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Case report

Diffuse idiopathic pulmonary neuroendocrine cell hyperplasia in a young man with hypoxia: a case report and review of the literature

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Summary. Diffuse idiopathic pulmonary neuroendocrine cell hyperplasia (DIPNECH) is a rare lung disease, which usually affects older women. This disease is often asymptomatic. For patients who are symptomatic, symptoms usually include cough and dyspnea. In this paper, we reported a 38-year-old man who suffered from chest pain for 3 months. CT scan findings revealed scattered nodules that were less than 1 cm. Spirometry was normal and the arterial oxygen saturation at room air was 85%. Open lung biopsy revealed DIPNECH. Patients with DIPNECH are mainly elderly women with symptoms including cough and dyspnea. However, we reported a young man with chest pain and hypoxia without dyspnea. DIPNECH can occur in male and female individuals at any age. (www.actabiomedica.it)

Key words: diffuse idiopathic pulmonary neuroendocrine cell hyperplasia

Introduction

Neuroendocrine tumors originate from neuroendocrine cells. Due to the scattering of these cells in the digestive and respiratory tracts, these two organs are the most common sites of such tumors. When neuroendocrine cell hyperplasia is idiopathic and limited to the epithelium, it is called diffuse idiopathic pulmonary neuroendocrine cell hyperplasia (DIPNECH). If this hyperplasia passes through the basement membrane and is less than 5mm in diameter, it is called Tumorlet, but if the diameter is more than 5mm, it is called carcinoid. (1) DIPNECH and Tumorlet can act as carcinoid precursors (1). DIPNECH was first described by Aguayo in 1992 (2). In carcinoids, there is a disturbance in the 11q3 region while it is not seen in Tumorlet (3). Therefore, this genetic mutation may be the cause of carcinoids. Most cases of Tumorlet and DIPNECH are presented in combination with other lung diseases like fibrosis and bronchiectasis (4). Hence, this cell proliferation is likely to be a tissue reaction.

Although carcinoid and neuroendocrine tumors account for about 1% to 2% of lung tumors (1,5), the incidence of DIPNECH and Tumorlet is unpredictable. Specific clinical symptoms have not yet been defined for Tumorlet and DIPNECH. However, most of the reported patients presented only symptoms including cough and shortness of breath. Most of the reported cases were middle age women who were non-smokers. In this study, we introduced a 38-year-old man who had hypoxia due to Tumorlet.

Case presentation

The patient was a 38-year-old non-smoker man without any history of diseases. He was admitted at a clinic with chest pain without dyspnea, cough, hemoptysis or constitutional symptoms. His vital signs were stable and there were bilateral inspiratory crackles in his both lungs. Arterial oxygen saturation was 85% at room air and the rest of the examination was normal.

Chest X-ray revealed diffuse bilateral nodular opacity. CT scan showed random bilateral diffuse nodules of about 3-9mm diameter (Figure 1). Spirometry was normal (FEV1/FVC = 83%, FEV1 = 3.6 L (78%), FVC = 4.3 L (81%). Open lung biopsy from RLL was carried out. In lung biopsy, small nodules of uniform cells were seen in the form of cell nests. These cells contained oval to spindle shaped nuclei, granular chromatin and eosinophilic cytoplasm (Figure 2). These cells in IHC were positive for NSE and chromogranin but negative for vimentin and actin. The cellular mitotic activity index was less than 7%; considering the morphology, positive neuroendocrine markers and low mitotic index, DIPNECH was diagnosed.

Discussion

Although about 90% of patients with Tumorlet and DIPNECH are old women, (6), our patient was a young man. Symptomatic patients usually have dyspnea and chronic cough. However, the patient in our study had only chest pain; he was hypoxic without any spirometric impairment.

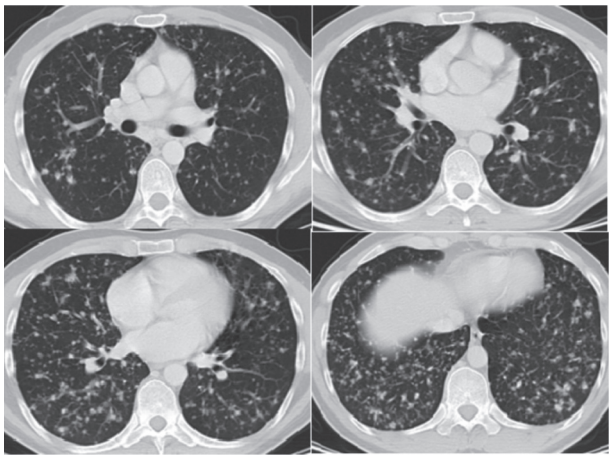

Figure 1. CT scan presents diffuse nodular opacity

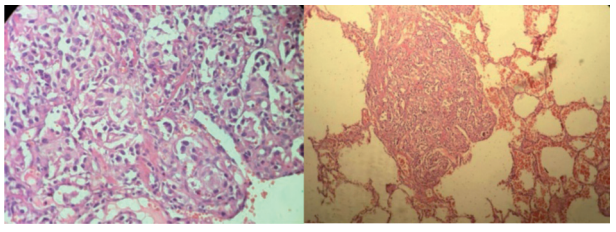

Figure 2. The nodules of the neuroendocrine cell nest pattern. The cells contain oval shaped nucleus and granular chromatin

Nearly 200 cases of DIPNECH have been introduced. DIPNECH may be detected accidentally in CT scan or pathology in patients who are evaluated for other reasons (6). If the patient is symptomatic, spirometry usually exhibits obstructive or restrictive patterns (7). In CT scan, the presence of scattered nodules in the lung, especially when accompanied by air trapping, is considered to be the typical finding of DIPNECH. (8) Tumorlet has been highly-absorbed in PET scan (9,10). Diagnosis of DIPNECH is usually based on open lung biopsy. Since the lesion originates from the bronchial epithelium, trans-bronchial lung biopsy or cryobiopsy can also be useful (9,11).

Marcheusky and colleagues proposed the criteria for diagnosis of DIPNECH by examining 70 pathology samples of surgical patients who had neuroendocrine cell hyperplasia (12). They found that patients who had at least three areas of Tumorlet in addition to multi-focal neuroendocrine hyperplasia were exposed to carcinoid, and that this criterion is necessary for the diagnosis of DIPNECH. However, since many patients are asymptomatic, this definition cannot be applied clinically. That is why Giulio and colleagues used the term DIPNECH syndrome or "DIPNECH with airway disease" (6). This term is used for those with a long term history of chronic pulmonary symptoms with an obstructive pattern in spirometry, abnormal findings in CT scans and neuroendocrine hyperplasia in pathology. At such circumstances, treatments should be focused on constrictive bronchiolitis

The course of the disease is different. Most patients are stable. However, some of them may develop advanced pulmonary obstructive diseases due to constrictive bronchiolitis, which can even lead to lung transplantation. If the patient is asymptomatic and has no progressive symptoms, no treatment is required. Tumorlet may transform to carcinoid and thus follow-up of the patient based on biopsy, clinical findings, spirometry, and imaging is recommended (13-15).

Based on the data in the literature and according to Marchevsky's pathological definition and Giulio's classification, we designed an algorithm to approach neuroendocrine hyperplasia (NECH) observed in the

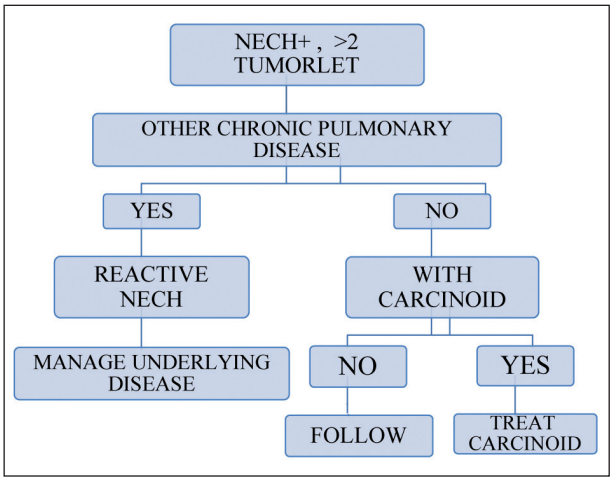

Figure 3. Flow chart to manage DIPNECH. NECH: neuroendocrine cell hyperplasia

pathology (Figure 3). This diagram provides a good concept for understanding of DIPNECH.

The uniqueness of our case was that, despite very low prevalence of the disease in men and at early ages, our patient was a young man. Moreover, the patient had hypoxia without a spirometric abnormality. DIPNECH seems to be associated not only with an obstructive mechanism but also with diffusion problems, leading to respiratory disorders. In our patient, chemotherapy was initiated due to hypoxia. However, after one year, there was no change in PFT and CT scans. Currently, the patient's functional class is suitable and he is not receiving any treatments.

Conflict of interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article

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