Not All That Wheezes is Asthma

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A 71-year-old non-smoking white female with no significant occupational exposure presents to the hospital with complaints of cough and shortness of breath that are not responding to her inhaler therapy. She has been having persistent shortness of breath and carries a diagnosis of asthma for which she follows up regularly with her pulmonologist. She is currently maintained on an inhaled corticosteroid and a long acting beta agonist for her asthma and was recently referred for allergy testing secondary to persistent symptoms while on her current therapy. The patient was admitted to the hospital for an asthma exacerbation with bronchitis. She underwent imaging including a chest x-ray which was unrevealing and a CT of the chest to rule out pulmonary embolism which revealed multiple sub-centimeter peripheral nodules and marked mosaic attenuation suggestive of air trapping. Further work-up with a PET CT showed mild metabolic activity of the larger nodules. Her pulmonary functioning tests revealed mild obstruction and a normal diffusion capacity. The patient underwent a surgical lung biopsy, which revealed multiple typical carcinoid tumorlets measuring less than 1 cm and proliferation of neuroendocrine cells consistent with neuroendocrine cell hyperplasia.

CT chest with contrast revealing multiple pulmonary nodules throughout both lung fields.

PET scan showing multiple pulmonary nodules largest of which is FDG avid, suspicious for diffuse idiopathic pulmonary neuroendocrine cell hyperplasia.

The diagnosis of DIPNECH can be challenging. Review of the literature shows a limitation in the use of serum biomarkers because neuroendocrine products cannot be broken down into readily measured levels. CT scan of the chest usually reveals small sub-centimeter nodules, which are less than 5mm in 60% of cases. Mosaic attenuation is also commonly found. Less common findings are ground glass opacities as well as bronchiectasis; however, no radiological finding is pathognomonic. The role of bronchoscopy is unclear as there are no specific findings on bronchiolar lavage although some reports of diagnoses of DIPNECH through trans-bronchial biopsies have been described. The gold standard for diagnosis is a surgical lung biopsy. In order to ensure histopathological diagnosis of DIPNECH, neuroendocrine cell hyperplasia must be seen. Carcinoid tumorlets are seen in more than 70% of patients including our patient. Various treatment strategies have been described including systemic/inhaled steroids, bronchodilators and lung resection.

The diagnosis and management of DIPNECH remains challenging because of varying presentation and lack of non-invasive testing. It requires a high index of suspicion in patients who have multiple small pulmonary nodules, especially in women with associated symptoms of cough and wheezing. Further case studies would be beneficial in order to better understand the diagnosis and management of this rare pulmonary condition. This case demonstrates the importance of clinicians maintaining a broad differential regarding common symptoms that are refractory to common therapies.

REFERENCES: