

Right Heart Failure as “Sole” Presentation of Carcinoid Syndrome

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Abstract Carcinoid tumors are rare neuroendocrine tumors that arise from neural crest amine precursor uptake decarboxylation cells. Most of carcinoid tumors originate in the midgut. The vasoactive secretory products of carcinoid tumor upon metastasis to liver reach systemic circulation as they bypass the metabolism by liver. 50% of patients with carcinoid syndrome eventually develop carcinoid heart disease. We here present a rare case of carcinoid tumor with metastasis to liver that solely presented with right heart failure. The patient did not have any symptoms of typical carcinoid syndrome features such as flushing, diarrhea, and bronchoconstriction.

Keywords: carcinoid syndrome, right heart failure, atypical presentation

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1. Introduction

Carcinoid tumors are rare neuroendocrine tumors that arise from neural crest amine precursor uptake decarboxylation cells. Carcinoid tumors mostly originate in the gastrointestinal tract, and less frequently from bronchus and gonads. Metastasis of gastrointestinal carcinoid to liver results in carcinoid syndrome by secreting a variety of bioactive secretory products including serotonin. These bioactive secretory products are usually inactivated by the liver. Bioactive secretory products from hepatic metastasis bypass this inactivation, reach the systemic circulation and cause typical carcinoid syndrome features such as flushing, diarrhea, and bronchoconstriction [1]. 50% of patients with carcinoid syndrome eventually develop carcinoid heart disease [2]. Till date, only three cases of carcinoid syndrome that solely presented as right heart failure has been reported [3,4]. We here present a case of a case of carcinoid syndrome in a 61 year-old-female that presently solely with right heart failure. The patient had no other reported carcinoid syndrome features and presented with right heart failure symptoms only.

2. Case Presentation

61-year-old postmenopausal female with past medical history of uterine fibroid and hypertension, presented with a four-week history of progressive abdominal distention,

bilateral lower extremity swelling, and exertional dyspnea. Exertional dyspnea was associated with orthopnea, paroxysmal nocturnal dyspnea, yellowish discoloration of the eyes and vague abdominal discomfort. She did not have a history of hepatitis or alcoholism. On physical examination, she was afebrile, blood pressure of 190/109 mmHg, HR 104 bpm, respiratory rate 20. She had scleral icterus, abdominal distension, and bilateral pitting grade II lower extremity edema. Lung auscultation revealed bilateral posterior-basal rales, and a holosystolic murmur was heard in the tricuspid area.

Laboratory investigations revealed elevated total bilirubin (1.2 mg/dl), elevated direct bilirubin (0.6 mg/dl), serum albumin ascites gradient of 2.2. Chest radiography showed cardiomegaly with small pericardial and pleural effusion. Electrocardiography revealed low voltage QRS complexes. Ultrasonography of abdomen revealed ascites, enlarged liver with multiple heterogeneous and echogenic lesions consistent with hepatic metastases. These findings were further confirmed by computed tomography of the abdomen that also revealed an irregularly shaped mesenteric mass of 4.4 x 4 x 3.4 cm, with no enlarged periaortic, iliac or inguinal lymph nodes (Figure 1 and Figure 2). Echocardiography (Figure 3) showed tricuspid valvular disease consistent with the carcinoid tumor, severe tricuspid regurgitation, right atrial dilation and right ventricular dilatation with a left ventricular ejection fraction of 58%, patent foramen ovale. Urinary 24 hour 5-hydroxyindoleacetic acid (5-HIAA) (75 mg/24 hours, normal <6mg/24 hours) and serum chromogranin-A levels (5400 ng/ml, normal 1.0-15 ng/ml) were significantly elevated. On liver biopsy, nests and cords of tumor cells

with pleomorphic hyperchromatic nuclei and eosinophilic granular cytoplasm were noted (Figure 4 and Figure 5). On immunohistochemical staining, all the tumor markers were negative with the exception of synaptophysin, chromogranin, CD56, CDX2, MOC-31, monoclonal CEA and uroplakin (Figure 6). Based on histology and the immunohistochemical staining, the diagnosis was

consistent with metastatic neuroendocrine carcinoma with a Ki 67 of 30%. Diffuse positivity of CDX-2 stain was suggestive of a neuroendocrine tumor from gastrointestinal tract possibly pancreatic or hepatobiliary origin. The patient was treated with octreotide and everolimus. She subsequently passed away following cardiac arrest.

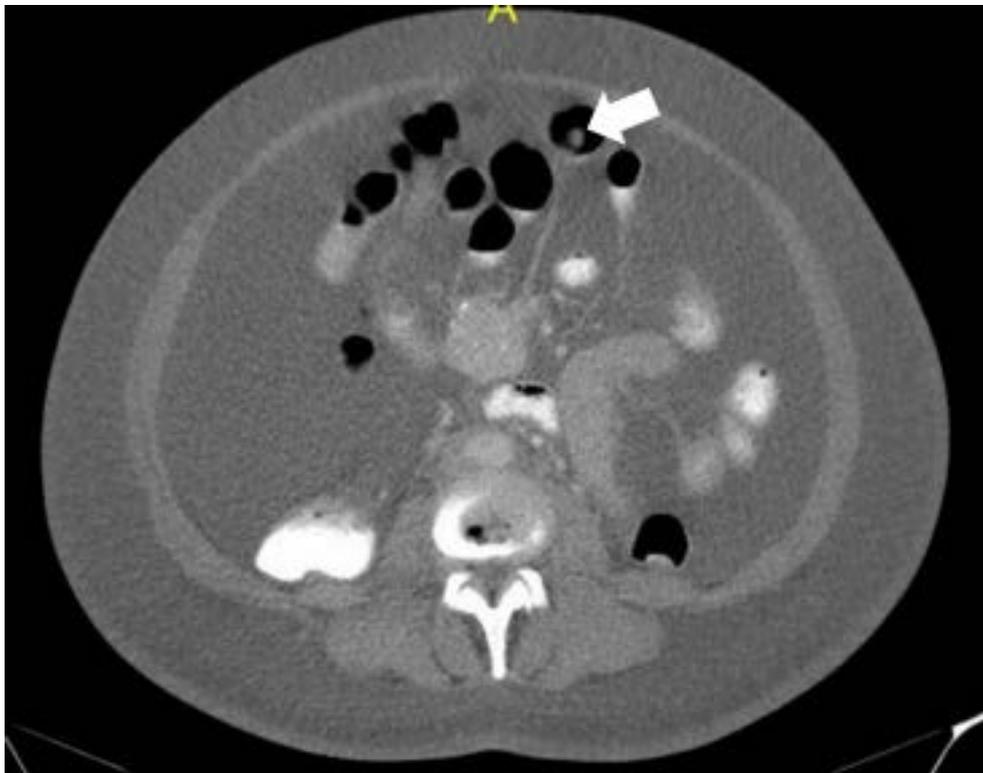


Figure 1. Computed tomography of the abdomen, white arrow indicating carcinoid tumor in midgut



Figure 2. Computed tomography of the abdomen, multiple metastases in liver and ascites can be appreciated.

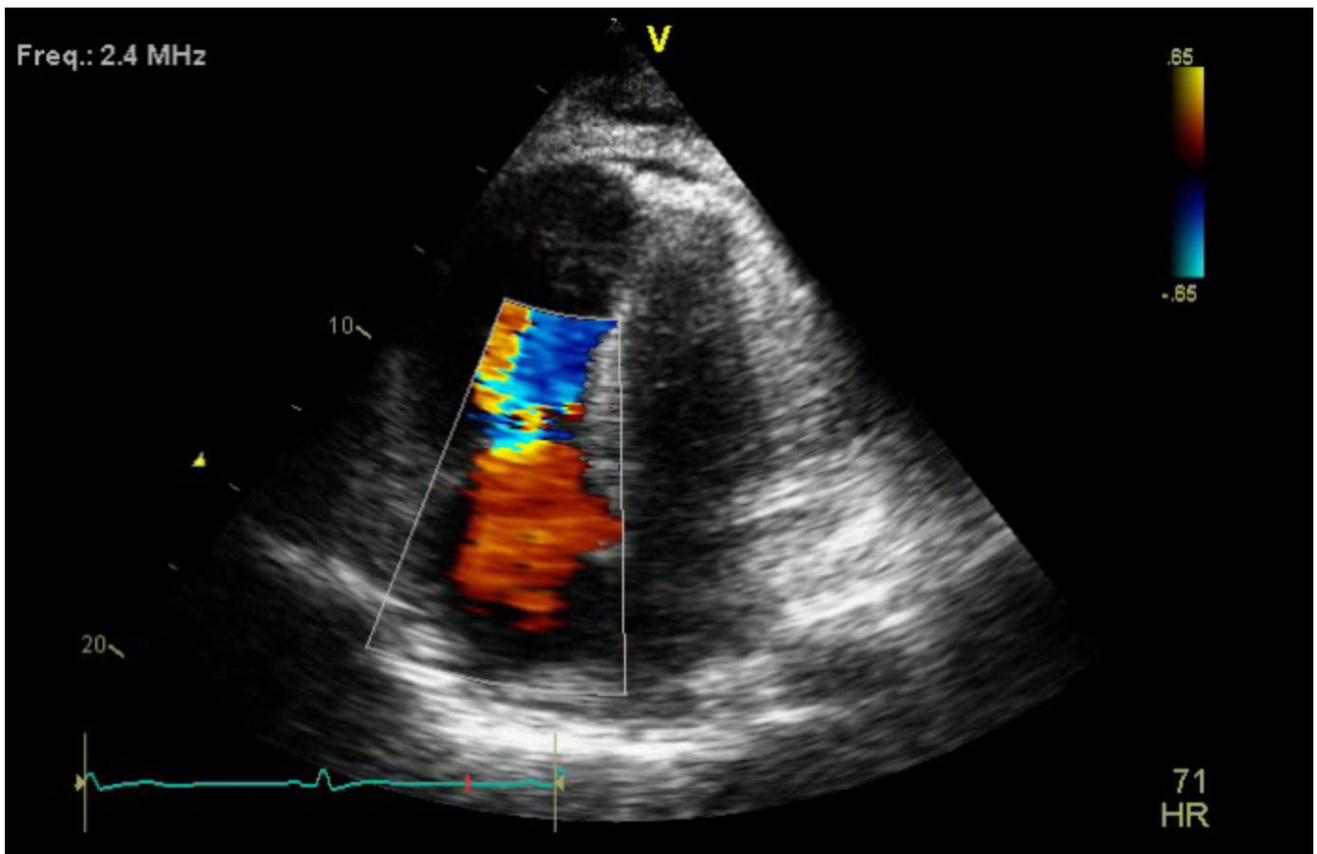


Figure 3. Transthoracic echocardiogram showing tricuspid flow reversal during right ventricular systole consistent with tricuspid regurgitation. Also right atrial and right ventricular dilation may be noted

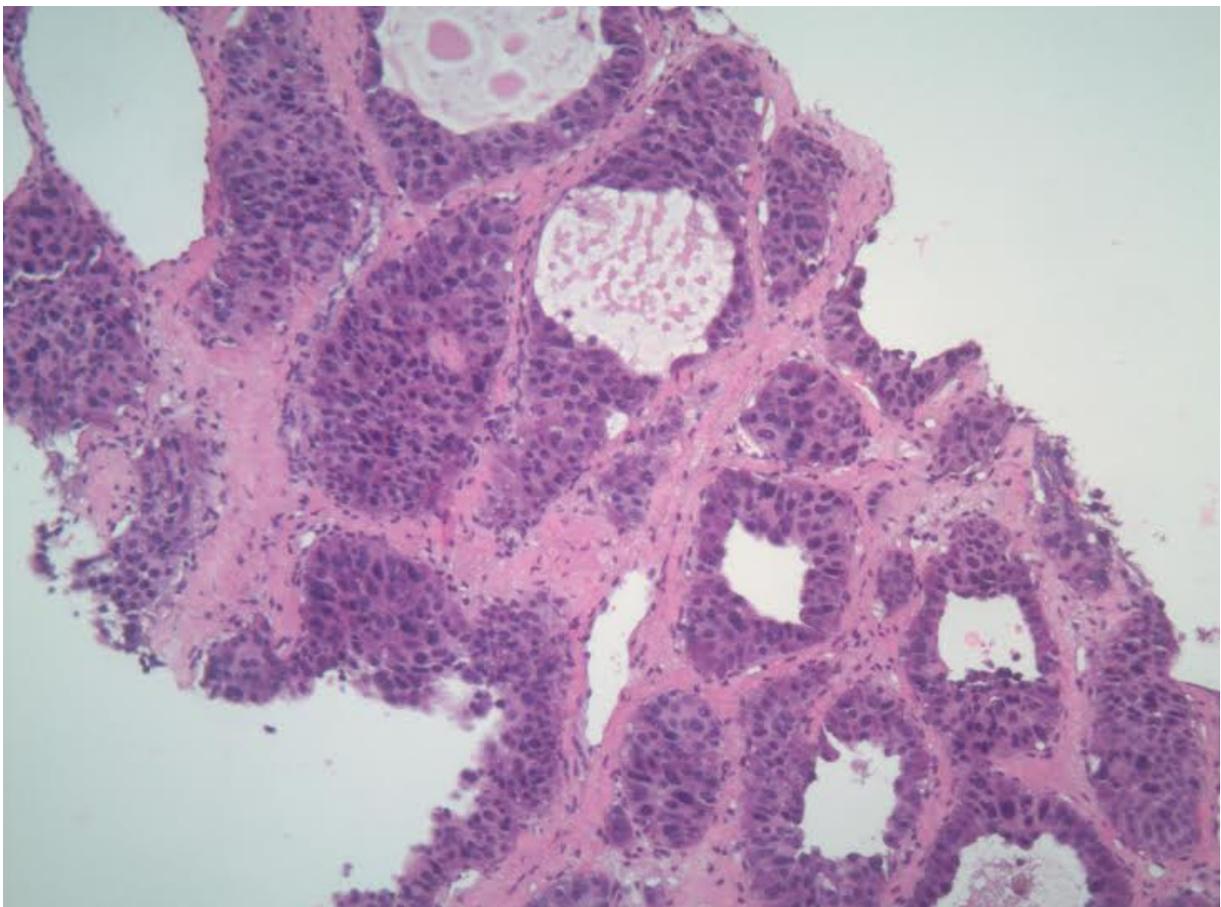


Figure 4. Hematoxylin-eosin staining (low magnification) of biopsy specimen of carcinoid liver metastases. Small round carcinoid cells nests are appreciable. Note that carcinoid cells have small round nuclei and pale blue cytoplasm

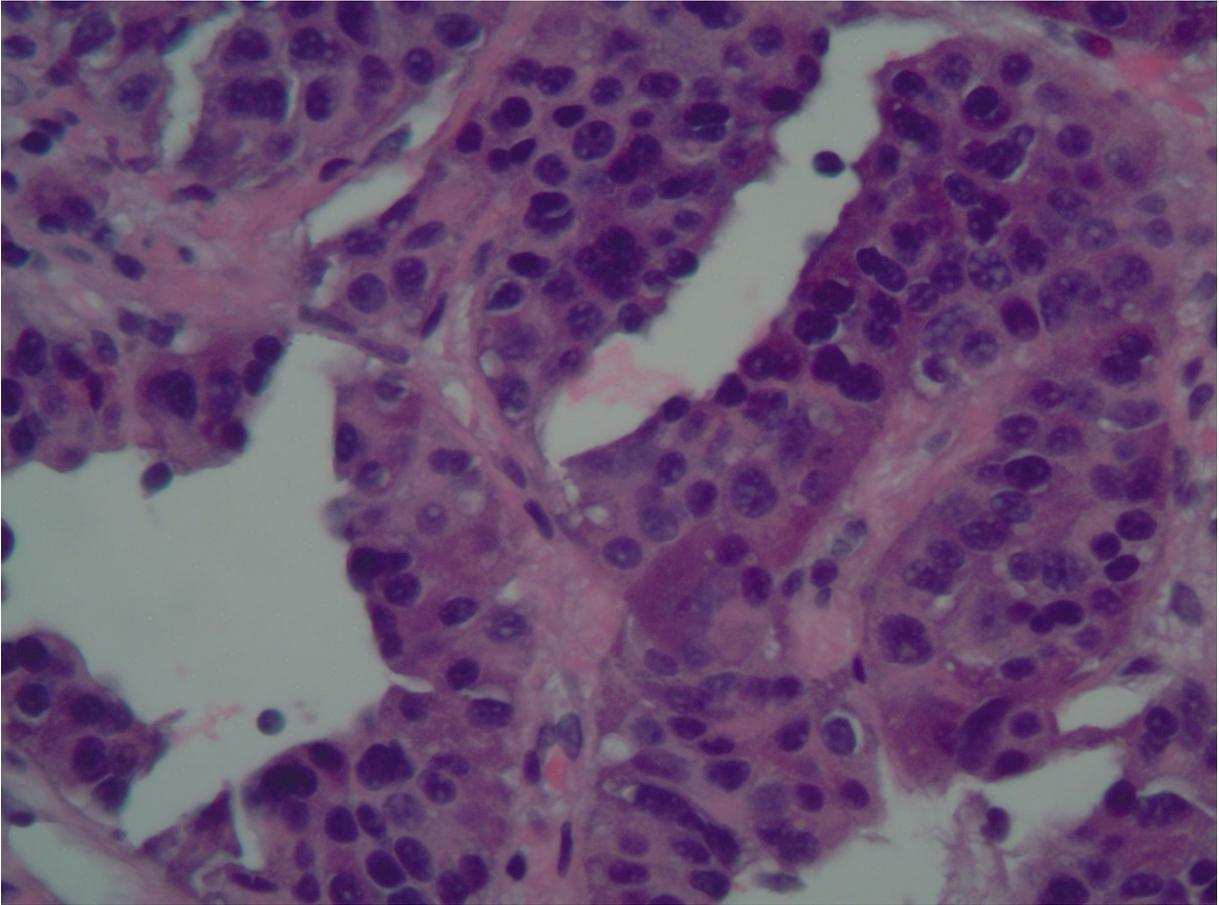


Figure 5. Hematoxylin-eosin staining (high magnification) of biopsy specimen of carcinoid liver metastases. Small round carcinoid cells nests are appreciable. Note that carcinoid cells have small round nuclei and pale blue cytoplasm with marked atypia

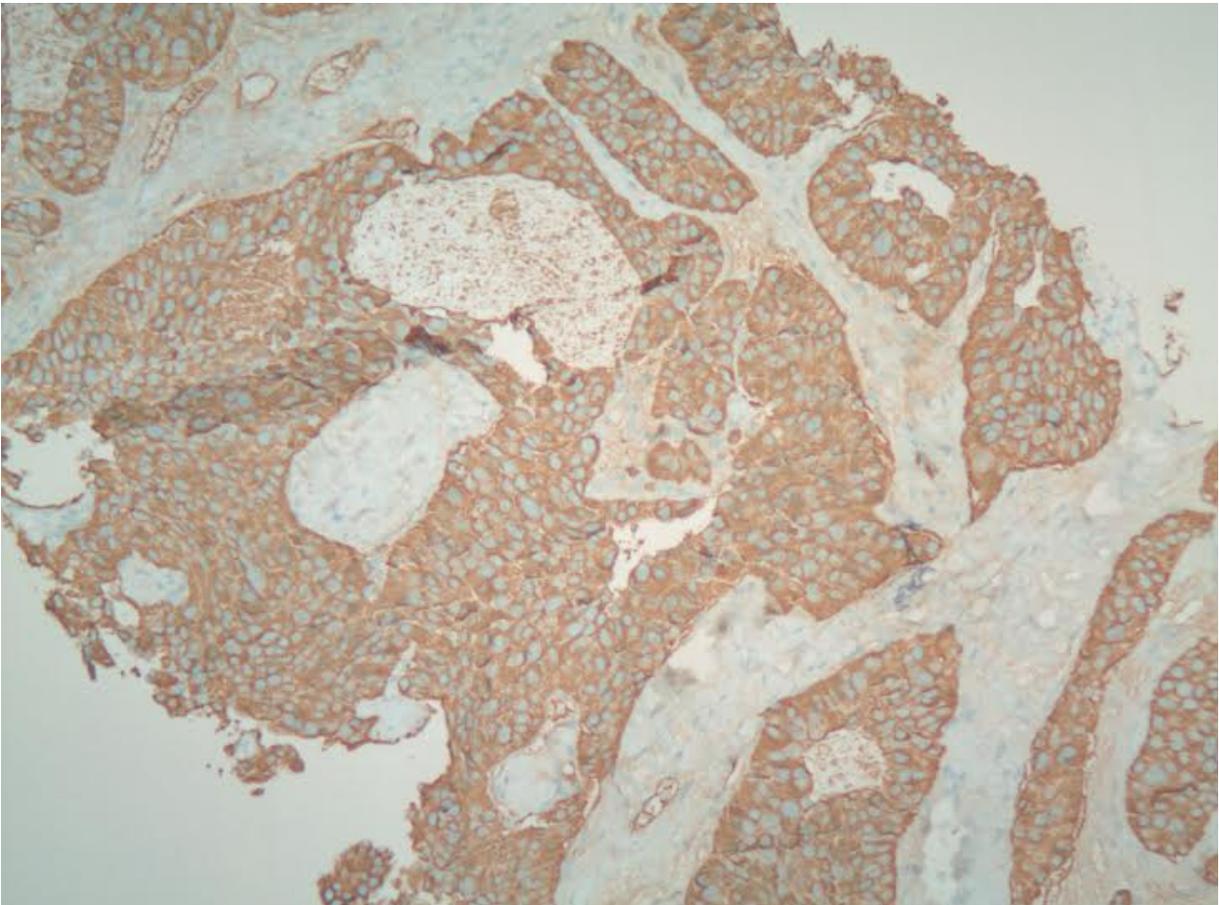


Figure 6. Chromogranin staining of biopsy specimen of carcinoid liver metastases (low magnification)

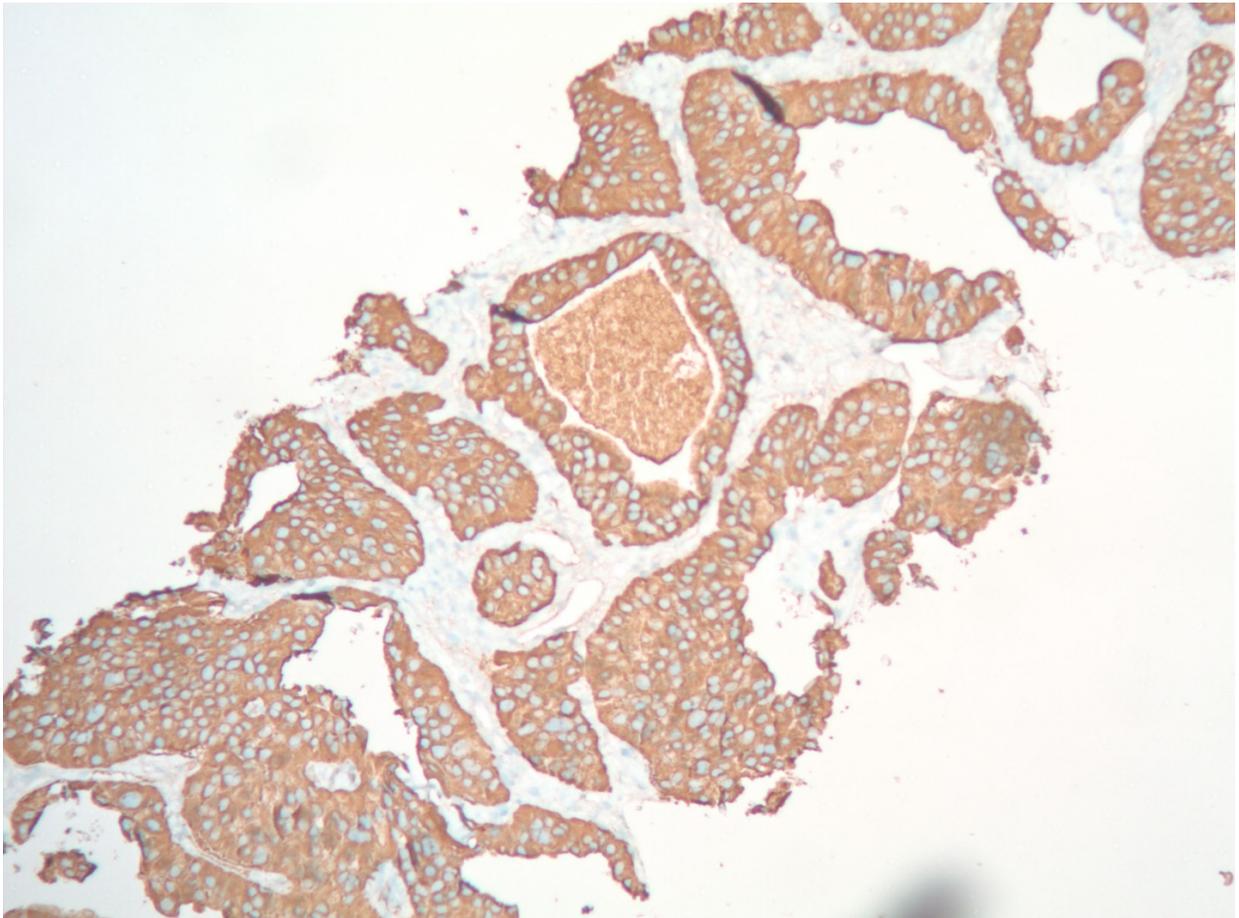


Figure 7. Chromogranin staining of biopsy specimen of carcinoid liver metastases (high magnification)

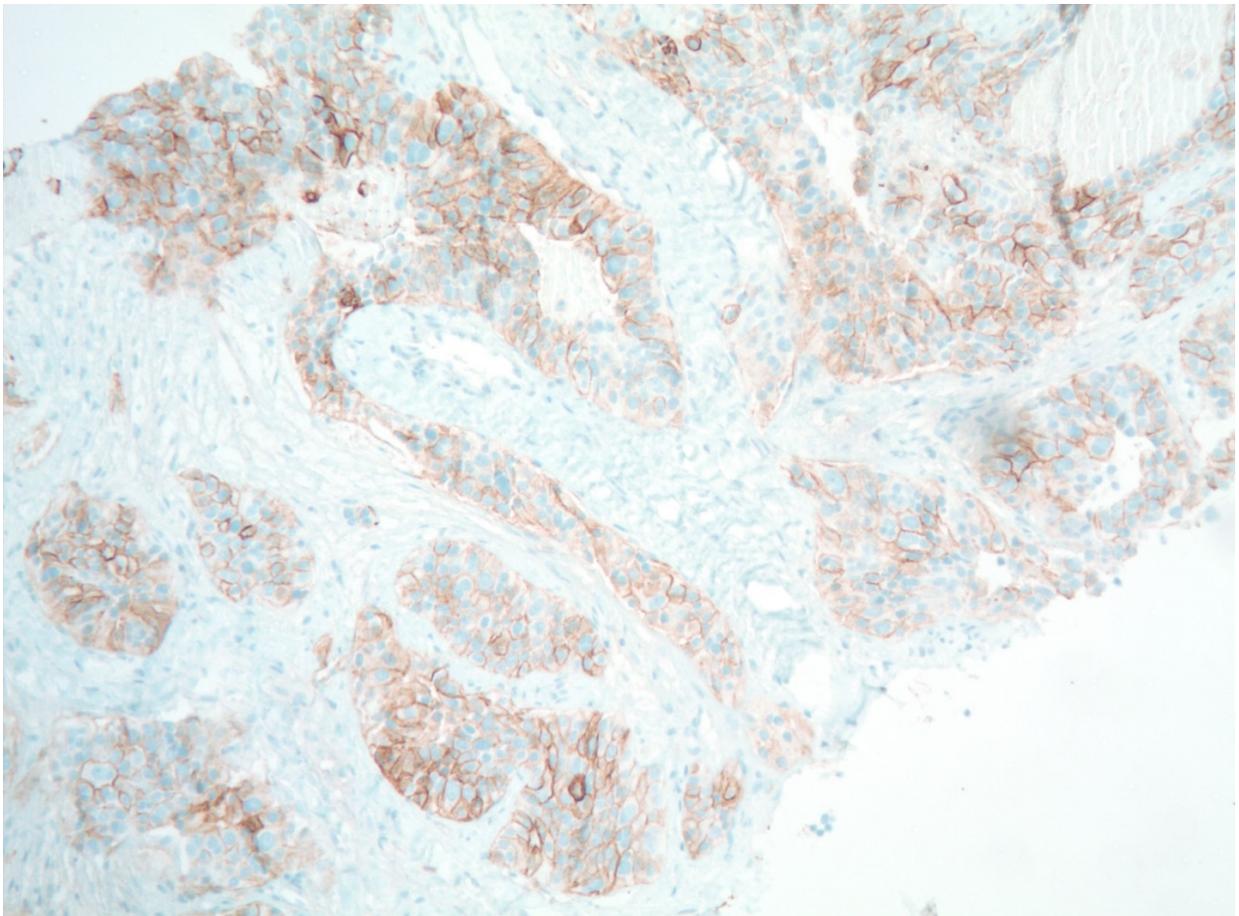


Figure 8. CD 56 immunohistochemical staining of biopsy specimen of carcinoid liver metastases (high magnification)

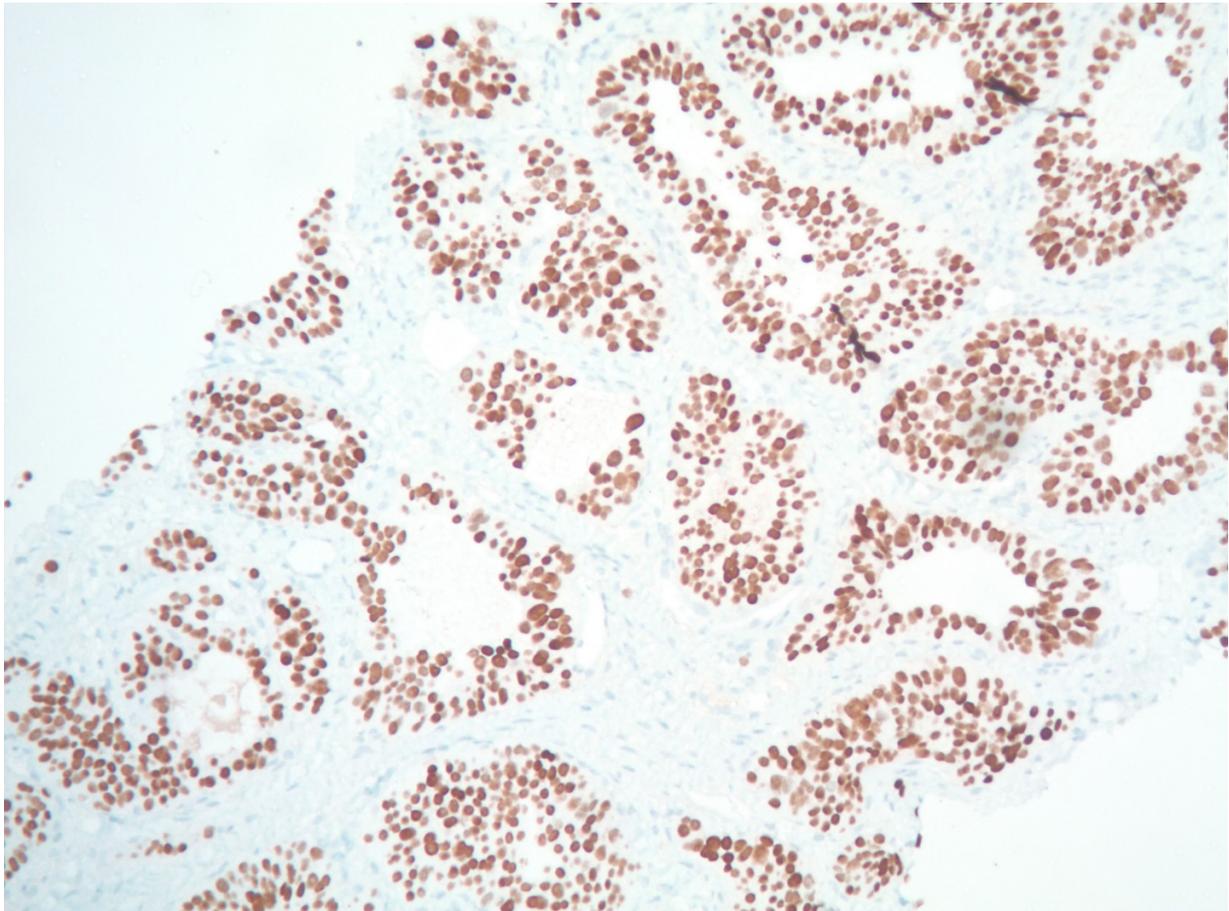


Figure 9. CDX2 immunohistochemical staining of biopsy specimen of carcinoid liver metastases (low magnification)

3. Discussion

Carcinoid tumors are rare neuroendocrine tumors that arise from neural crest amine precursor uptake decarboxylation cells [1]. Gastrointestinal tract, mostly ileum and the appendix of midgut are the commonest site where carcinoid tumors originate. The bioactive substances secreted by gastrointestinal carcinoid tumors are degraded in the liver. However, upon metastasis of midgut gastrointestinal carcinoid tumors into the liver, the bioactive substances escape the degradation in the liver thus causing carcinoid syndrome which is characterized by clinical features like flushing, diarrhea, and bronchoconstriction [1]. Carcinoid heart disease is seen in 50% of the patients with carcinoid heart disease [2]. Carcinoid heart disease is a result of the paraneoplastic effect of bioactive substances secreted from the carcinoid tumor/ tumor metastasis. Such bioactive substances secreted by carcinoid include serotonin (5-hydroxytryptamine), histamine, tachykinins, and prostaglandins [2].

Bioactive substance-induced endocardial fibrous plaque formation is the characteristic pathological finding. Endocardial fibrosis is typically seen in inferior vena cava, right heart chambers, tricuspid valve and pulmonary valve. Left heart involvement is noted in association with patent ductus arteriosus, extensive liver metastasis or bronchial carcinoid. The preferential right heart involvement is most likely related to inactivation of the vasoactive substances by the lungs. Endocardial fibrosis affects valve leaflets, tendinous chords and papillary muscles of valves resulting in valvular regurgitation, stenosis or both [5,6,7]. Till date, only three cases of carcinoid syndrome that

solely presented with right heart failure has been reported [3,4]; to the best of our knowledge the case presented here is the fourth such case.

4. Conclusion

Right heart failure due to right heart valvular fibrosis happens in 50% of the patients with carcinoid syndrome. Carcinoid syndrome rarely presents solely with right heart failure. The reasons for such atypical presentation is yet to be understood.

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