CASE REPORT

Surgical Management of Incidental Appendiceal Paraganglioma

A Rare Case Report and Review of Literature

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Abstract

We report a case of paraganglioma of the appendix in a 78-year-old male who presented with right upper quadrant pain, gallstones, and nausea. To the best of these author's knowledge, this is the one of the first cases of a pure paraganglioma of the appendix reported in the literature. The rarity of this disease makes it difficult to isolate clear predictors of malignancy. Lifelong follow up in patients with chromaffin cell tumors is mandatory. Immunohistochemical analysis is considered a crucial step in diagnosis of paraganglioma. These tumors stain positive for a wide variety of markers including synaptophysin, chromogranin, and S100, along with demonstrating a low nucleus to cytoplasm ratio. We do believe that an accurate diagnosis of paraganglioma of appendix was rendered.

INTRODUCTION

The first paraganglioma in the literature was discovered in 1956 by Masson. Few other reports have been documented. Two that were similar to our case include a 40-year-old female with appendiceal paraganglioma with malignant features and a 47-year-old male who was found to have appendiceal paraganglioma with a presentation consistent with acute appendicitis.[1,2]

Paragangliomas represent 10% of catecholamine producing tumors. The annual incidence of paraganglioma is estimated at 1/100,000. The male to female ratio is 1.8/1. The ages of presentation are 23-83; however, it is most common in the 5th decade of life. Paragangliomas are rare neuroendocrine chromaffin tumors that arise from neural crest cells. They are histologically similar to pheochromocytomas and are distinguished from pheochromocytomas by their location. Pheochromocytomas arise from the adrenal medulla wheras paragangliomas are located at extra-adrenal sites—most commonly along the sympathetic or parasympathetic chain.[3] While paragangliomas are usually nonfunctioning, some have been found to secrete catecholamines causing clinical symptoms such as sweating, hypertension, and tachycardia.[4] They range from cervical region to the pelvic region and are related to the autonomic nervous system. Multiple theories exist to explain their formation.[1-9] Some cases are reported in patients with genetic syndromes such as Von-Hippel Lindau, neurofibromatosis, multiple endocrine neoplasia, and Carneys syndrome.[5]

Because the visceral organ involvement is so rare, most of the paraganglioma literature is limited to single case studies. They are most commonly found in small bowel, rarely in gastric locations and even more limited to the appendix.[5] Abdominal pain is most common in symptomatic paragangliomas of the visceral organs; however, most are discovered incidentally.[5]

Diagnosis with CT and MRI are useful to determine features of tumor, site, number, and malignancy associated with other neoplasms such as in hereditary syndromes.
Histopathologically, paragangliomas are identified with the classic finding of Zellballen formations (uniform cells surrounded by spindle cells).

While there is still no agreed upon criteria to determine malignant potential of paragangliomas, the World Health Organization (WHO) states that the presence of metastases or tumor spread in sites were chromaffin tissue is not usually found makes it malignant. Treatment for paragangliomas is multimodal

and can include open or minimally invasive surgery, nuclear medicine, chemotherapy, radiotherapy, and biological target agents.

CASE PRESENTATION

A 78 year old Caucasian male was referred to the general surgery clinic by his primary care physician regarding right upper quadrant abdominal pain, cholelithiasis, and an appendiceal mass that was incidentally discovered on CT scan. Upon initial presentation, the patient reported that he was experiencing postprandial right upper quadrant pain. He described the pain as dull and achy in nature without radiation. He noted that the pain was associated with a decrease in appetite. He denied fever, chills, nausea, vomiting, changes in bowel habits, and changes in urination.

The patient's past medical history was significant for essential hypertension, hyperlipidemia, pituitary tumor, benign prostatic hypertrophy, hypothyroidism, and chronic osteoarthritis. All of his diseases were being managed by his primary care physician with the medications listed in Table 1.

Table 1: HOME MEDICATIONS

Medication	Dosage	Frequency
Alfluzosin	10 mg	Daily
Aspirin	81 mg	Daily
Celecoxib	200 mg	Daily
Clonazepam	0.5 mg	Daily
Fosinopril	20 mg	Daily
Levothyroxine	88 mcg	Daily
Simvastatin	20 mg	Daily
Zolpidem	10 mg	Nightly

The patient reported a distant surgical history significant for back and shoulder surgery. An evaluation of the patient's social history revealed a distant history of tobacco use, occasional alcohol consumption, and no use of illicit drugs.

Vital signs at the time of presentation, a complete review of systems and physical exam

findings are presented in Tables 2, 3 and 4, respectively.

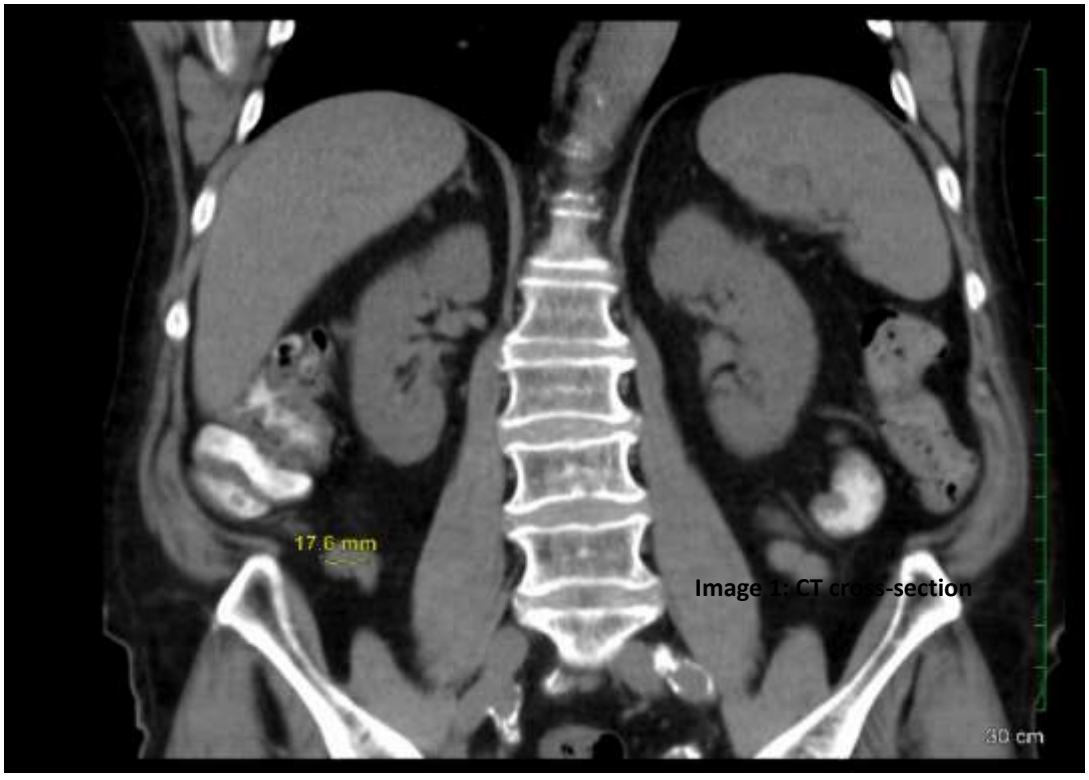
Table 2: VITAL SIGNS	
Blood pressure	141/81 mmHg
Heart rate	60 beats/min
Oxygen saturation	97% on room air
Height	193 cm
Weight	107 kg
BMI	28.73 kg/m^2

Table 3: REVIEW OF SYSTEMS	
Constitutional	Negative for fevers and chills.
HEENT	Positive for occasional headaches due to pituitary tumor. Stable vision. Stable hearing.
Respiratory	Positive for mild shortness of breath with exertion.
Cardiovascular	Negative for chest pain, palpitations, and syncope.
Gastrointestinal	Right sided abdominal pain localized to the right upper quadrant without radiation described as dull and achy. Negative for nausea, vomiting, constipation, diarrhea.
Genitourinary	Reported some difficulty with urination due to BPH.
Musculoskeletal	Reported chronic joint pain due to OA without new or worsening joint pain.

Table 4: PHYSICAL EXAM	
General	Sitting in exam room chair in no apparent distress. Well dressed, well nourished. Appears stated age. Answers questions appropriately.
Head/Neck	Normocephalic, atraumatic. Supple neck. No JVD. No thyromegaly.
Lungs	Clear to auscultation bilaterally. Unlabored work of breathing. Equal chest rise and fall.
Cardiovascular	Regular rate and regular rhythm. No murmur, rub, or gallop.
Abdomen	Soft, non-distended, non-peritoneal. Bowel sounds present in all four quadrants. Tenderness to deep palpation in the RUQ and RLQ. (+) Murphy sign. (+) McBurney point. (-) Rovsing sign.
Extremities	Full range of motion.

During the initial consultation, the CT exam findings were discussed with the patient. CT scan demonstrated a small layer of stones dependently located within the gallbladder and 1.8 cm soft tissue mass at the tip of the appendix. Image 1 depicts a section of the CT scan that demonstrates the appendiceal mass.

Image 1: CT cross-section



At the time of consultation, the patient agreed to under a laparoscopic cholecystectomy with intraoperative cholangiogram for his symptomatic cholelithiasis. He also agreed to undergo a laparoscopic appendectomy with possible right hemicolectomy.

In the operating room, a diagnostic laparoscopy was performed. It demonstrated an appendix that was curved distally with an apparent mass located at the tip. The appendix was non-edematous and non-inflamed. A laparoscopic appendectomy was performed in typical fashion. The appendiceal specimen was sent to pathology for intraoperative frozen section. There were no signs of adenocarcinoma or carcinoid tumor. The removed appendix is depicted in Images 2 and 3.

Image 2: Removed Appendix

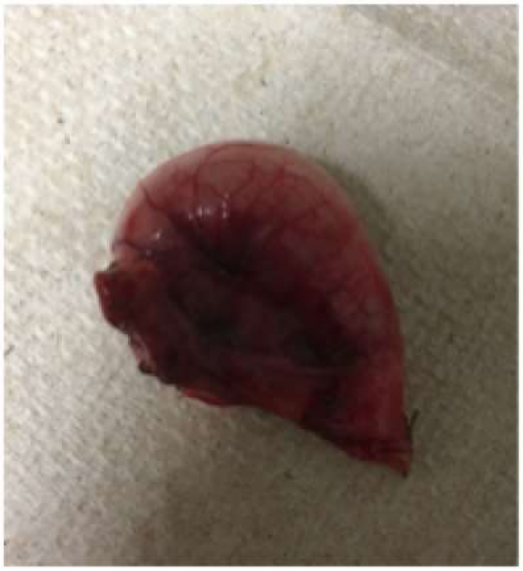
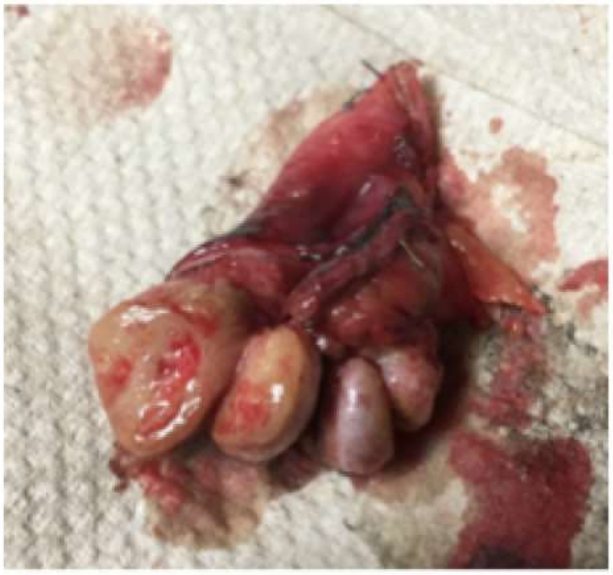


Image 3: Appendix Cross-Section



Final appendiceal pathology revealed paraganglioma with the following immunohistochemical staining.

- Positive for synaptophysin, chromogranin, and OCT-4.
- Focally positive for CK Oscar, CAM 5.2, and TCK.
- Negative for CK-7, CK-20, GATA-3, vimentin, and Glypican-3

Following his laparoscopic cholecystectomy and laparoscopic appendectomy, the patient was referred to oncology for follow up. A PET/CT scan was conducted and demonstrated nodular metabolic activity in the inferior left thyroid concerning for a possible metabolically active thyroid nodule. A follow-up thyroid ultrasound was negative. The patient underwent a total thyroidectomy and was diagnosed with a Hurthle cell tumor.

METHODS USED

Current literature related to paragangliomas was utilized. The literature was accessed via the electronic library provided by the Arizona College of Osteopathic Medicine at Midwestern University. An online search of textbooks, journal articles, and credible websites yielded additional resources and information. Priority was given to the most recent publications and to those that specifically dealt with paragangliomas. The patient's medical records were also utilized to complete the case presentation portion of this report.

DISCUSSION/CONCLUSION

The majority of reported paragangliomas of the gastrointestinal tract are found in the upper gastrointestinal tract; most commonly within the duodenum. There are two reported cases of neuroendocrine tumors of the appendix that presented as acute appendicits and were subsequently discovered to be gangliocytic paragangliomas after histopathologic examination following appendectomy[1,2] There remains a paucity of reported incidental paragangliomas of the appendix reported in the literature.

Of note, there is a single reported case of an asymptomatic incidental paraganglioma of the mesoappendix. Intially, the mass was palpated on physical exam and was origianlly thought to be of ovarian origin. Upon surgical exploration, the mass was identified within the mesoappendix. Histopathology demosntred no gangliocytic component.[10]

The patient presented in this report was initially evaluated in the surgery office regarding cholelithiasis and a suspicious mass in the tip of the appendix that was demonstrated on CT exam. Imedially following appendectomy, a longitudinal transection of the appendix was conducted that had appearance similar to carcinoid. Frozen section was unable to rule out carcinoid. At that time, an appendectomy was considered sufficient given that the mass was less than 2 centimeters in size and that it was located at the tip of the appendix. Final pathology revealed findings consistent with paraganglioma.

The majority of paragangliomas from the base of the skull to the bladder are sympathetic paragangliomas.[3] With the exception of headaches, our patient reported no symptoms typical of cathecholamine excess: hypertension, palpatations, sweating, pallor, and tachycardia. Our patient's long term headaches were attributed to a benign pituitary

tumor that had been diagnosed many years prior to our evaluation. Given the patient's presentation, we had little suspicion of a catecholemine producing paraganglioma.

If suspected of being a cathecholamine secreting paraganglioma, management preoperatively should be similar to the management of pheochromocytoma; control of hypertension by alpha blockade with secondary utilization of beta blockade for refractory hypertension. Paragangliomas, whether symptomatic or asymptomatic, should have a work up consisting of urine and plasma metanephrines. When clinical suspicion is absent prior to surgical removal, FDG-PET /CT should be done to rule out any metastatic disease.

CONFLICTS OF INTEREST

None declared.

FUNDING

None

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