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Case Report

Neuroendocrine Tumor Involving the Epicardium

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Keywords
Neuroendocrine tumors · Epicardium · Carcinoid tumors · Carcinoid syndrome · Carcinoid heart · Metastasis

Abstract
Neuroendocrine tumors (NETs) are rare malignancies that usually arise from the digestive tract or lungs. Metastases of NETs to the heart (epicardium) are a rare complication. We present a case of a metastatic NET involving the epicardium.

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Background

Neuroendocrine tumors (NETs) derive predominantly from enterochromaffin or Kulchitsky cells [1]. They are rare malignancies that arise from the digestive tract, lungs, or rare primary sites such as the kidneys or the ovaries. The age-adjusted incidence in the United States for nonpancreatic primaries is about 4.7 per 100,000 persons [1–3]. The annual incidence is higher for males and African Americans. The median age at diagnosis is 63 years. The incidence continues to rise in the United States and globally for both pancreatic and nonpancreatic primary sites [4]. Likely more cases are getting diagnosed incidentally with imaging being done for other unrelated reasons.

Clinical symptoms are in general not specific or they may correlate with the location of the tumor and be organ related. NETs can be classified as functional or nonfunctional. NETs

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are functional when a specific clinical syndrome is caused by the excessive production of hormones by the tumor cells. Approximately two-thirds of NETs are functional [5]. Nonpancreatic functional NETs are also referred to as carcinoid tumors. Carcinoid syndrome and its symptoms (chronic flushing, diarrhea, wheezing, etc.) usually present in patients with metastatic carcinoid tumors of the distal small bowel and proximal colon [4, 6, 7]. The classic carcinoid syndrome-related symptoms are present in about 20% of patients with NETs [8]. Most cases present with nonfunctioning NETs. Given the indolent nature and longevity of patients with NETs, metastases to rare sites are increasingly being seen.

Case Presentation

The patient is a 63-year-old African-American previously healthy male with a longstanding history of metastatic NET. He was initially diagnosed in 2011 after developing intractable abdominal pain. He underwent exploratory abdominal surgery with resection of a 1.3-cm tumor involving the small bowel with extension into the mesenteric adipose tissue. Pathology showed a well-differentiated NET, characterized by predominantly nested architecture, with uniform round to oval nuclei with evenly distributed granular chromatin and a moderate amount of amphophilic cytoplasm. The lesion had an infiltrative growth pattern, with extension into the mesenteric adipose tissue. Immunohistochemical stains were positive for chromogranin and pancytokeratin Ki-67 showed a low proliferative index (less than 2% tumor nuclei staining). Twelve regional lymph nodes were resected and 2 revealed metastatic carcinoid. There was evidence of perineural and lymphatic invasion. Surgical margins were negative. He was followed with observation only.

In July 2016, the patient presented to an emergency room with abdominal pain. A CT scan showed an ileus and multifocal hepatic lesions. A CT-guided biopsy of one of the liver lesions was performed. Pathology showed fragments of liver parenchyma infiltrated by small monotonous blue cells with salt-and-pepper chromatin and minimal cytoplasm (Fig. 1). Immunohistochemical stains were again positive for pancytokeratin, chromogranin, synaptophysin, and CD56. The Ki-67 proliferative rate was low (<2% tumor nuclei staining). Based on histological features and immunohistochemistry, these findings confirmed the presence of a well-differentiated NET (G1 NET). 24-h urine 5-HIAA was elevated at 149.9 mg/24 h. He had a negative colonoscopy. A CT scan of the chest revealed no intrathoracic abnormalities concerning for metastatic involvement. He initiated therapy with everolimus; however, he stopped it about 2 months after due to tolerability issues.

In November 2016, he underwent an octreotide scan that showed increased radiotracer activity in the pelvis, liver, and right side of the heart (Fig. 2, 3). He subsequently underwent cardiac MRI that showed a 2.5-cm well-circumscribed mass along the epicardial surface in the right atrioventricular groove (Fig. 2b). Cardiac chamber size and function were normal. Estimated left ventricular ejection fraction was 53%. There was no abnormal myocardial enhancement to suggest infarct, scars, or infiltrative process.

He was evaluated by cardiothoracic surgery; however, due to the location and the extent of the operation likely requiring possible right coronary artery bypass grafting in addition to the presence of metastatic disease, surgery was not recommended.

He restarted everolimus; however, quickly after initiating it he continued to have a worsening performance status with malnutrition and failure to thrive and elected to enroll into hospice.

Discussion

In a Surveillance Epidemiology and End Results Program (SEER) database report of over 11,000 carcinoid cases, the vast majority were located in the gastrointestinal tract (55%) and the bronchopulmonary system (30%) [9]. Although carcinoid tumors have been described in almost every organ, only few cases of metastatic carcinoid tumor spreading to the heart have been reported.

Carcinoid heart disease, on the other hand, is a separate but recognized cardiac complication in patients with advanced NET and carcinoid syndrome that involves deposition of plaques on the endocardial surface of the valves or subvalvular apparatus causing valvular heart disease. It is believed to be mediated by the vasoactive substances secreted by the tumor (serotonin, prostaglandins, histamine, bradykinin, etc.) [10, 11]. However, cases of metastatic carcinoid masses to the heart are sparse.

A Mayo Clinic series published in 2002 highlighted a total of 11 patients who were found to have carcinoid tumors to the heart. Of these 11 patients, 5 patients had metastatic carcinoid tumors identified at autopsy. Surgical removal was accomplished in 5 out of 6 patients. All patients had symptomatic carcinoid syndrome as well, confirmed by increased levels of urinary 5-HIAA. On pathologic review, all the metastases were intramyocardial (40% in the right ventricle, 53% in the left ventricle, and 7% in the left ventricular septum). The average size was 1.8 ± 1.2 cm. Systolic ejection fraction was preserved in all patients. Survival from the diagnosis of metastatic carcinoid tumor was 6.3 ± 5 years [12]. In our particular patient's case, it involved the epicardium (Fig. 2).

Concluding Remarks

Metastatic spread of NET to the heart is a very rare complication. With better treatment and imaging modalities being readily available (e.g., Gallium Dotatate Scan, now approved specifically for NET patients), these rare sites of metastases will increasingly get recognized. Patients should be evaluated and treated in centers specializing in the care of NET patients.

Statement of Ethics

Written informed consent was obtained from the patient for the publication of this case report.

Disclosure Statement

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Author Contributions

We certify that all individuals listed as authors of this paper have participated in conceptualizing the research or content of the manuscript, in writing or critically editing the manuscript, and/or in analysis of data presented in the manuscript.

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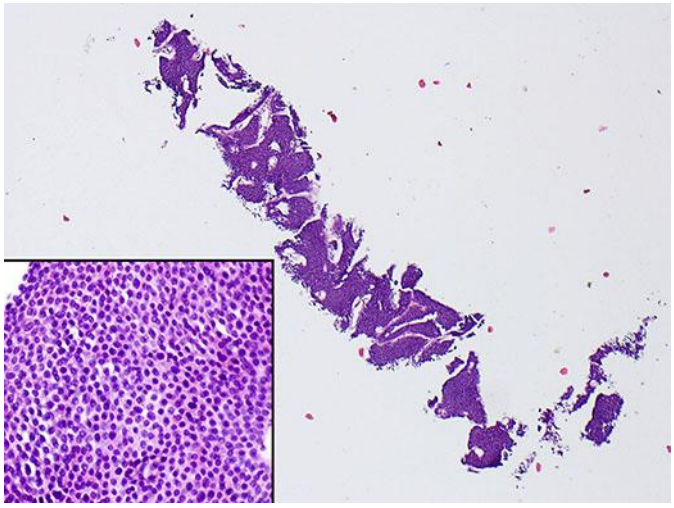

Fig. 1. Liver biopsy of well-differentiated metastatic neuroendocrine tumor (G1 NET) at low (4×) and high power (40×) (**inset**).

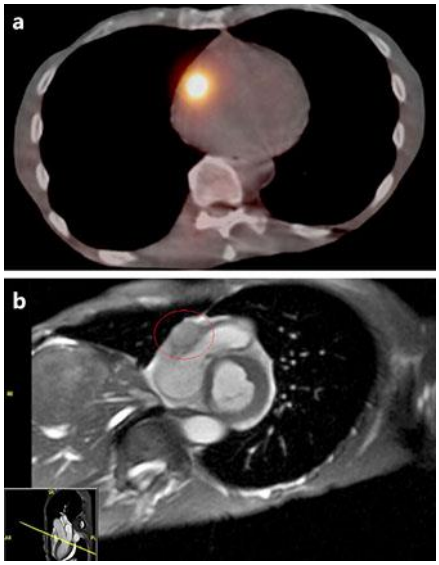

Fig. 2. **a** Octreoscan showing focal increased radiotracer activity in the right lower mediastinum, which correlates with an enhancing mass along the epicardial surface in the right atrioventricular groove. **b** Cardiac MRI showing an abnormal 2.5-cm well-circumscribed rapidly enhancing mass along the epicardial surface in the right atrioventricular groove, consistent with metastatic carcinoid.

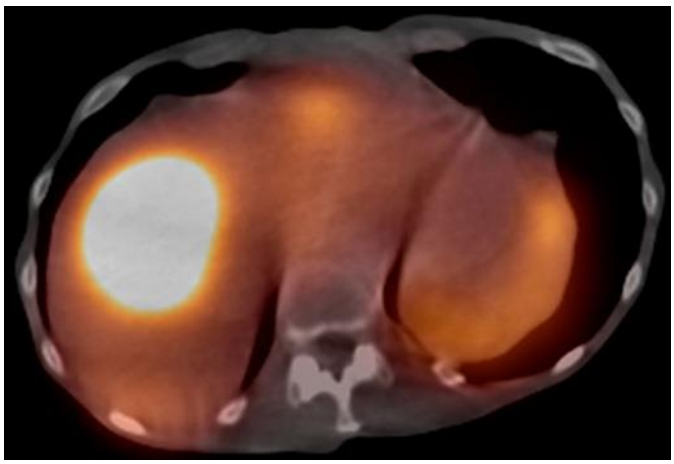

Fig. 3. Octreoscan showing increased radiotracer activity within the liver that correlates with multiple hepatic metastatic carcinoid.