Case Report

Diffuse idiopathic pulmonary neuroendocrine cell hyperplasia: Unusual presentation

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Submission: 27-05-2018
Accepted: 14-06-2018

Abstract:

Diffuse idiopathic pulmonary neuroendocrine cell hyperplasia (DIPNEC) is an abnormal proliferation of pulmonary neuroendocrine cells that occur without underlying etiology. Here, we report a unique case of 55-year-old female with unusual presentation of DIPNECH and thymoma and on the background history of Crohn's disease that might point toward an autoimmune phenomenon. To the best of our knowledge, there were no previous reports of DIPNECH with either thymoma or Crohn's disease. DIPNECH has premalignant potential and reported in association with carcinoid and non-small cell lung cancer; however, its autoimmune association never reported. The presence of multiple lung nodules along with evidence of small airway disease should alert the physician to include DIPNECH as part of the differential diagnosis given its malignant potential. The prognosis is variable and depends on the presence or absence of underlying malignancy as well as the severity of airflow obstruction.

Keywords:

Crohn's disease, diffuse idiopathic pulmonary neuroendocrine cell hyperplasia, thymoma

Pulmonary neuroendocrine cells (PNECs) are normal specialized epithelial cells lining the tracheobronchial tree and can present solitary or in the cluster. PNECS are normally few as human grow in comparison to the fatal lung. An abnormally high rate of PNECS proliferation can occur with different respiratory disorders that are associated with hypoxia.[1] When the proliferation occurs without obvious reasons, the term Diffuse Idiopathic Pulmonary Neuroendocrine Cell Hyperplasia (DIPNEC) is applied. DIPNECH is considered premalignant lesion by the last update from the World Health Organization (WHO).[2] Here, we report a patient with DIPNECH that coincides with a diagnosis of thymoma and on background history of Crohn's disease. We believe that this is the first report of such association.

Case Report

A 55-year-old female presented to our outpatient clinic with prolong history of productive cough associated with wheezes for the last 5 years associated with recurrent chest infection requiring outpatient treatment with oral antibiotics along with a short course of oral steroid. She is a nonsmoker or passive smoker. There is no family history of malignancy. Her background history is significant for Crohn's disease since 2014 treated with azathioprine. On physical examination, auscultation was significant for bibasilar fine inspiratory crackles. There were no wheezes. The rest of examination was unremarkable.

Pulmonary function test (PFT) – Forced vital capacity (FVC) 2.53 L (73%), forced expiratory volume in 1 s (FEV1) 2.36 L (87%), FEV1/FVC 93%, total lung capacity

Access this article online

Quick Response Code:

Website: www.thoracicmedicine.org

DOI: 10.4103/atm.ATM_159_18

How to cite this article: Alrajhi NN, Paramasivam MP, Alboukai AA, Alrikabi AC, Alhamad EH. Diffuse idiopathic pulmonary neuroendocrine cell hyperplasia: Unusual presentation. Ann Thorac Med 2019;14:161-3.

4.10 L (80%) and corrected diffusion capacity for carbon monoxide DLCOcor 6.79 mm/min/kPa (82%).

Review of high-resolution computed tomography of the chest revealed that hyperinflated lung with evidence of small airway disease showing bronchiolar wall thickening representing mild bronchiectasis associated with peribronchiolar nodularity along with air trapping suggestive of bronchiolitis. It is associated with variable size nodular infiltrates seen more in the upper lobes and along the bronchovascular distribution. The presence of radiologic evidence of bronchiolitis along with lung nodules rises the suspicion of DIPNECH. The mediastinal window showed large anterior mediastinal soft-tissue mass with no mediastinal or hilar lymphadenopathy [Figure 1].

Computed tomography (CT)-guided fine-needle aspiration of the anterior mediastinal mass confirmed the diagnosis of thymoma [Figure 2].

She underwent surgical lung wedge biopsy from middle lobe and lingular lobe of both lungs at the time of thymectomy. The histopathology of the lung biopsy revealed foci of neuroendocrine cell hyperplasia (tumorlet). Immunohistochemical showed that the cells are positive for CK7, TTF1, and chromogranin [Figure 3].

As thymoma was the WHO Type B2 and the margin of the resection was involved by the thymoma, she underwent radiotherapy of 22 sessions. She remains stable and on regular follow-up.

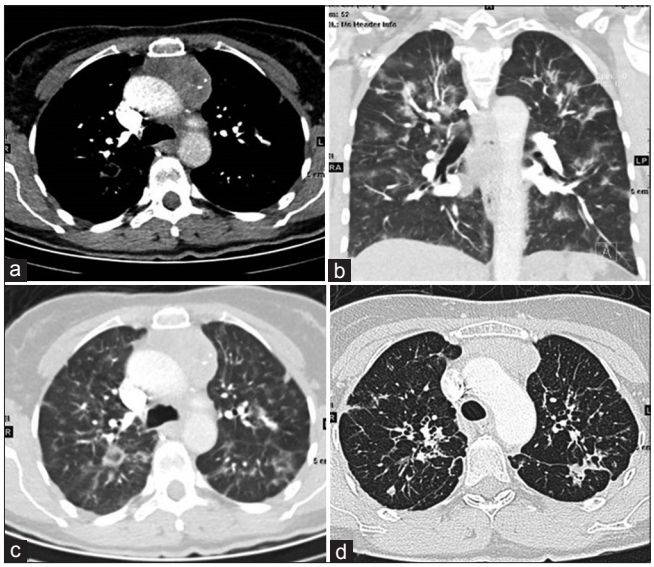

Figure 1: High-resolution computed tomography of the chest. (a) The mediastinal window showed large anterior mediastinal mass. (b and c) Coronal and axial lung view showing evidence of bronchiolitis with presence small airway bronchiolar wall thickening suggestive of mild bronchiectasis associated with peribronchiolar nodularity along with air trapping. It is associated with variable size nodular infiltrate. (d) High-resolution computed tomography in May 2017 showed progression of peribronchial fibrotic streaks

Discussion

Our case demonstrates unique presentation of DIPNECH with a concomitant diagnosis of thymoma and on the background of Crohn's disease. Up to our knowledge, there are no previous reports of DIPNECH with either thymoma or Crohn's disease.

The diagnosis of DIPNECH is made in appropriate clinical scenario of obstructive symptoms along with PFT findings of obstructive ventilator defect and/or air trapping in conjunction with CT findings of lung nodules with or without signs of small airway disease. Restrictive and normal PFT finding has been reported as well.[3] In some cases, the patient can be asymptomatic, and diagnosis is made through incidental finding of lung nodule.[4] Lung biopsy is required to confirm the diagnosis and to rule out carcinoid tumor in the presence of lung nodule. The gold standard test is surgical lung biopsy as it provides the ideal sufficient sample given the nature of its patchy bronchiolar involvement that can be missed by conventional transbronchial biopsy.[5]

Up to date, there is no consensus in treating DEIPNECH. The management largely depends on presence and severity of symptoms as well as the severity of airflow obstruction on PFT. Therapeutic options include surgical resection, steroid, somatostatin analog, and cytotoxic therapy. Watch and see approach can be considered in asymptomatic patient with regular clinical follow-up.[5]

Prognosis is variable and depends on the degree of constrictive bronchiolitis and its associated airflow obstruction as well as its presence of associated malignancy. Davis SJ and coworkers estimate 5-year

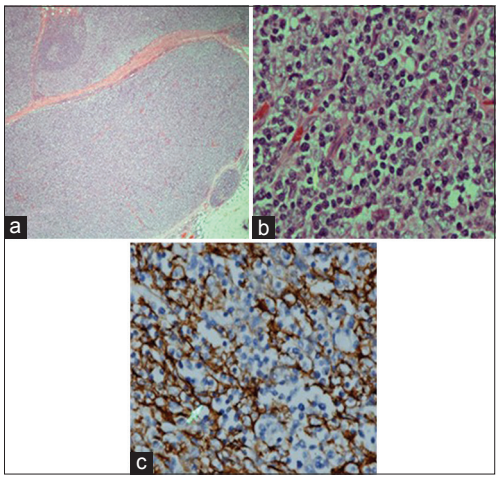

Figure 2: Biopsy from anterior mediastinal mass consistent with thymoma. (a) Lobules of thymoma, Type B2 (H and E, ×40). (b) Numerous mature T lymphocytes and epithelial-like cells with large vesicular nuclei (H and E, ×600). (c) Epithelial cells stain positive for cytokeratin 7 (IHC, ×600)

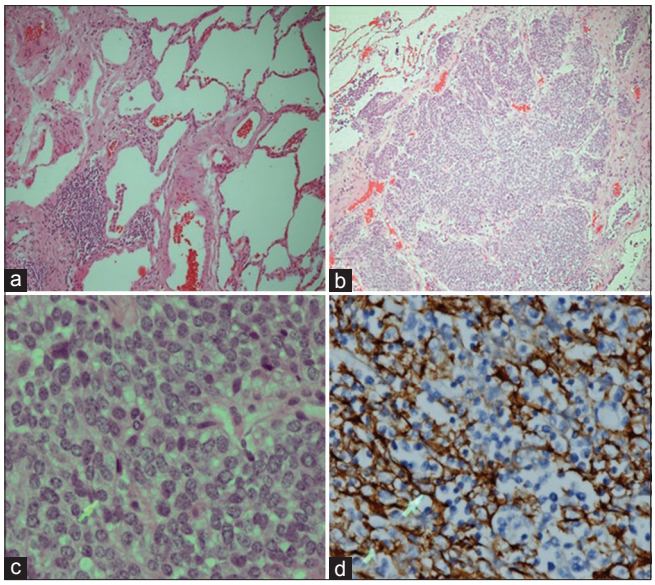

Figure 3: Surgical lung biopsy showed diffuse idiopathic pulmonary neuroendocrine cell hyperplasia. (a) Peribronchiolar inflammation and focal widening of some alveolar walls (H and E, ×40). (b) A lung nodule of proliferating neuroendocrine cells consistent with tumorlet (H and E, ×1100). (c) Neuroendocrine cells showing "salt and pepper" nuclear chromatin (arrowhead, H and E, ×600). (d) Tumorlet lung nodule stains positive for chromogranin (Chromogranin, ×400)

survival rate of 83%. Progressive airflow obstruction secondary to obliterative bronchiolitis can be stabilized with steroid therapy, but in other cases would require lung transplantation. DIPNECH is considered premalignant lesion according to the latest WHO update and serial radiologic monitoring in the presence of lung nodule and low threshold for surgical biopsy of >0.5 cm or increasing size nodule due it is carcinoid potential.[5]

DEPNICH has been reported in the patient with a current or previous history of intrathoracic or extrathoracic malignancies. Thymoma is associated with other autoimmune disorders, such as systemic lupus erythematosus and Sjogren's syndrome.[6]

Up to our knowledge, this is the first case reported the presence of DEPNICH in association with Crohn's disease and with thymoma. This might point toward a possible underlying autoimmune stimulus for PNECs to proliferate, however, its autoimmune association not demonstrated.

In summary, here, we report a unique case of DIPNECH in a patient with Crohn's disease and thymoma. The presence of multiple lung nodules along with evidence of small airway disease should rise the suspicion of DIPNECH as part of the differential diagnosis given its malignant potential.

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.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Koliakos E, Thomopoulos T, Abbassi Z, Duc C, Christodoulou M. Diffuse idiopathic pulmonary neuroendocrine cell hyperplasia: A case report and review of the literature. Am J Case Rep 2017;18:975-9.
2. Gosney JR. Diffuse pulmonary neuroendocrine cell hyperplasia. In: Travis WD, Brambilla E, Burke AP, Marx A, Nicholson AG, editors. WHO Classification of Tumors of the Lung, Pleura, Thymus and Heart. 4th ed. Lyon. IARC. 2015. pp.78-9.
3. Lim C, Stanford D, Young I, McCaughan B, Cooper W. Diffuse idiopathic pulmonary neuroendocrine cell hyperplasia: A report of two cases. Pathol Int 2010;60:538-41.
4. Miller RR, Müller NL. Neuroendocrine cell hyperplasia and obliterative bronchiolitis in patients with peripheral carcinoid tumors. Am J Surg Pathol 1995;19:653-8.
5. Rossi G, Cavazza A, Spagnolo P, Sverzellati N, Longo L, Jukna A, *et al*. Diffuse idiopathic pulmonary neuroendocrine cell hyperplasia syndrome. Eur Respir J 2016;47:1829-41.
6. Jiang Y, Dai X, Duan L, Zhou Y. The coexistence of autoimmune rheumatic diseases and thymomas. Adv Clin Exp Med 2017;26:237-43.