CASE REPORTS

Well-Differentiated Neuroendocrine Tumor—A Low b-Grade Tumor's Aggressive Course and Dismal Outcome: A Case Report

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ABSTRACT

Introduction: Incidence of well-differentiated neuroendocrine tumors (NETs) of the colon and rectum is increasing and is now approximately 1 per 100,000 in the US. NETs are either well-differentiated (indolent) or poorly differentiated (aggressive). The majority of these tumors are found incidentally during screening colonoscopies and rarely are associated with symptoms of hormonal syndrome, even during the advanced stage. Metastatic well-differentiated NETs of the colon and rectum are incurable, hard to treat, and associated with a poor prognosis and survival rates similar to colorectal adenocarcinoma survival.

Case Presentation: A 56-year-old man presented to our clinic with right-sided weakness and a 40-pound weight loss during the previous 2 months. A neurologic examination was remarkable for atrophy of the right trapezius muscle and decreased strength in the right upper extremity. Imaging revealed extensive blastic and lytic lesions involving the axial skeleton, a large rectal mass, a large necrotic nodal mass extending from the left iliac region to the level of the left renal veins, and multiple necrotic liver metastasis. Liver lesion fine-needle aspiration findings were consistent with metastatic well-differentiated neuroendocrine carcinoma.

Discussion: This case illustrates how a low-grade tumor can have an aggressive course with poor outcomes. Metastatic well-differentiated NETs of the colon and rectum remain difficult to treat because evidence is scarce. More research is needed on this topic.

INTRODUCTION

Well-differentiated neuroendocrine tumors (NETs) of the colon and rectum, also known as hindgut carcinoids, are increasingly diagnosed in the US, with an annual incidence of 1 per 100,000.^{1,2} Most of these tumors are found incidentally during screening colonoscopies. Approximately 50% of patients are asymptomatic, but rectal bleeding, pain, and change in bowel habits may occur for some.³ These tumors rarely cause symptoms of hormonal syndromes such as flushing or diarrhea, even during the metastatic stage.³ The mean age at diagnosis is 56 years.² In general, NETs are divided into well-differentiated (indolent) and poorly differentiated (aggressive) categories. Well-differentiated (low- and intermediate-grade) NETs also are known as carcinoid tumors or

grades 1 and 2 neuroendocrine tumors, respectively.² Prognosis for early-stage, well-differentiated NETs of the colon and rectum is good, with 5-year overall survival of 88%. Once metastasized, however, these tumors are associated with a poor prognosis similar to prognosis for metastatic colorectal adenocarcinoma, with a 5-year survival rate of 32%.²

CASE PRESENTATION

A 56-year-old man with an unremarkable medical history arrived at the Emergency Department with right-sided weakness and an inability to hold objects in his right hand. He also had lost 40 pounds during the previous 2 months. On examination, his cranial nerves were intact and a motor examination was remarkable for atrophy of the right trapezius

Figure 1. Two magnetic resonance images of the cervical spine reveals skeletal lesions: A, sagittal image; B, magnified sagittal image of the same region showing lesions.

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Figure 2. An octreoscan illustrates multiple areas of uptake in the liver and a large rectal mass: A, anatomical image in transverse section; B, fusion image in transverse section; C, fusion image in coronal section.

muscle. Strength was 4/5 in the right upper extremity with decreased muscle tone. Reflexes were 2/4 throughout, and the bilateral Hoffmann sign and bilateral pectoral reflex were absent. A sensory examination was remarkable for decreased pinprick in the right C6-C8 territory. Normal gait and the Romberg sign were not present. The rest of his neurologic examination was unremarkable. Brain magnetic resonance imaging findings were negative for intracranial pathology but revealed lesions in the cervical spine. A cervical spine magnetic resonance image revealed both blastic and lytic lesions involving the skeletal structures but not the spinal cord (Figure 1A and B). A computed tomography (CT) scan of the chest, abdomen, and pelvis with contrast revealed mixed blastic and lytic lesions involving the axial skeleton, a large rectal mass, a large (9-cm) necrotic nodal mass extending from the left iliac regions to the level of the left renal veins, and multiple

liver metastasis including a large necrotic mass involving the entire right lobe of the liver that measured 17 x 12 x 13.9 cm. An octreoscan showed increased radiotracer uptake, indicating a rich somatostatin receptor tumor (Figure 2 A-C). Prostate-specific antigen, carcinoembryonic antigen, and alpha-fetoprotein tumor marker findings were negative. Fine-needle aspiration (FNA) of a liver lesion was consistent with metastatic well-differentiated neuroendocrine carcinoma (Cam 5.2 marker, positive [strong and diffuse]; synaptophysin marker, positive [strong and diffuse]; CD56 marker, positive [strong and diffuse]; Figure 3A-C). We obtained another FNA of the large necrotic nodal mass in the left flank, and final pathology was consistent with well-differentiated neuroendocrine carcinoma most likely originating from the rectum. The patient was started on octreotide injections as an outpatient, but he continued to experience disease progression and developed

difficulty with urinating and defecating. A repeat CT of the chest, abdomen, and pelvis confirmed disease progression. The patient ultimately required a laparoscopic diverting loop sigmoid colostomy to help him defecate. He subsequently was admitted to hospice care and died. The case timeline appears in Figure 4.

DISCUSSION

Lack of relevant data makes it a challenge to treat metastatic well-differentiated colorectal NETs.⁴ Current treatment options are extrapolated from the treatment regimen for midgut NETs; these options include somatostatin analogs, interferon alpha, hepatic arterial embolization, and surgical cytoreduction.⁴ Chemotherapy is not effective for this disease, and no data support its use for rectal NETs. These colorectal NETs are not associated with carcinoid syndrome; nevertheless, octreotide injections are used for its growth inhibitory effect.^{5,6}

Figure 3. Liver biopsy images: A, 200x magnification; B, 400x magnification; C, positive synaptophysin stain (showing neuroendocrine differentiation).

Figure 4. Event timeline from initial presentation to death.

CT = computed tomography; FNA = fine-needle aspiration.

Octreotide injections should be strongly considered, especially if there is evidence of somatostatin receptor expression by increased radiotracer uptake on octreoscan.⁴ Interferon alpha may be considered when metastatic colorectal NETs progress during octreotide injection treatment; however, the side effect profile is a major issue. Cytoreductive therapy, particularly with liver-only metastasis, can improve quality of life for patients with NETs.⁴ ❖

Disclosure Statement

The author(s) have no conflicts of interest to disclose.

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