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Images in Hospital Medicine

Neuroendocrine Tumor Presenting as Hypoxic Respiratory Failure in a Patient with Patent Foramen Ovale

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A 61-year-old male with a past medical history of diabetes mellitus and hyperlipidemia presented to the hospital with progressively worsening hypoxic respiratory failure. He was a non-smoker and had no prior history of lung disease. On admission, his oxygen saturation was 86% and remained between 86-90% on high-flow oxygen with FiO2 of 100% and 60 L/minute flow. He reported intermittent non-bloody watery diarrhea, facial flushing after showering, and anorexia with a 50lbs unintentional weight loss in the preceding six months. Initial labs showed a hemoglobin of 18.3g/dL [Nl:13.2-16.6g/dL] and erythropoietin level of 23.1mIU/ml [Nl:2-18.5mIU/ml], suggestive of secondary polycythemia. CT-pulmonary-angiogram was negative for pulmonary embolism but revealed diffuse hilar lymphadenopathy. CT-abdomen showed intra-abdominal lymphadenopathy and a 1 cm lesion in the left hepatic lobe (**Figure 1**). His hypoxic respiratory failure refractory to supplemental oxygen therapy was concerning for a shunt. An echocardiogram with bubble study demonstrated an EF of 56%, a dilated right ventricle, and a severely dilated right atrium with 4+ tricuspid regurgitation (TR) caused by annular dilation and very rigid, immobile tricuspid leaflets with restricted motion and a patent foramen ovale (PFO) with a significant right to left shunting. Based on the patient's symptoms of flushing, diarrhea, and hepatic lesion with hilar lymphadenopathy, a metastatic neuroendocrine tumor (NET) was suspected. He was started on octreotide while awaiting liver biopsy and underwent a right heart catheterization with PFO closure using a septal-occluder device. These interventions resulted in the resolution of his hypoxia. The patient's 24-hour urine 5-HIAA was 146 [Nl:<7.7mg/day] and liver biopsy showed metastatic well-differentiated NET grade 1. The patient was continued on octreotide and referred to oncology.

Carcinoid tumors (CT) are NETs that primarily develop from the gastrointestinal tract and bronchopulmonary system, with an incidence of around 2/100,000 annually.[1,2] CTs are generally indolent and secrete a variety of vasoactive substances, including serotonin, histamine, and prostaglandins.[3] Vasoactive substances enter the systemic circulation in individuals with extensive liver or lung metastases when hepatic or pulmonary cells fail to metabolize them, resulting in carcinoid syndrome (CS).[3] Vasoactive chemicals may also reach the systemic circulation in individuals with PFO and when the initial tumor is situated in the bronchi.[3–5] CS commonly manifests as episodic facial flushing, diarrhea, bronchoconstriction, tachycardia, hypotension, and carcinoid heart disease (CHD).[4,5] CHD typically presents as valvular heart disease (isolated TV regurgitation), coronary artery vasospasm in individuals with nonocclusive coronary artery disease, arrhythmias, and direct myocardial involvement from tumor metastases.[4,5] CHD is diagnosed based on strong clinical suspicion, biomarker levels (5-HIAA), and cardiac imaging. Management

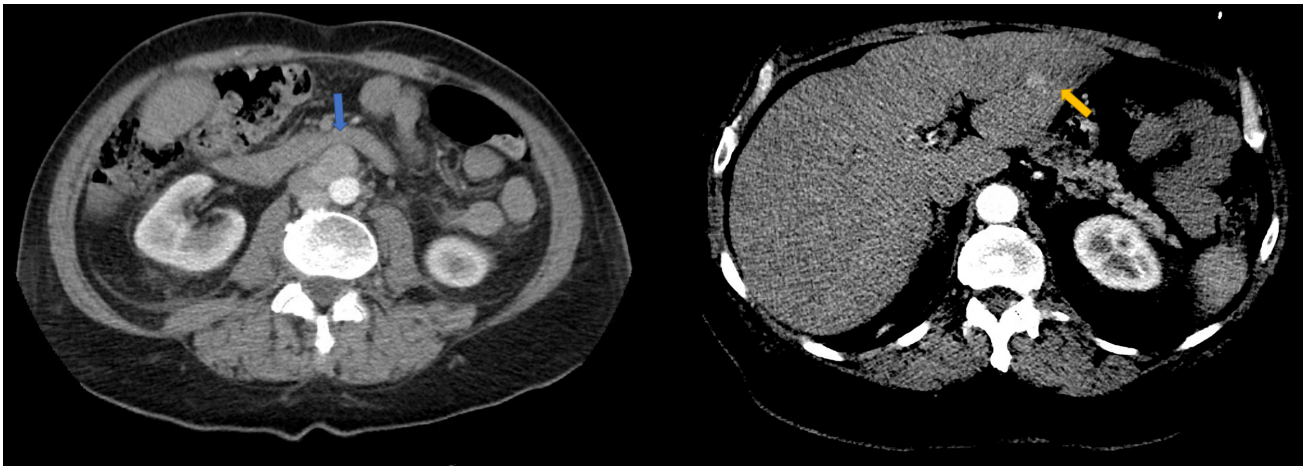

Figure 1. Axial section of the CT abdomen demonstrating intra-abdominal lymphadenopathy (blue arrow) and a 1 cm lesion in the left hepatic lobe (yellow arrow)

includes somatostatin analogs (octreotide) that limit serotonin release and lower 5-HIAA levels, diuretics to regulate fluid balance, and surgical repair of CHD.[6]

In conclusion, our report highlights a unique case of right-sided valvular involvement with NET in a patient with PFO causing shunting of deoxygenated blood presenting as chronic hypoxic respiratory failure unresponsive to supplemental oxygenation, with compensatory polycythemia. It also underlines the significance of looking for PFO in individuals with clinical indications of CS/CHD without metastatic lung lesions.

AUTHOR CONTRIBUTIONS

All Authors (AC, KS, SD, AK) have reviewed the final manuscript prior to submission. All the authors have contributed significantly to the manuscript, per the ICJME criteria of authorship.

- Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND
- Drafting the work or revising it critically for important intellectual content; AND
- Final approval of the version to be published; AND
- Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

DISCLOSURES

The authors have no conflicts of interest to disclose.

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