J Med Sci 2020;40(4):190-193
DOI: 10.4103/jmedsci.jmedsci_162_19

CASE REPORT

Pulmonary Neuroendocrine Tumor in a Young Male

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Pulmonary neuroendocrine tumor is a subtype of lung cancer, which does not have favorable outcome. The small-cell and large-cell variants of this cancer comprise 20% of all lung cancers. However, large-cell neuroendocrine tumor (LCNET) is not frequent and seen in about less than 3% of cases of lung cancer. Here, we describe a young nonsmoker male with the unholy triad of LCNET, newly diagnosed diabetes mellitus, and skin metastasis.

Key words: Lung cancer, chemotherapy, histopathological examination, paraneoplastic syndrome, neuroendocrine tumor

INTRODUCTION

Neuroendocrine tumors (NETs) of the lung constitute a heterogeneous group of cancers, originating from neuroendocrine cells in the pulmonary and bronchial epithelium. The large-cell tumor is the latest variant to be introduced addition to the three classic subtypes, namely small cell, typical carcinoid, and atypical carcinoid.[1] Although NET contributes to up to 20% of all lung cancers, large-cell variant is not common and seen in only 3% of cases. Similar to small-cell variant, they have a predilection for old age, male sex, and smokers.[2] However, the peripheral site of lung affliction by the tumor stands in contrast to the central involvement in case of small-cell tumor. Unfortunately, the tumor usually is of high grade and has dismal prognosis in the absence of a universal therapeutic regimen. Cough and hemoptysis are uncommon presentations, whereas paraneoplastic syndromes are even rare. Lymph node involvement is common at the diagnosis. However, the clinical presentations in our case were doubly unique: skin metastasis and diabetes mellitus in a nonsmoking young male.

CASE REPORT

A 22-year-old male presented to the emergency department with complaints of right-sided chest pain and cough with expectoration for 15 and 5 months, respectively. The chest pain was insidious in onset, gradually progressive, and located on the right side of the thorax. Cough was associated with a moderate amount of mucoid expectoration which was nonfoul-smelling and was not associated with any diurnal or postural variation. The patient also complained of loss of appetite and significant weight loss. There was no history of fever, breathlessness, hemoptysis, and hoarseness of voice. The patient also did not report any past history of either anti-tubercular therapy intake or any previous major surgical procedures. The patient had never smoked and was a teetotaler. On physical examination, the patient was conscious and oriented with pallor seen on palpebral conjunctiva. There was no evidence of peripheral lymphadenopathy, digital clubbing, or pedal edema. Systemic examination revealed the presence of a rounded swelling on the left side of anterior abdominal wall just below the left costal margin [Figure 1]. The swelling was painless, mobile, hard, and nonfluctuant with dimensions of 1.0 cm × 1.5 cm.

Routine blood investigations showed hemoglobin of 5.2 g/dl and a total leukocyte count of 12600 cells/mm^3 with a differential count of 77% neutrophils and 20% lymphocytes. His random blood sugar levels were elevated at 426 mg/dl. The corresponding fasting and postprandial values were also deranged at 246 mg/dl and 389 mg/dl, respectively, making the diagnosis of new-onset diabetes mellitus evident. Chest X-ray

Received: September 04, 2019; Revised: October 23, 2019; Accepted: February 25, 2020; Published: April 22, 2020
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How to cite this article: Bajpai J, Jain A, Kant S, Pradhan A, Bajaj DK. Pulmonary neuroendocrine tumor in a young male. J Med Sci 2020;40:190-3.

in the posteroanterior view demonstrated opacity in the right upper lobe of the lung [Figure 2]. Sputum smear for acid-fast bacilli was performed which turned out to be negative.

His abdominal ultrasound showed peripancreatic lymph nodes (largest measuring 2.58 cm × 2.35 cm) and retroperitoneal lymph nodes, largest being 4.07 cm × 3.05 cm. An endocrinology consultation was sought in which the cause of the diabetes was established as due to paraneoplastic syndrome and parenteral insulin therapy was initiated. A peripheral smear (general blood picture) was also done which showed hypochromic and anisocytic red blood cells and no immature cells. A contrast-enhanced computed tomography of the thorax was done which showed a large, heterogeneous mass lesion in the posterior part of the right upper lobe with lobulated margins [Figure 3].

A transthoracic biopsy was performed, and the microscopic examination unveiled the presence of sheets of medium-to-large round cells with high nuclear-to-cytoplasmic (N/C) ratio, hyperchromatic nuclei, and scant cytoplasm [Figure 4]. Immunohistochemistry was positive for cytokeratin and synaptophysin. Fine-needle aspiration cytology from the anterior abdominal wall swelling was also suggestive of metastasis from large-cell neuroendocrine tumor (LCNET). All the above features were consistent with the diagnosis of NET-large-cell type with stage IV. The patient was administered chemotherapy with cisplatin and etoposide and thereafter discharged with advice to report for subsequent cycles after 3 weeks. During the second cycle of chemotherapy, he developed massive hemoptysis which did not respond to conservative measures, and the patient ultimately succumbed to the disease.

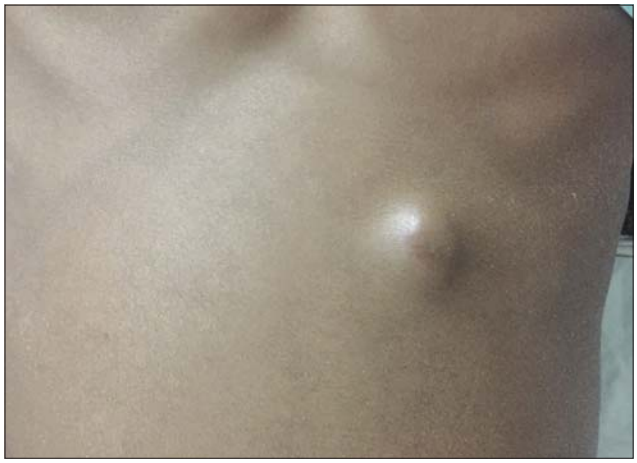

Figure 1: Cutaneous swelling on the left aspect of the anterior abdominal wall

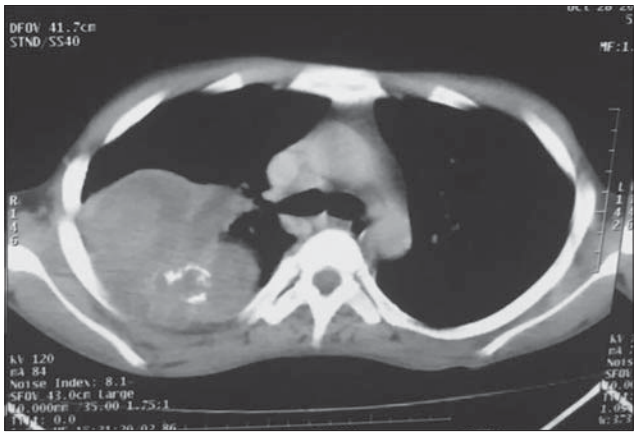

Figure 3: Contrast-enhanced computed tomography of the thorax in mediastinal window depicting speculated intrathoracic mass in the right upper zone

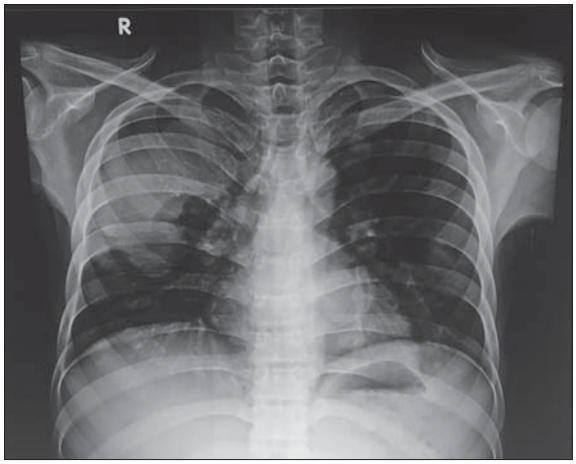

Figure 2: Chest X-ray demonstrating a heterogeneous opacity in the right upper zone of the lung

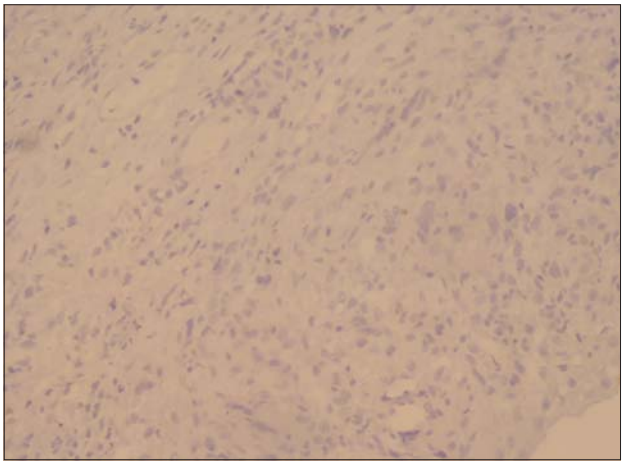

Figure 4: Histopathological examination of a biopsy specimen from the intrathoracic mass revealed the presence of sheets of medium-to-large round cells having high nuclear-to-cytoplasmic ratio with hyperchromatic nuclei and scant cytoplasm (H and E, ×400)

DISCUSSION

The lungs are the second-most common predilection site for NETs (first being the gastrointestinal tract!).[1,2] The World Health Organization criteria for pulmonary NET (2015) has classified them into the following subtypes: typical carcinoid, atypical carcinoid, LCNET, and small-cell NET.[3] Among these, small-cell NET and LCNET carry a poor prognosis as compared to the rest as they exhibit rapid tumor growth and early distant metastasis. LCNET has been further defined as "a large-cell carcinoma showing histologic features such as organoid nesting, trabecular, rosette-like, palisading patterns that suggest neuroendocrine differentiation and in which the latter can be confirmed by immunohistochemistry or electron microscopy."[3] Among the subtypes of NET, large-cell carcinomas are aggressive and carry a poor prognosis, as evidenced in our case by metastasis to anterior abdominal wall and to peripancreatic lymph nodes which manifested as diabetes mellitus. Although they are strongly associated with tobacco smoking, in the present case, the patient was a nonsmoker.[4] The treatment options for localized disease are surgical resection with mediastinal lymph node sampling.[5] There is no role of adjuvant radiotherapy in resected lung NETs even in the setting of positive lymph nodes. In case of advanced diseases, however, chemotherapy with cisplatin and etoposide has shown to be efficacious, with up to 75% of response observed in some studies.[6]

The epidemiological presentation of laNET in our case was unique – the young age and nonsmoker status. The clinical manifestations of skin metastasis and diabetes mellitus were also novel. Paraneoplastic syndromes are signs or symptoms that occur as a result of organ or tissue damage at locations remote from the site of the primary tumor or metastases. Paraneoplastic syndromes associated with lung cancer can impair various organ functions, and the list is myriad, including neurologic, endocrine, dermatologic, rheumatologic, hematologic, ophthalmological, glomerular, and coagulopathy syndromes.[7] LCNET-associated diabetes was possibly related to ectopic adrenocorticotropic hormone (ACTH) syndrome which in effect is an endogenous ACTH-dependent form of Cushing's syndrome with elevated ACTH and cortisol levels. Multiple organ metastases were, hence, found in the current patient. To the best of our knowledge, only a few cases of cutaneous metastasis of LCNET have been reported. Hence, this unholy constellation of LCNET, skin metastasis, and diabetes mellitus is worth a mention.

There is no standard treatment of pulmonary LCNET, and only a few data are available primarily from the case series. As it is a very rare disease, randomized clinical trials are difficult to be conducted. Primary surgery should be the first option in operable patients (TNM stages I and II). In early stages, lobectomy or pneumonectomy are the preferred choices because they may improve survival in the absence of lymph node metastases at mediastinal sampling.

The role of radiotherapy in the treatment of local or advanced pulmonary LCNET is still unclear, but some authors suggest its use in the setting of locally advanced disease. Prophylactic cranial irradiation, which is largely used in limited small-cell lung cancer after the partial or complete response to chemotherapy, is not currently recommended in pulmonary LCNET patients.[8]

CONCLUSION

LCNETs are aggressive tumors with a dismal prognosis. Although mostly seen in elderly smoking males, our case happened to be a young and nonsmoker male. Skin metastasis and paraneoplastic syndromes are features which are infrequently manifested. In the advanced stage, platinum-based chemotherapy with palliative care is the treatment of choice.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that his name and initials will not be published, and due efforts will be made to conceal his identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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