Diffuse idiopathic pulmonary neuroendocrine cell hyperplasia: Case report and review of literature

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SUMMARY
Diffuse idiopathic pulmonary neuroendocrine cell hyperplasia is a rare condition affecting mostly women in the fifth and sixth decades of life. Here we present a case of its accidental finding in the lung parenchyma of a 56-year-old non-smoker female. In the periphery of the right middle lobe, linear and nodular proliferations were detected in the wall of the small bronchi and terminal and respiratory bronchioles. Under the pleura, several tumorlets were located. Immunohistologically, neuroendocrine cells were positive with antibodies against chromogranin A, synaptophysin, CD56, serotonin (weak positivity of some cells only), calcitonin, GRP/bombesin, cytokeratin 7 and TTF-1.

Keywords: diffuse idiopathic pulmonary neuroendocrine cell hyperplasia – tumorlets – neuroendocrine tumors – immunohistochemistry

Difuzní idiopatická hyperplázie neuroendokrinních buněk: popis případu a přehled literatury

SOUHRN
Difuzní idiopatická plicní hyperplázie neuroendokrinních buněk je vzácné onemocnění, které postihuje většinou ženy v 5. a 6. dekádě života. Prezentujeme náhodný nález tohoto onemocnění u 56-leté ženy, nekuřačky. Na periferii středního laloku pravé plíce byla zjištěna lineární a nodulární proliferace neuroendokrinních buněk ve stěně malých bronchů a v terminálních a respiračních bronchiolech. Pod pleurou bylo zjištěno několik tumorletů. Imunohistologicky neuroendokrinní buňky reagovaly pozitivně s protilátkami proti chromograninu, synaptofysinu, CD56, serotoninu (slabá pozitivita jen některých buněk), kalcitoninu, GRP/bombesinu, CK7 a TTF-1.

Klíčová slova: difuzní idiopatická hyperplázie neuroendokrinních buněk – tumorlety – neuroendokrinní tumory – imunohistochemie

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Diffuse idiopathic pulmonary neuroendocrine cell hyperplasia (DIPNECH) is a rare condition. As of the year 2011, only 49 cases were published (1). According to the World Health Organization (WHO) DIPNECH is considered as a generalised proliferation of scattered single cells, small nodules (neuroendocrine bodies), or linear proliferations of pulmonary neuroendocrine cells in the mucosa and submucosa of the small bronchi and bronchioles (2,19). Initially, there is linear proliferation mostly beneath the superficial columnar epithelium. As a rule, the lesions are found in the periphery of the lung. The patients have no significant clinical symptoms and the condition is usually diagnosed accidentally during general examination. Most commonly, women in the fifth and sixth decades of life are affected (2,3). However, the disease may develop at any age. DIPNECH is considered to be a precursor of tumorlets and certain G1 and G2 neuroendocrine tumors (carcinoids and atypical carcinoids) (18). Centrally located G1 and G2 tumors are more frequent and typically characterized by more prominent clinical signs associated with narrowing of the larger bronchi. In their proximity, hyperplastic neuroendocrine cells may also appear but these changes do not correspond to DIPNECH (3,4). The study of DIPNECH may aid in understanding the development of pulmonary neuroendocrine tumors.

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MATERIAL AND METHODS

A 65-year-old female patient with no significant complaints reported frequent coughs six years previously. An X-ray of the lungs as part of a preventive physical examination revealed a poorly defined lesion of approximately 4 cm in diameter in the periphery of the right middle lobe. The bronchoscopy was not performed. Subsequently, a right middle lobectomy was performed.

Immunohistochemistry. Immunohistochemical evaluation was carried out using the avidin-biotin complex (ABC) method. Positive and negative controls were used. The following antibodies were used (with working dilutions stated in brackets): CK20, clone Ks 20.8 (prediluted); CK7, clone OV-TL 12/13 (1:50); polyclonal rabbit anti-human gastrin (1:2000); polyclonal rabbit anti-human somatostatin (1:1000); monoclonal mouse anti-human serotonin, clone 5HT-H209 (1:100); and polyclonal rabbit anti-human glucagon (1:1000); all antibodies produced by Dako Glostrup, Denmark; monoclonal rabbit anti-TTF-1, clone G21-G (1:100), DB Biotech; synaptophysin, clone 27G12 (1:100); chromogranin A, clone 5H7 (1:100); and monoclonal mouse anti-CD56 (NCAM), clone 1B6; produced by Novocastra, Newcastle-upon-Tyne, UK; monoclonal mouse anti-neuron-specific enolase (NSE), clone MIG-N3 (prediluted); Biogenex; rabbit anti-pancreatic polypeptide, clone 18-0043