Case Report

Metastatic Squamous Cell Cancer with Unknown Primary Origin in the Mediastinal Lymph Node

M Agca, A Kosif[1]

Departments of Pulmonology and [1]Thoracic Surgery, University of Health Sciences Istanbul Sureyyapasa Chest Diseases and Thoracic Surgery Training and Research Hospital, Istanbul, Turkey

Abstract

Metastatic tumors with unknown primary origin are a group of heterogeneous tumors with undetectable primary tumor site on admission. They have the common properties of rapid and aggressive progression and unpredictable metastases. They form 3%–5% of all cases with cancer and the fourth-most common cause of cancer-related deaths. The histological type of these tumors is commonly (90%) adenocarcinoma, whereas 5% are squamous cell carcinomas. Metastasis is observed in the liver, lungs, and bones. Mediastinal lymph node metastasis is extremely rare. They have a poor prognosis and the mean survival is shorter than a year. The case we have presented is a rare case due to its mediastinal lymph node involvement among tumors with unknown origin and squamous cell histological subtype.

Keywords: *Mediastinal lymph node, neoplasm, unknown primary tumor*

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Introduction

Tumors with unknown origin are a group of heterogeneous tumors with undetectable primary origin on admission despite a detailed anamnesis, a careful clinical examination, and the use of radiological methods, although histologically confirmed to be a metastatic carcinoma.[1] They are the 7th or 8th most common carcinoma types and the 4th most common cause of cancer-related deaths.[2] Their incidence is 7–12/100,000/year.[3] The rapid and aggressive progression properties of these tumors are related to the absence of a symptom of the primary tumor. The primary origin cannot be determined despite autopsy examination in 15%–25% of the cases. The unpredictable nature of metastases is related to the uncommon sites of primary tumor metastases. As an example, bone metastases are generally suggestive of breast or prostate cancers, whereas tumors with unknown primary origin are generally suggestive of pulmonary, hepatic, or renal carcinomas.[4]

The primary tumor is of pulmonary or pancreas in most of the cases.[4,5] Metastases are frequently observed in the liver, lungs, or bones, and lymph node metastasis is less common. Lymph node involvement in the mediastinum is extremely rare.[6,7] The histopathological type is adenocarcinoma in most of the cases, whereas squamous cell carcinoma is rare.[3,8]

Herein, a 63-year-old male patient with a mediastinal lymph node tumor of unknown origin has been presented.

Case Report

A 63-year-old male patient presented with complaints of chronic cough and hiccup. His history included hypertension, diabetes mellitus, and a cerebrovascular event in 2007. His family history was unremarkable. He had smoked 50 packs/year. Physical examination findings were normal. Laboratory findings included the following: leukocyte count: 4.7 × 10^3/mm^3, hemoglobin: 13.3 g/dL, hematocrit: 40.8, platelet: 299/uL 10^3/mm^3, glucose level: 87.7 mg/dL, urea: 19.1 mg/dL, creatinine: 1.38 mg/dL, albumin: 4 g/dL, and lactate dehydrogenase (LDH): 215. Other biochemical findings were within the normal ranges. Computed tomography (CT) of the thorax revealed

Address for correspondence: Dr. M Agca, Department of Pulmonology, Sureyyapasa Chest Diseases and Thoracic Surgery Training and Research Hospital, Basıbuyuk Mahallesi, Maltepe 34854, Istanbul, Turkey.
E-mail: agcameltem@yahoo.com

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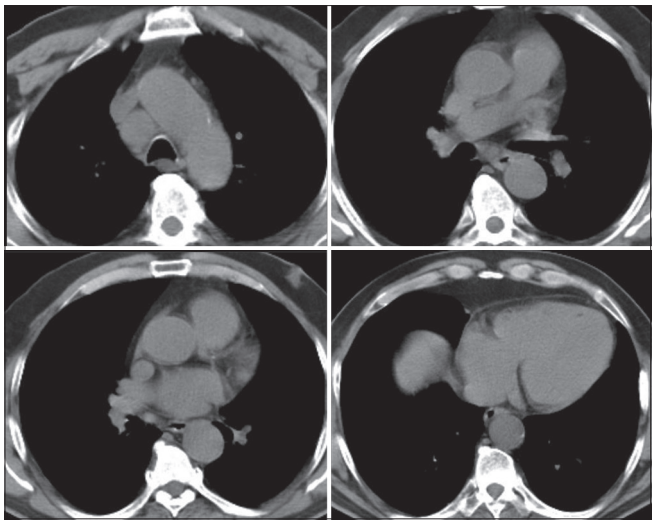

Figure 1: Mediastinal section of the case in thoracic computed tomography, lymphadenopathy in 4R

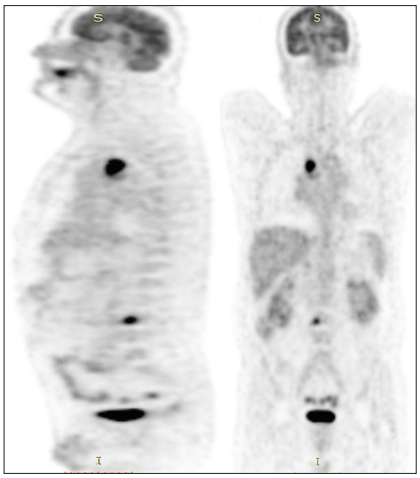

Figure 2: Positron emission tomography/computed tomography showing lymphadenopathy in the mediastinum and a lytic lesion was observed in the L3 vertebra

enlarged 2R and 4R lymph nodes in the mediastinum, the larger being 26 mm [Figure 1]. No endobronchial lesion was observed on fiber-optic bronchoscopy (FOB). The pathology of the biopsy material obtained from the carena of the superior left and right lobe margins revealed mild edema and bronchial epithelium. No acid-resistant bacilli were observed in the lavage sample, and no microbial growth was observed. Cytological analysis revealed alveolar macrophages, polymorph cells, and lymphocytes. Since FOB failed to make a diagnosis, endobronchial ultrasonography and transbronchial needle aspiration were performed onto 2R and 4R lymph nodes. No malignancy was observed. Due to the presence of a suspicious malignancy, positron emission tomography/CT (PET/CT) was performed, and lymphadenopathies were observed in the mediastinum (SUV_{max}: 29.7). A lytic lesion was observed in the L3 vertebra as well, with a SUV_{max} of 16.2 [Figure 2]. Hypermetabolic foci were detected neither in the bilateral pulmonary parenchyma nor in the remaining sites of the body. Magnetic resonance imaging of the brain was normal. The patient underwent biopsy from the 4R via mediastinoscopy. Its pathology revealed malignant tumor metastasis. In the immunohistochemical study, tumor cells stained positively with P6 and CK7 and negatively with CD20, HMB45, S-100, TTF1, and prostate-specific antigen. The pathology report revealed that the present immunoprofile did not suggest a significant primary focus. The patient was accepted as squamous cell carcinoma with unknown origin by the oncology department and underwent chemo-radiotherapy. Exitus was observed 1 year after the diagnosis.

Discussion

Herein, we presented a case of squamous cell carcinoma in a mediastinal metastatic lymph node with unknown primary origin.

Tumors with unknown primary origin constitute 3%–5% of all cancers. It is generally observed at the sixth decade and is more frequent in men. A detailed medical history should be obtained and physical examination should be performed for the diagnosis. Whole blood analysis, blood biochemistry analysis, occult blood in the feces, urinary analysis, pulmonary X-rays, and abdominal, thoracic, and pelvic tomography were performed, and the decision for localization of the biopsy was made.[4] In the autopsies, location of the primary tumor is generally detected within the lungs, liver, pancreas, or the gastrointestinal (GI) tract.[5] The most important step in the diagnosis is histopathological evaluation. Immunohistochemical analysis may suggest the primary origin of the tumor and determine the response to therapy and prognosis.[2]

Tumors with unknown primary origin generally appear with clinical findings of the metastatic origin. The most frequent metastatic tissues are the liver, lungs, pleura, and bones, and multiple organ metastases are present in most of the cases (60%).[4] Lymph node metastases are most frequently observed in the cervical, supraclavicular, axillary, and inguinal lymph nodes.[9] Cases with mediastinal lymph node metastasis are extremely rare. In our case, two foci of metastasis were detected, one being a mediastinal lymph node.

There are five histological subtypes as follows: good, moderate, and poorly differentiated adenocarcinoma; squamous cell carcinoma; poorly differentiated carcinoma; meuroendocrine tumor; and undifferentiated carcinoma.[10] In a wide case series, the most frequently reported type is adenocarcinoma.[3,8] The rate of

squamous cell carcinomas is only 5%.[7] Adenocarcinoma is more common among women, whereas squamous cell carcinoma is more common among men.[3] Histopathologically diagnosed adenocarcinomas are suggestive of prostate cancer in men and axillary lymph node metastasis is suggestive of breast cancer in women.[2] PET/CT is highly diagnostic in the head-and-neck and pulmonary cancers, especially with the squamous cell subtype.[2,10] Endoscopic examinations should be performed in a selected group of patients in the presence of symptoms and findings in the systemic and laboratory evaluation of the patient suggestive of the primary malignancy. As an example, in the presence of respiratory complaints, bronchoscopy and, in the presence of abdominal complaints and/or occult blood in feces, endoscopy should be recommended.[2] The case in our report was a smoker and had respiratory complaints; therefore, the examinations we performed were mainly of pulmonary carcinoma. Endoscopy was not performed due to the absence of GI complaints, anemia, or occult blood in feces, and no GI system-related symptom in the radiological examinations.

Several hypotheses have been put forth about the development of carcinomas with unknown primary origin. One of them is the transfer of benign epithelial inclusion to malignant cells in the lymph node. The other one is the very small nature of the tumor that cannot be detected in clinical evaluations or autopsy. Due to the immune defense mechanisms of the patient, disappearance of the tumor has been accepted as a possible cause.[6]

Prognosis of tumors with unknown primary origin is poor, and the mean survival is 4–12 months. These tumors are generally resistant to chemotherapy.[10] Its prognosis depends on patient's age, gender, performance score, histopathological subtype of the tumor, serum LDH level, and metastasis type.[2] Prognosis is better if the metastasis is limited to the lymph node and if the histopathology is other than adenocarcinoma.[5] However, localization of the involved lymph node is important as well; for example, supraclavicular lymph node involvement is a poor prognostic factor.[4] Hepatic metastasis is a poor prognostic factor independent from the histological subtype, and the mean survival is limited to 1–2 months. Survival is reduced in the adenocarcinoma metastasis of the remaining organs.[5]

The treatment is based on chemotherapy since the disease is a systemic metastasis.[4] If the cellular subtype cannot be determined in mediastinal lymph node metastases, the case is accepted as non-small cell cancer, and chemotherapy and radiotherapy are performed onto the mediastinum.[7] In our case, chemotherapy was started following the diagnosis; however, he died 1 year later.

This case should emphasize that, in case of a metastatic cancer in mediastinal lymph nodes, the diagnosis of "tumors with unknown primary origin" should be considered, which has an aggressive progression and a poor prognosis, which is known to be considerably frequent.

Declaration of patient consent

The authors certify that they 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.

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Conflicts of interest

There are no conflicts of interest.

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