Case Report

Atypical carcinoid tumor of the lung: A rare entity

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ABSTRACT

Carcinoids account for approximately 2% of all lung tumors, and the atypical carcinoids (ACs) are much rarer than typical carcinoid. Here, we report a rare case of AC tumor of the lung. A 50-year-old female patient presented with left-sided chest pain for 1 year, cough for 6 months, and loss of appetite for 6 months. Contrast-enhanced computed tomography scan of the thorax revealed an ill-defined heterogeneously enhancing soft-tissue attenuation lesion in the mediastinum following which transthoracic biopsy was done. Histomorphology and immunohistochemistry were consistent with AC, a neuroendocrine tumor. Combination chemotherapy consisting of cisplatin and etoposide was administered as initial chemotherapy.

KEY WORDS: Atypical carcinoid, intrathoracic mass, neuroendocrine tumor

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INTRODUCTION

Carcinoid tumors arise from Kulchitsky cells of the bronchial epithelium which are the stem cells having neuroendocrine activity. Tumors can develop from these neuroendocrine cells in many different organs, the most common being the lungs, the appendix, the small intestine (duodenum), the rectum, and the pancreas.[1] The World Health Organization categorized neuroendocrine tumors as small-cell lung carcinoma, large-cell neuroendocrine carcinoma (LCNEC), typical carcinoid (TC), and atypical carcinoid (AC).[2] Carcinoids account for approximately 2% of all lung tumors, and ACs are much rarer than TC. Bronchopulmonary system is involved in 25%–30% of all neuroendocrine tumors. The increase in age-adjusted incidence rates of bronchopulmonary carcinoids and neuroendocrine tumors in general over the past 30 years for all genders and races is attributed mainly to improvements in histopathological diagnosis and classification and to the more frequent use of endoscopic procedures.[3] It is usually diagnosed at 60 years of age. A female predominance was described by Modlin *et al.* and others.[4,5] A female predominance only for patients under the age of 50 years was described by Quaedvlieg *et al.* suggesting hormonal influence.[6]

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CASE REPORT

A 50-year-old woman nonsmoker presented with left-sided chest pain for 12 months, cough for 6 months, and loss of appetite for 6 months. On examination of the respiratory system, dullness on percussion and decreased breath sounds on auscultation were found on the left interscapular region with no features of mediastinal shift. It was suggestive of a space-occupying lesion. The clinical examination of the rest of the system revealed no abnormality. Routine blood investigations were within normal limits. For confirming the clinical findings and further evaluation, chest X-ray was done which was suggestive of left-sided

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homogeneous opacity in the upper zone probably an intrathoracic mass lesion. On further investigation, contrast-enhanced computed tomography (CECT) scan of the thorax [Figure 1] revealed that the lesion was seen encasing branches of the arch of the aorta completely and the arch of the aorta partially and seen abutting them with ill-defined fat plane. Transthoracic fine-needle aspiration cytology and tru-cut biopsy of the left lung mass were done for histopathology and immunohistochemistry. Histopathology revealed tissue infiltration by a tumor disposed in nests and trabeculae. The tumor cells are polygonal with moderately pleomorphic nuclei, granular chromatin, and moderate amount of eosinophilic cytoplasm. Mitotic figures (3/10 high-power fields [HPFs]) and apoptotic bodies are evident [Figure 2]. Immunohistochemistry [Figure 3] was positive for chromogranin, and Ki-67 proliferation index was 5%. It was negative for cytokeratin-7 (CK-7), thyroid transcription factor-1, and CK-5/6. These findings were consistent with AC.

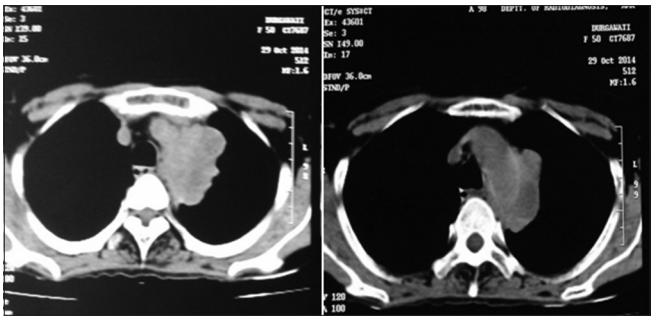

Figure 1: Contrast-enhanced computed tomography scan of the thorax showing that the lesion is encasing branches of the arch of the aorta completely and the arch of the aorta partially

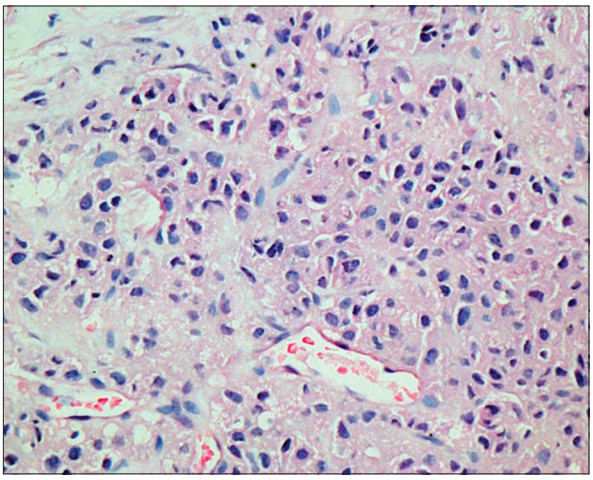

Figure 2: Histopathology of atypical carcinoid showing tissue infiltration by a tumor disposed in nests and trabeculae. The tumor cells are polygonal with moderately pleomorphic nuclei, granular chromatin, and moderate amount of eosinophilic cytoplasm. Mitotic figures (3/10 high-power fields) and apoptotic bodies are evident

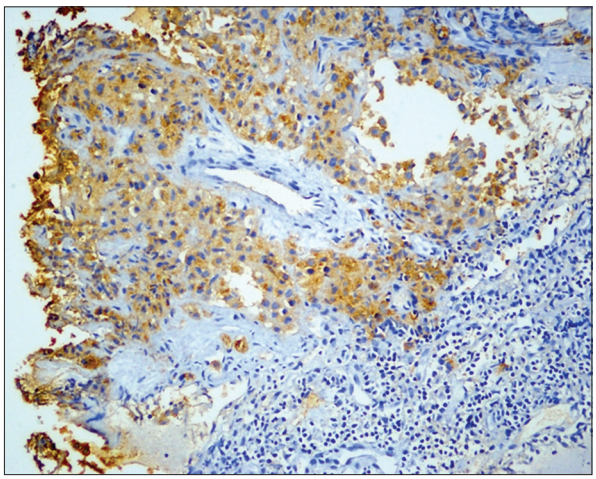

Figure 3: Immunochemistry of atypical carcinoid positive for chromogranin

DISCUSSION

Carcinoid tumors are commonly found in the gastrointestinal tract, followed by the tracheobronchial tree.[1] Kulchitsky cells found in the bronchopulmonary mucosa give rise to carcinoid tumors.[1] Bronchial carcinoid tumors may be asymptomatic or may present with wheezing, dyspnea, cough, hemoptysis, and recurrent pneumonia due to bronchospasm and obstruction.[6] Variability in clinical presentation may lead to delay in diagnosis or even misdiagnosis. The differential diagnosis of a patient with symptoms of bronchial obstruction, bronchospasm, and hemoptysis includes an obstructing bronchial carcinoma, endobronchial metastasis, hamartomas, aspirated foreign body, asthma, and chronic obstructive pulmonary disease.

Chest X-ray and CECT scan of the thorax can detect space-occupying lesion, and the diagnosis can be confirmed by bronchoscopic biopsy and/or CT-guided needle biopsy depending on accessibility. Bronchial carcinoid usually appears as a pinkish to reddish vascular mass, attached to the bronchus by a broad base, may have a polypoid appearance. Diagnosis can be made by an experienced bronchoscopist based on appearance, biopsy is helpful in diagnosis, and bronchial brushing for cytopathological examination is often futile.[7]

Of the bronchial carcinoids, TC is nearly nine times more common than AC.[8] The former is usually well-differentiated tumors of histologically ordered structure, larger than 5 cm, and exhibits <2 mitoses/10 HPFs. Necrosis is often not seen. While AC shows an atypical appearance with 2–10 mitoses/10 HPFs. Necrosis is present, and they tend to be more aggressive. They have a higher probability to metastasize, to recur, and to have a worse outcome and prognosis.[9] The mean age of presentation was 51 years for AC while it was 43 years for TC.[10] In this case, the age of presentation was 50 years, which almost corresponds to the average age reported in the literature. Smoking cigarettes or exposure to tobacco smoke has not been found to have any associations with bronchial carcinoids.[11]

AC usually presents at a more advanced stage than typical ones. Thus, an accurate histological diagnosis is imperative for further management. In 2005, Mineo *et al*. published that AC has a higher probability for developing micrometastases and hence has a more aggressive clinical behavior. Even small tumors located in the periphery of the tracheobronchial tree may metastasize suggesting that nodal micrometastases do not correlate with tumor size and stage. Immunohistochemical detection of micrometastases using chromogranin A and CK as markers allows for more accurate staging.[12]

Surgery is the mainstay for the treatment of both typical and atypical bronchial carcinoids. Our patient did not undergo surgery as the lesion was encasing branches of the arch of the aorta completely and the arch of the aorta partially. With AC, lobectomy and pneumonectomy are the most common options while with TC, bronchial sleeve resection which involves removal of less tissue solves the purpose as they are not as aggressive as AC.[13] Bronchoscope-guided resection can be curative for entirely intraluminal endobronchial carcinoid tumors without evidence of bronchial wall involvement or suspicious lymphadenopathy. Bleeding during biopsy or resection is a potential complication and may lead to airway compromise. Thus, rigid bronchoscopy may be preferable against flexible bronchoscopy. Surgical resection, with bronchoplastic techniques (i.e., sleeve, wedge, or flap resection) to preserve lung parenchyma, is the preferred treatment of choice for bronchial carcinoid, once the diagnosis is confirmed.[14]

Chemotherapy may be considered for adjuvant or neoadjuvant therapy with surgery and for advanced disease. There are no prospective trials addressing the benefit of chemotherapy with or without radiation therapy for resected bronchial carcinoids. Hence, the role of adjuvant therapy of a bronchial carcinoid is controversial. Patients receiving adjuvant chemotherapy with lymph node involvement and treated with surgical resection alone had a high likelihood to develop recurrent disease and a significantly unfavorable outcome. The data just took into account LCNEC and small-cell lung carcinoma. Chemotherapy regimens administered in small-cell lung cancer therapy, including platinum plus etoposide, should usually be an option like LCNEC.[15] Octreotide, somatostatin receptor analog, can be used for control of symptoms caused by tumor's secretion of peptide and amines.

Histology is the most important prognostic factor for bronchial carcinoid. AC has a worse prognosis and high rate of recurrence than TC.[9] In the latter group, the 5-year survival ranges from 89% to 92% and from 66.7% to 75% in the former group. The 10-year survival was 82%–88.9% for TC and 50%–56% for AC, which is explained by the more aggressive behavior in the latter group.[5,11]

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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