervical lymph nodes was indicative of NEC, which was positive for cytokeratin, Chromogranin A, neuron-specific enolase (NSE) and synaptophysin in immuno-histochemical (IHC) staining, and it was negative for human leukocyte and cytoplasmic antigens and thyroid transcription factor-1. Moreover, Ki-67 labeling was 15%, which was confirmative of NEC.

The patient refused chemotherapy and left the treatment. Six months later, he presented again with deterioration of cough and dyspnea. Following that, four courses of chemotherapy were planned with 2-week intervals. After the second course of chemotherapy, the patient was

**Corresponding author:* Elham Ghalenavi, Pulmonologist, Lung Disease Research Center, Faculty of Medicine Mashhad University of Medicine Sciences, Mashhad, Iran. Tel/Fax: +985138598818; E-mail: ghalenavie@mums.ac.ir

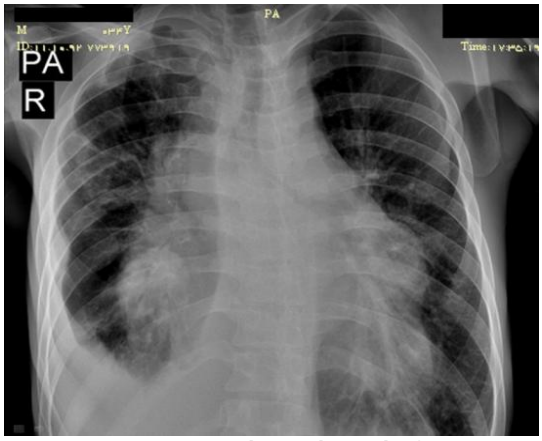

Figure 1. Postero-anterior chest radiograph of a patient with mediastinal NEC, showing the right mediastinal mass and the right-sided pleural effusion

referred to the hospital with severe dyspnea, orthopnea and facial edema.

Investigation

On admission, the patient showed signs of superior vena cava syndrome (SVCS). The chest CT-scan indicated the enlargement of the previous mass and the severe constriction of superior vena cava (SVC) vein. The right hilar nodes and the right main bronchus were involved, and multiple pulmonary nodules with the maximum diameter of 27×17mm were found in the apical segment of the right lower lobe (Figure 3). Furthermore, the patient presented with interlobular septal thickening and abdominal lymphadenopathy.

Differential diagnoses

Lung cancer and non-Hodgkin lymphoma were the most significant differential diagnoses in our patient, which are also the most common causes of SVCS. However, they were ruled out by pathological and IHC assays.

Treatment

The patient received hypofractionated radiotherapy (5 courses per day, 400 cGy). As a result, the symptoms of SVCS subsided and he was scheduled for chemotherapy. The patient's chemotherapy regimen was based on cisplatin and etoposide.

Outcome and follow-up

The patient was followed-up monthly via phone and he was enquired about the alleviation of symptoms and his ability to return to career. Six months after hospital discharge, the chemotherapy courses were repeated. In total, he received four chemotherapy courses after discharge from the hospital, and 20 months after diagnosis, the patient remained alive and is now symptom-free.

Discussion

Mediastinal NEC of unknown primary-site is a rare tumor, which originates from thymus in most of the cases.

According to the literature, only five cases of primary NEC in the mediastinum have been reported (1), all of which have been found in male patients, including our case. This might be suggestive of the male gender propensity of this disease. However, more cases need to be documentated in order to confirm this hypothesis.

The age range of the NEC patients is 35-65 year. Our patient was 33 years old, when the symptoms started to appear (1-4).

There is another report of a patient with SVCS in the literature (1). Our patient is the second case of mediastinal NEC presented with SVCS in the course of his disease.

According to the literature, the overall survival in the previous cases was 11 months (range: 2-13 month). On the other hand, the median survival of unknown primary NEC of other organs was 15.5 months (range: 11.6-40 month)(1,5). In our case, the patient survived 20 months after the diagnostic biopsies.

Different pathological characteristics are associated with NEC, and IHC assay is known to have a pivotal role in its diagnosis (1,6).

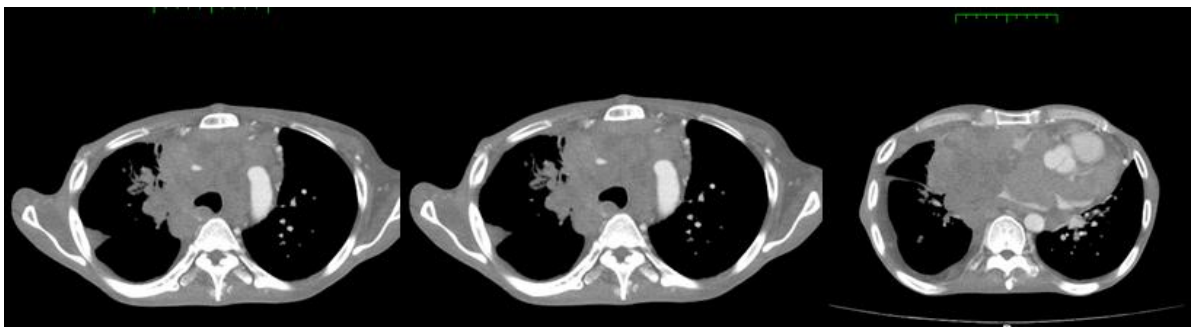

Figure 2. Contrast-enhanced chest CT scan of a patient with mediastinal NEC, showing a large right-sided mediastinal mass, extended to the right hemi-diaphragm with the encasement of SVC

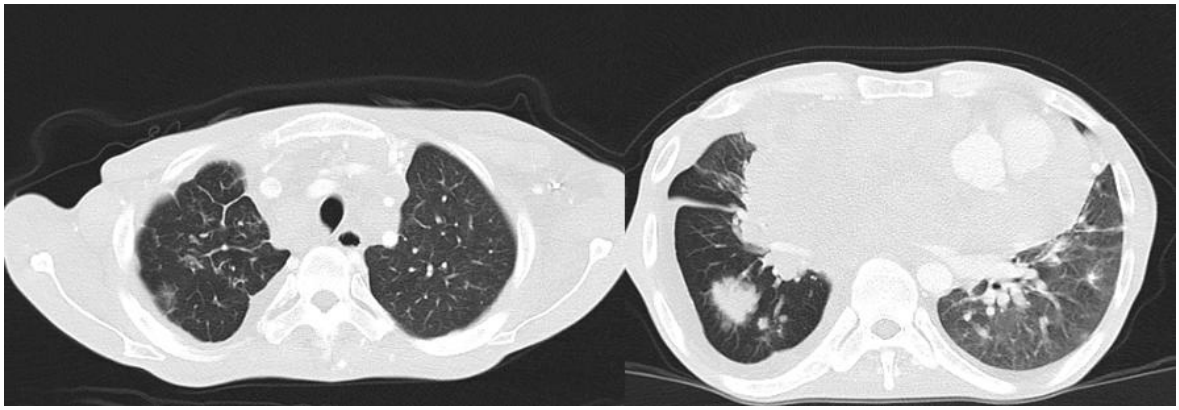

Figure 3. Parenchymal window of chest CT scan of a patient with mediastinal NEC, showing septal thickening and right lower lobe mass

Unfortunately, adequate information is not available on the treatment of this invasive tumor. It is mainly due to the heterogeneity of these tumors, which restricts the diagnosis, effective treatment and prognosis (5). Various chemotherapy regimens have been used in the treatment of mediastinal NEC. According to several studies, large cell NEC (LC-NEC) is associated with shorter survival and more relapses (7) in comparison to non-small cell lung cancer (NSCLC), while it has a better survival than small cell lung cancer (SCLC) (8).

Adjuvant chemotherapy with basic regimens of SCLC (platinum-etoposide) is likely to result in a better outcome (1). Thus, it could be inferred that chemotherapy regimen has a key role in the improvement of the outcome in such cases.

Furthermore, hyperfractionated, accelerated radiation therapy is considered effective in restricting tumor growth compared to other conventional methods such as accelerated fraction radiation therapy. It is probably because malignancies with rapid growth and regeneration are more sensitive to intensified fractionation protocols (9). In our case, there was a dramatic response to hypofractionated radiation therapy.

Learning points

- Mediastinal NEC of unknown-origin is a rare malignancy. Therefore, early diagnosis of the cases might assist in the better management of the disease.
- Currently, there are not any specific treatment protocols for mediastinal NEC, and the chemotherapy regimens used in these cases vary in different studies.

NEC has no pathognomonic signs and symptoms. Consequently, adequate knowledge of this disease could contribute to the early and appropriate diagnosis.

Conflict of Interest

The authors declare no conflict of interest.

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