ACS Case Reviews in Surgery
Vol. 1, No. 6

Non-Functional Paraganglioma Masquerading as Local Nodal Recurrence in Postresection Colon Adenocarcinoma Patient

AUTHORS:
Leah Winer, MD; Sarah M. Kling, MD; Anthony J. Prestipino, MD; James P. Casey, MD; Pankhuri Jha, BS; Ernest L. Rosato, MD, FACS; Scott D. Goldstein, MD, FACS, ASCRS

CORRESPONDENCE AUTHOR:
Dr. Scott D. Goldstein
Department of Surgery
Division of Colon and Rectal Surgery
Thomas Jefferson University
1100 Walnut Street
Suite 500
Philadelphia, PA 19107
(215) 570-1464
scott.goldstein@jefferson.edu

AUTHOR AFFILIATIONS:
Thomas Jefferson University
Sidney Kimmel Medical College
Philadelphia, PA 19107

Background	A 64-year-old woman presented nine months after a right hemicolectomy for stage II colon adenocarcinoma with findings concerning for metastatic disease or local nodal recurrence on surveillance imaging. The patient's surveillance imaging began with a CT scan. After the CT scan at nine months was abnormal, the patient was worked-up with an MRI, PET-CT scan and colonoscopy. Preoperative and postoperative CEA levels were always normal, ranging from less than 0.5 to 1.2 ng/mL.
Summary	This rare case reports on a patient with presumed local nodal recurrence of colon adenocarcinoma found on routine nine-month postoperative surveillance imaging that turned out to be a non-functional paraganglioma. Non-functional paragangliomas are often asymptomatic. Most non-functional paragangliomas are found incidentally or due to mass effect, but are otherwise asymptomatic because they do not secrete catecholamines. CT imaging is 90 percent sensitive for identifying paragangliomas; however, our patient's tumor went undetected as such and was treated as a metastasis of her colon adenocarcinoma. This patient's CT scan revealed a new 8mm lesion in the right inferior liver, suggesting metastasis. Follow up PET-CT scan did not detect a hepatic lesion, but it did identify a hypermetabolic focus concerning for an enlarged peripancreatic lymph node near the superior mesenteric vein. The patient underwent an exploratory laparotomy with enucleation of the mass, which was later pathologically identified as a paraganglioma with low malignant potential. Treating a paraganglioma without knowledge increases the risk of morbidity and mortality from surgical intervention. Manipulation of the paraganglioma can cause release of catecholamines, even in non-functional tumors; it can additionally cause hemodynamic instability much like a pheochromocytoma. Patients with paragangliomas would benefit from alpha- and beta-adrenergic blockade for intraoperative protection from a catecholamine surge. Radiologic surveillance in patients with colorectal cancer is critical to identify metastases, recurrence, or new primary tumors.
Conclusion	Identifying asymptomatic paragangliomas preoperatively proves to be challenging and holds potential harmful implications to patients if undiagnosed prior to surgery. Non-functional paragangliomas are often asymptomatic and found incidentally. If operated on unknowingly, without appropriate alpha and beta-blockade, massive amounts of catecholamines may be released upon surgical manipulation of the tumor, leading to hemodynamic instability and possibly death.

Keywords	Paraganglioma; non-functional paraganglioma; colon adenocarcinoma; surveillance imaging; local nodal recurrence

DISCLOSURE:
The authors have no conflicts of interest to disclose.

To Cite: Winer L, Kling SM, Prestipino AJ, Casey JP, Jha P, Rosato EL, Goldstein SD. Non-Functional Paraganglioma Masquerading as Local Nodal Recurrence in Postresection Colon Adenocarcinoma Patient. *ACS Case Reviews in Surgery.* 2018;1(6):14-17.

Case Description

Colon adenocarcinoma is the third most common cancer in the United States. Locally invasive tumors without nodal or metastatic involvement can be surgically removed with curative intent. To optimize postoperative survival, patients require five years of radiographic, colonoscopic, and carcinoembryonic antigen (CEA) marker surveillance for the early detection of metastases or new primary tumors. Here, we discuss a unique case of a patient with a retroperitoneal paraganglioma discovered incidentally nine months after resection of her stage II colon adenocarcinoma.

A 64-year-old African American woman with a history of hypertension, osteoarthritis, and asthma presented to an outside hospital in early July 2013 with several months of abdominal pain, dyspnea and fatigue, and a hemoglobin of 5.5 g/dL. Her blood pressure was well-controlled on lisinopril-hydrochlorothiazide 20–25mg. On colonoscopy, there was an ulcerated, fungating, and malignant-appearing mass with no evidence of abdominal wall involvement that partially obstructed the proximal ascending colon, preventing scope traversal. Biopsy revealed adenocarcinoma, and CT confirmed a right-sided colonic mass and associated mesenteric lymphadenopathy without distant metastasis or evidence of abdominal wall involvement. In anticipation of surgery, the patient transferred care to Thomas Jefferson University Hospital. At this time, the patient's preoperative CEA level was 0.6 ng/mL.

On July 29, 2013, the patient underwent a laparoscopic-to-open right hemicolectomy; the case was converted because of tumor bulk and invasion into the posterior abdominal wall. Final surgical pathology was consistent with a 6 cm, moderately differentiated, stage T4b cecal adenocarcinoma. All margins and 25 lymph nodes were negative, and the patient was discharged to home on postoperative day 4. Microsatellite instability (MSI) testing of the tumor specimen was negative. In September 2013, the patient's first postoperative CT scan showed neither mass nor recurrence, and her post-resection CEA was less than 0.5 ng/mL.

In October 2013, the patient began adjuvant 5-fluorouracil, oxaliplatin and leucovorin (FOLFOX) therapy. Just after the patient's twelfth and final cycle in March 2014, a surveillance CT scan detected a new 8 mm lesion in the right inferior liver suggesting metastasis; this finding, however, was inconsistent with her low CEA of 1.2 ng/mL. Neither a follow-up MRI nor positron emission tomography (PET)-CT scan with ^{18}F-FDG in April 2014 detected the hepatic lesion. No liver biopsy was performed. However, the MRI and PET-CT did identify a hypermetabolic focus of 4.12 SUV concerning for an enlarged peripancreatic lymph node near the superior mesenteric vein (Figure 1).

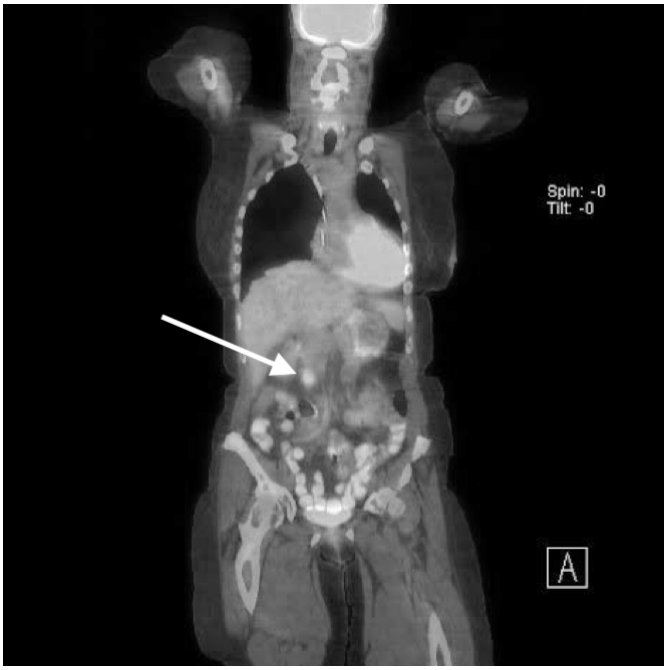

Figure 1. PET-CT imaging with 18F-FDG displaying a hypermetabolic focus. This suggests an enlarged lymph node adjacent to the superior mesenteric vein and inferior to the splenoportal confluence abutting the pancreatic head. The focus demonstrates a maximum SUV of 4.12. The 8 mm right inferior hepatic lesion seen on a previous CT scan is below the resolution of the PET-CT.

Throughout this workup, the patient remained asymptomatic with a benign abdominal examination, and surveillance colonoscopy found no concerning pathology.

In June 2014, the patient underwent an exploratory laparotomy for possible removal of any metastatic foci of her primary cancer. Inspection of the root of the mesentery revealed an encapsulated, red-hued mass distinct from the pancreatic parenchyma that appeared to arise from the lower border of the pancreatic head on the inferior aspect of the inferior mesenteric vein. The mass was enucleated circumferentially, measuring 2.3 x 1.8 x 1.5 cm. Frozen-section immunostaining and histology were consistent with a diagnosis of paraganglioma with low malignant potential (Figure 2). Her intraoperative blood pressure remained stable throughout. A white nodule seen on the peritoneum was biopsied and was negative for malignancy.

A piece of the omentum excised during the procedure was found to be an inflammatory nodule with no evidence of malignancy. All subsequent CT scans and tumor marker levels returned as normal.

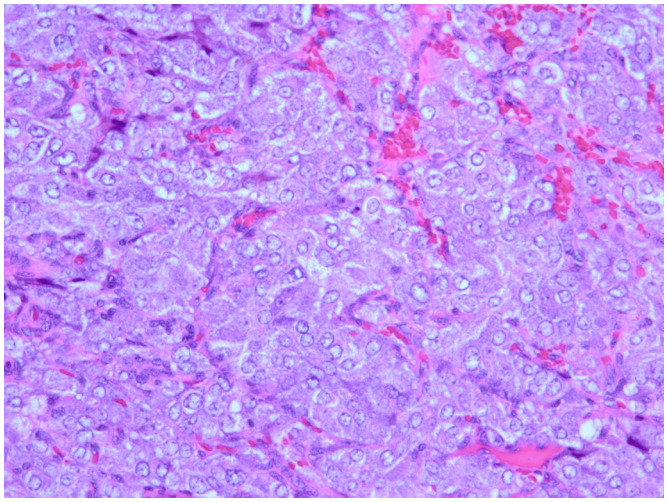

Figure 2. Hematoxylin and eosin stained section at 400x magnitude showing a richly vascular tumor comprised of fairly uniform alveolar groups of neoplastic cells ("zellballen") characteristic of paraganglioma. Consistent with paraganglioma, this section also stained strongly positive for neuroendocrine markers chromogranin A and synaptophysin; immunostain for S100 protein was also positive. Stains for pancytokeratin and AE1/AE3 melan A were negative. Focally, the tumor demonstrated extension through the thin capsule without obvious mitotic figures or tumor necrosis.

Discussion

Paraganglia are small, extra-adrenal organs comprised primarily of chromaffin cells—specialized neuroendocrine cells of embryonic neural crest origin—and are classified as either sympathetic or parasympathetic based on their anatomic distribution. Sympathetic paraganglia are found symmetrically along the paravertebral axis, from the superior cervical ganglion to the bladder, whereas parasympathetic ganglia are localized to the skull base and neck.[1]

Paragangliomas are richly vascular, encapsulated neuroendocrine tumors that can develop from paraganglia wherever they are distributed, most commonly in the head and neck. They are closely related to pheochromocytomas, chromaffin cell tumors of the adrenal gland, and represent 10 percent to 18 percent of all chromaffin-tissue tumors.[1] Paragangliomas are rare—their estimated incidence is 1 in 300,000 and are equally distributed among men and women.[2] Depending on their biochemical activity, paragangliomas are categorized as either functional or non-functional. Functional paragangliomas comprise 30 to 60 percent of the tumors and are so-named because they produce and secrete catecholamines, which cause paroxysms of hypertension, palpitations, tremors, headache and diaphoresis.[3] Non-functional paragangliomas lack this activity and are physiologically silent. They usually come to physician attention through genetic screening, complaints related to mass effect on head and neck structures or incidental discovery on CT or MRI. In one series, only 20 percent of patients with benign paragangliomas had documented catecholamine hypersecretion; the majority presented secondary to mass effect or incidental imaging findings.[1,4] Although most paragangliomas are benign, surgical resection is recommended to prevent metastasis, which occurs in 20 to 42 percent of cases.[3] Radiation is a viable alternative for poor surgical candidates.[1,4]

As illustrated by our case, preoperative planning and surgical management are challenging in asymptomatic patients with incidental abdominal masses. Despite CT imaging, which is 90 percent sensitive for paragangliomas and the modality of choice for localization, our patient's tumor was undetectable.[3] PET imaging also failed to elucidate the correct preoperative diagnosis, and accordingly, the mass was treated as a metastasis. The diagnosis became clear only after complete pathologic evaluation. In fact, 27 percent of patients with benign, incidental thoracic or abdominal paragangliomas require pathologic examination of resected specimens for definitive diagnosis as preoperative imaging and gross intraoperative inspection are insufficient.[4] Patients who undergo resection of undiagnosed paragangliomas are at increased risk for morbidity and mortality because surgical manipulation of even non-functional tumors can cause transient release of catecholamines and hemodynamic instability. Thus, whenever a paraganglioma is suspected, patients should receive alpha- and beta-adrenergic blockade as protection from intraoperative catecholamine hypersecretion.

To the best of our knowledge, this is the first case of colon adenocarcinoma and a sporadic, non-functional paraganglioma presenting within one year of each other. The coincidence of paragangliomas and solid organ tumors is not itself uncommon because 10 to 50 percent of paragangliomas are hereditary, manifesting alongside other neoplasms in autosomal dominant diseases such as neurofibromatosis type 1, von Hippel-Lindau disease, Carney triad, and multiple endocrine neoplasia type 2.[1] However patients with these syndromes typically present with functional paragangliomas, and colon adenocarcinoma is rarely involved. Given our patient's presentation and lack of family history, her tumors were deemed unrelated and genetic screening was deferred.

Conclusion

PET-CT imaging identified a hypermetabolic mass in the superior abdomen of a patient nine months after her right hemicolectomy for colon adenocarcinoma. Given her lack of symptoms and the suspicion that this lesion was related to her colon cancer, the patient underwent an exploratory laparotomy less than three months later with enucleation of what turned out to be a non-functional, retroperitoneal paraganglioma. This unique case highlights both the challenges involved in the diagnosis of asymptomatic chromaffin-tissue tumors and the importance of radiologic surveillance in patients with colorectal cancer.

Lessons Learned

Asymptomatic paragangliomas can masquerade as metastases or local recurrence in patients with previously resected malignancies. This case highlights the importance of surveillance imaging in these patients as well as the challenge in identifying non-functional paragangliomas preoperatively.

References

1. Young WF. Paragangliomas: Clinical Overview. *Ann N Y Acad Sci.* 2006;1073:21-29.
2. McNicol AM. Histopathology and immunohistochemistry of adrenal medullary tumors and paragangliomas. *Endocrinol Pathol.* 2006;17(4):329-336.
3. Sangster G, Do D, Previgliano C, et al. Primary Retroperitoneal Paraganglioma Simulating a Pancreatic Mass: A Case Report and Review of the Literature. *HPB Surg.* 2010;2010:645728.
4. Erickson D, Kudva YC, Ebersold MJ, Thompson GB, van Heerden JA, Young WF Jr. Benign paragangliomas: clinical presentation and treatment outcomes in 236 patients. *J Clin Endocrinol Metab.* 2001;86(11):5210-5216.