A Massive Retroperitoneal Tumor – An Unusual Presentation of a Rare Primary Pancreatic Neoplasm

Devin J. Clegg

University of Tennessee at Knoxville

Ryan Hammond

University of Tennessee at Knoxville

Ryan K. Schmock

University of Tennessee at Knoxville

Ryan Sauls

University of Tennessee at Knoxville

Lisa Duncan

University of Tennessee at Knoxville

Laura M. Enomoto (✉ lenomoto@utmck.edu)

University of Tennessee at Knoxville

Case Report

Keywords: Pancreatic tumor, benign abdominal tumor, pancreatic lipoma, hamartoma

Posted Date: February 21st, 2022

DOI: <https://doi.org/10.21203/rs.3.rs-1374921/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Abstract

Background:

The differential diagnosis for retroperitoneal masses is broad, and includes pancreatic lipomatous hamartoma, a rare but benign disease process. Hamartoma describes outgrowth of tissue native to the organ in which it occurs and is considered a malformation rather than a true neoplasm. Pancreatic hamartomas consist of less than 1% of all hamartomas, and few cases of pancreatic lipomatous tumors with distinct components of pancreatic hamartoma have been described. These tumors are difficult to diagnose on imaging and biopsy alone and can appear malignant with potential for significant mass effect on surrounding organs, leading to surgical intervention for definitive diagnosis.

Case Presentation:

A 57-year-old male presented with right upper quadrant pain radiating to his left side and back. Ultrasound demonstrated cholelithiasis and an incidentally discovered large retroperitoneal mass. Computed tomography (CT) imaging demonstrated a 14.4 x 4.6 x 16 cm heterogenous, fatty-appearing retroperitoneal mass displacing the colon and small bowel, while abutting the aorta and inferior vena cava (IVC) with no obvious invasion of surrounding structures. He underwent laparoscopic cholecystectomy with biopsy of the mass. Biopsy demonstrated benign adipose tissue and no evidence of malignancy, and his care was transferred to our facility. His postoperative course was complicated by acute congestive heart failure that ultimately delayed definitive surgical intervention for nine months. Progressive growth of the mass was noted on serial imaging as his cardiopulmonary status was optimized. Preoperative CT revealed a 20.2 x 28.2 x 14.1 cm with worsened mass effect on surrounding structures.

The patient underwent open resection of the retroperitoneal mass with en bloc resection of the third and fourth portions of the duodenum and the uncinate process of the pancreas. The final pathologic diagnosis was benign lipomatous proliferation with features most consistent with pancreatic lipomatous hamartoma (PLH), with specimen weight of 3810g and overall dimensions of 35 x 27 x 14 cm.

Conclusions:

PLH is an extremely rare benign tumor, which is notoriously difficult to diagnose with imaging and biopsy alone. This case highlights the difficulty delineating benign from malignant tumors of the pancreas and retroperitoneum.

Background

Pancreatic lipomatous hamartoma (PLH) is an incredibly rare, benign disease process that has been rarely described in the current literature. The term hamartoma refers to the focal outgrowth of cells and tissues native to the organ in which it occurs, and is considered a malformation rather than a true

neoplasm (1). Pancreatic hamartomas account for less than 1% of all hamartomas and 10% of primary mesenchymal tumors of the pancreas (1–3). Pancreatic masses consisting of lipomatous contents include lipoma, liposarcoma, lipomatous pseudohypertrophy, and other fat-containing neoplasms such as perivascular epithelioid cell tumor and malignant neoplasm with lipoid degeneration.

Very few cases of pancreatic lipomatous tumors with distinct components of pancreatic hamartoma have been described. Reports have suggested radiographic and pathologic features that are suggestive of both pancreatic hamartomas and pancreatic lipomatous hamartomas, such as no dilatation of the main pancreatic duct, well-defined slight hyperintensity or iso-intensity on T2 weighted imaging, and iso-intensity on diffuse weighted imaging, with obvious progressive enhancement (2, 4). Despite this, these tumors are notoriously difficult to diagnose on imaging and biopsy alone, as they can often appear similar to retroperitoneal liposarcomas and other benign or malignant tumors.

Case Presentation

A 57-year-old male presented to an outside facility with right upper quadrant pain that radiated to his left side and back. Right upper quadrant ultrasound demonstrated gallbladder wall thickening, cholelithiasis, and a large retroperitoneal mass. Magnetic resonance cholangiopancreatography (MRCP) was performed that again demonstrated gallbladder wall thickening with cholelithiasis and a large fatty mass of the right retroperitoneum (Figure 1). He underwent laparoscopic cholecystectomy with intraoperative cholangiogram and biopsy of the retroperitoneal mass. Biopsy demonstrated benign adipose tissue with no evidence of malignancy. His postoperative course was complicated by a bile leak requiring multiple percutaneous drainage procedures. During the management of the bile leak, he developed atrial fibrillation with rapid ventricular response requiring cardioversion, with the subsequent development of anasarca and acute congestive heart failure. Computed tomography (CT) of the abdomen and pelvis demonstrated a 14.4 x 4.6 x 16 cm heterogenous, fatty appearing retroperitoneal mass displacing the colon and small bowel, while abutting the aorta and inferior vena cava (IVC) with no obvious invasion of surrounding structures (Figure 2). The patient was then referred to our center for further management of the retroperitoneal mass.

The patient is a non-smoker, with previous medical history significant only for hypertension. Family history was significant for ovarian cancer in a daughter, but no other reported malignancies. His abdominal exam demonstrated well-healed port site scars, right upper quadrant percutaneous drain, without a clearly palpable abdominal mass given body habitus. Given the concern for a retroperitoneal sarcoma, he underwent staging CT thorax which demonstrated no evidence of metastasis. He required multiple readmissions for heart failure exacerbations and ultimately underwent left heart catheterization which demonstrated mild irregularities. The left ventricular ejection fraction was 25% with global hypokinesia and a personal wearable defibrillator and implantable cardioverter defibrillator (ICD) was recommended. It was recommended that any surgical intervention was delayed by at least 90 days until his cardiac function could improve. He sought a second opinion and ultimately the personal wearable defibrillator was removed, and he continued to demonstrate improvement.

Repeat CT of the abdomen and pelvis was performed seven months after initial presentation, demonstrated enlargement of the fatty retroperitoneal mass, measuring 20.2 x 28.2 x 14.1 cm (Figure 3). The lesion was causing mass-effect on the right kidney, proximal duodenum, right colon, inferior liver, IVC, and pancreas. Thin internal septations were apparent within the mass. The patient was ultimately deemed an acceptable cardiac risk for surgical intervention nine months after initial diagnosis on imaging.

The patient underwent open resection of the retroperitoneal mass. The mass abutted the common bile duct, portal vein, superior mesenteric artery and vein, aorta and IVC, was densely adherent to the uncinate process of the pancreas and encased the third and fourth portions of the duodenum. Because of these intraoperative findings, surgical extirpation was required with en bloc resection of the third and fourth portions of the duodenum and the uncinate process of the pancreas, with duodenojejunostomy (Figure 4). The intraoperative planes were obscured by adhesions related to previously placed percutaneous drains for the management of his post-cholecystectomy bile leak. Post-operatively the patient required percutaneous drain placement for a pancreatic fistula and was managed on total parenteral nutrition (TPN) and octreotide.

Tumor pathology was initially reviewed at our institution and was ultimately sent to an outside referral center for further analysis after it demonstrated pervasive pancreatic ducts and acinar cells. The specimen had a gross weight of 3810 grams with overall dimensions of 35 x 27 x 14 cm. The ultimate final pathologic diagnosis was benign lipomatous proliferation with features most consistent with pancreatic lipomatous hamartoma (PLH) (Figure 5). Histological examination demonstrated lobulated mature adipose tissue with interspersed benign pancreatic tissue between the lobules. The benign pancreatic component included pancreatic ducts and acinar tissue. Both the adipocytic and epithelial component lacked any features of malignancy, including atypia, mitotic figures, hyperchromasia, or necrosis. MDM2 (Mouse Double Minute 2 homolog) FISH (Fluorescence in situ) was performed and showed no amplification. The differential included pancreatic lipomatosis, pancreatic lipomatous hamartoma, and well-differentiated lipomatous neoplasm including lipoma and well-differentiated liposarcoma. The lack of MDM2 amplification helped to exclude well-differentiated liposarcoma, while the presence of epithelial elements argued against lipoma. Based on the size of the presenting mass, and these unique histologic findings, the tumor was most consistent with pancreatic lipomatous hamartoma.

Discussion

The literature pertaining to pancreatic lipomatous hamartoma is scarce. This disease process is poorly understood due to both its rarity, difficulty in establishing a diagnosis without surgical resection, as well as its radiographic similarity to many other retroperitoneal tumors (5, 6). Pancreatic hamartomas account for less than 1% of hamartomas from all sites, and represents only 10% of primary mesenchymal tumors of the pancreas (2). They have been described in case reports and case series, with less than ten of these reports found during literature search. Many of these reports describe smaller tumors that are found incidentally in asymptomatic patients, lesions that were resected due to concern for a malignant process

of the pancreas or retroperitoneum, or tumors in patients with vague abdominal complaints likely due to other causes. The number of recent cases being reported has increased, likely due to the advancement in imaging quality and frequency of use (4). All tumors reported in the literature were small, averaging approximately 2-4 cm in diameter, with some patients presenting with multifocal lesions (2, 4, 6–8). There is a report of a large pancreatic lipoma mimicking a well-differentiated liposarcoma, which ultimately measured 6.4 x 6.0 cm (8). These reports vary considerably from our patient described above, as the tumor ultimately had a gross weight of 3810 grams with overall dimensions of 35 x 27 x 14 cm and was rapidly growing in a symptomatic patient. However, all these patients ultimately underwent complete resection to determine if these lesions represented a malignancy as it could not be ruled out with imaging, serum markers, or biopsy alone. Extensive surgery was often required, with many patients undergoing pancreaticoduodenectomy (2–4, 6, 8).

The primary indication for surgical resection in this patient population is most often due to the inability to rule out a malignant process with imaging, laboratory analysis, and biopsy alone. The determination of pancreatic lipomatous hamartoma is made during histological analysis, which has now been more well-defined. This includes a microscopic description of small to medium-sized ductal structures, lined by columnar epithelium without atypia, surrounding by disarranged acini with various amounts of fibrous stroma (1, 2, 4). Well-formed islets of Langerhans are not common, and Pauser and colleagues have defined criteria for the diagnosis of pancreatic hamartoma as (a.) forming a well-demarcated mass, (b.) being composed of mature acini and ducts with distorted architecture, and (c.) lacking discrete islets of Langerhans (1, 9, 10). Immunohistochemically, both acinar cells and ductal cells are positive for epithelial markers, and the acinar cells are positive for exocrine markers, similar to normal pancreatic tissue. Stromal spindle cells may express CD34 and CD117, but are usually negative for S100, SMA, desmin and bcl-2, although it appears S100 positivity differs in some tumors in the adipose tissue (1, 2, 7). These are similar findings to the tumor resected in our patient, demonstrating lobulated mature adipose tissue with interspersed benign pancreatic tissue between lobules. The benign pancreatic component included pancreatic ducts and acinar tissue, with both adipocytic and epithelial component lacking any features of malignancy. Further analysis ultimately showed negative MDM2 amplification by FISH analysis, which was most consistent with PLH (Figure 5).

Diagnosis by imaging is extremely difficult due to the similarity to other lipomatous tumors, but recent case series have suggested some findings that may suggest the diagnosis of PLH after review of all reported cases. The majority of PLH are well-demarcated cystic and solid lesions, with progressive or late enhancement on contrasted CT or MRI (Magnetic Resonance Imaging). They are most often located in the head or uncinate process of the pancreas. MRI can depict the solid component as an iso-low intensity of T1 weighted image and an iso-high on T2 weighted image (3, 4). FDG-PET (Fluorodeoxyglucose Positron Emission Tomography) demonstrated uptake in approximately 20% of patients reviewed, which may lead to the misdiagnosis of the lesions as pancreatic adenocarcinoma (4). Many of these lesions remain stable over time on serial imaging, unlike the rapid growth demonstrated in our patient (4). The MRCP performed on our patient demonstrated multiple irregular nodular soft tissue densities with increased T2WI signal. Contrast CT imaging noted multiple internal septae without evidence of progressive or

late enhancement but noted increased vascularity. Due to the size of our patient's mass, there was significant mass effect on all surrounding major organs and vascular structures with difficulty discerning invasion, which differentiates this patient from other reported cases.

Consistent with the literature, our patient did not demonstrate any significant laboratory abnormalities including lipase, amylase, Carcinoembryonic Antigen (CEA), Carbohydrate Antigen 19-9 (CA 19-9) or other serum tumor markers. On core needle biopsy of the mass, it did not demonstrate any findings concerning for malignancy and was consistent with lipoma. This is also consistent with the literature and represents much of the difficulty with the diagnosis of these tumors without surgical resection. While imaging characteristics can appear benign, biopsy of lesions can lead to false-negatives due to sampling error in larger lesions. This is despite core needle biopsy being the suggested method of sampling, with reported 95% concordant diagnosis for adipocytic tumors after excision (11).

The cases reported often do not include detailed intraoperative descriptions, but those that do often reported intimate involvement with the head or uncinate process of the pancreas and surrounding structures, often necessitating a pancreaticoduodenectomy (2, 3, 6, 8, 12). This is consistent with our patient's findings, although the tumor was able to be resected with a portion of the uncinate process and duodenum without formal pancreaticoduodenectomy (Figure 4).

The management of retroperitoneal and pancreatic masses varies broadly, depending on the histological subtype and concern for malignancy. CT guided core needle biopsy is recommended if anatomically possible, or reports have suggested the use of endoscopic ultrasound (EUS)(13). Patients should undergo appropriate staging work-up with CT imaging of the chest, abdomen, and pelvis, as well as serum tumor markers such as CEA and CA 19-9. If resection is performed, a microscopically margin-negative resection is recommended, as failure to achieve this increases the risk of local recurrence. There are no formal guidelines for surveillance for resected PLH due to their rarity, and the true risk of local recurrence is unknown. Surveillance after resection of retroperitoneal or abdominal sarcomas is recommended based on histology and grading, with the majority undergoing history and physical exam every 3-6 months for 5 years with CT imaging, and then annually thereafter for at least 10 years (14), so it seems reasonable to follow large PLH with imaging for at least 5 years due to an unknown risk of local recurrence.

The management of these clinically ambiguous masses ultimately results from ongoing discussion of risks and benefits. As there is significant difficulty in determining if these lesions are truly benign or malignant without surgical resection, the decision to continue surveillance or proceed to the operating room depends on provider and patient preference, as well as suitability to undergo often extensive resection. In the case that we now present, the patient was symptomatic due to mass effect with rapid growth of the tumor over his period of preoperative medical optimization, making concern for malignancy significantly higher, and after extensive discussion, we elected to proceed with resection. Concerning features that may obviate the need for resection include tumor growth, large size, symptomatology such as biliary or intestinal obstruction, weight loss, early satiety and poor appetite, or intractable abdominal pain. Recommendation for resection is often difficult since many patients are asymptomatic with small,

incidentally found lesions, with unknown biologic behavior in the setting of potentially high morbidity operations. There is no evidence in current literature that PLH can undergo malignant transformation, and there have been no reports of rupture or bleeding resulting from these tumors (1, 3, 4, 6).

Our patient demonstrates many similarities with those previously reported, but also stands out as having a significantly larger tumor, being symptomatic due to mass effect, and demonstrating rapid growth during a short period of time. The ambiguity in the diagnosis of PLH and differentiating it from malignant tumors such as retroperitoneal liposarcoma, pancreatic carcinoma and other more common tumors, often leads to highly morbid surgical resection and postoperative diagnosis based on histology. More information is certainly needed to determine guidelines and recommendations in the surveillance and management of suspected PLH, especially with a recent increase in detection and reporting likely due to more frequent use of high-quality imaging for other purposes. This case highlights this need, as it differs significantly from those previously reported. Pancreatic lipomatous hamartoma should be included in the differential diagnosis of all retroperitoneal or pancreatic masses with unrevealing tumor markers and biopsy pathology, and with the imaging findings described, but treated with extreme caution as to not overlook the possibility of a hidden malignant process.

Abbreviations

Pancreatic lipomatous hamartoma (PLH)

Magnetic resonance cholangiopancreatography (MRCP)

Computed tomography (CT)

Inferior vena cava (IVC)

Implantable cardioverter defibrillator (ICD)

Total parenteral nutrition (TPN)

Mouse Double Minute 2 homolog (MDM2)

Fluorescence in situ (FISH)

Magnetic Resonance Imaging (MRI)

Fluorodeoxyglucose Positron Emission Tomography (FDG-PET)

Carcinoembryonic Antigen (CEA)

Carbohydrate antigen 19-9 (CA 19-9)

Endoscopic Ultrasound (EUS)

Declarations

Ethics approval and consent to participate: Not applicable.

Consent for publication: Written consent obtained.

Availability of data and materials: Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

Competing interests: The authors declare that they have no competing interests.

Funding: The authors have no funding to report.

Author's contributions: DJC contributed to the organization and writing of the manuscript, as well as patient care. RH contributed to the literature review and writing of the manuscript. RKS contributed to the writing of the manuscript, revisions and editing, as well as patient care. RS contributed to the histological examination and pathological diagnosis, as well as the creation of histological figures. LD contributed to the histological examination and pathological diagnosis, as well as the creation of histological figures. LE contributed to the writing of the manuscript, revisions and editing, as well as patient care.

Acknowledgements: We would like to acknowledge Julia R. Caudill, NP for the fantastic care she provides for our patients.

References

1. Basturk O, Askan G. Benign Tumors and Tumorlike Lesions of the Pancreas. *Surg Pathol Clin*. 2016 Dec;9(4):619–41.
2. Zhou B, Li G, Xu S, Zhan C, Zheng X, Yan S. Pancreatic lipomatous hamartoma mimicking other pancreatic tumor: a case report and literature review.:7.
3. Cui H, Lian Y, Chen F. Imaging findings for pancreatic Hamartoma: two case reports and a review of the literature. *BMC Gastroenterol*. 2020 Dec;20(1):37.
4. Katayama H, Azuma K, Koneri K, Murakami M, Hirono Y, Hatta S, et al. A typical case of resected pancreatic hamartoma: a case report and literature review on imaging and pathology. *Surg Case Rep*. 2020 Dec;6(1):107.
5. Tanaka M, Ushiku T, Ikemura M, Takazawa Y, Igari T, Shimizu M, et al. Pancreatic Lipomatous Hamartoma: A Hitherto Unrecognized Variant. *Am J Surg Pathol*. 2018 Jul;42(7):891–7.
6. Matsushita D, Kurahara H, Mataka Y, Maemura K, Higashi M, Iino S, et al. Pancreatic hamartoma: a case report and literature review. *BMC Gastroenterol*. 2016 Dec;16(1):3.
7. Yamaguchi H, Aishima S, Oda Y, Mizukami H, Tajiri T, Yamada S, et al. Distinctive Histopathologic Findings of Pancreatic Hamartomas Suggesting Their “Hamartomatous” Nature: A Study of 9 Cases. *Am J Surg Pathol*. 2013 Jul;37(7):1006–13.

8. Xiao R-Y, Yao X, Wang W-L. A huge pancreatic lipoma mimicking a well-differentiated liposarcoma: A case report and systematic literature review. *World J Clin Cases*. 2019 Aug 26;7(16):2352–9.
9. Pauser U, Kosmahl M, Krušlin B, Klimstra DS, Klöppel G. Pancreatic Solid and Cystic Hamartoma in Adults: Characterization of a New Tumorous Lesion. *Am J Surg Pathol*. 2005 Jun;29(6):797–800.
10. Pauser U, da Silva MTS, Placke J, Klimstra DS, Klöppel G. Cellular hamartoma resembling gastrointestinal stromal tumor: a solid tumor of the pancreas expressing c-kit (CD117). *Mod Pathol*. 2005 Sep;18(9):1211–6.
11. Thavikulwat AC, Wu JS, Chen X, Anderson ME, Ward A, Kung J. Image-Guided Core Needle Biopsy of Adipocytic Tumors: Diagnostic Accuracy and Concordance With Final Surgical Pathology. *Am J Roentgenol*. 2021 Apr;216(4):997–1002.
12. Shin DH, Rho SY, Hwang HK, Lee WJ, Kang CM. A case of pancreatic hamartoma pathologically confirmed after robot-assisted pancreaticoduodenectomy. *Ann Hepato-Biliary-Pancreat Surg*. 2019;23(3):286.
13. Suzuki R, Irisawa A, Hikichi T, Shibukawa G, Takagi T, Wakatsuki T, et al. Pancreatic Lipoma Diagnosed Using EUS-FNA. A Case Report. 2009;4.
14. von Mehren M, Randall RL, Benjamin RS, Boles S, Bui MM, Ganjoo KN, et al. Soft Tissue Sarcoma, Version 2.2018, NCCN Clinical Practice Guidelines in Oncology. *J Natl Compr Canc Netw*. 2018 May;16(5):536–63.

Figures

Figure 1

MRCP performed at outside facility on presentation.

Figure 2

Subsequent CT imaging during management of post-operative bile leak.

Figure 3

CT imaging for surveillance prior to surgery.

Figure 4

Surgical specimen including retroperitoneal tumor, uncinate process of the pancreas and portion of duodenum.

Figure 5

Pancreatic Lipomatous Hamartoma. (A) Cystically dilated duct with benign epithelium, stroma, and smooth muscle in background of mature adipose tissue (10X). (B) Benign pancreatic acinar tissue and fibrous stroma with mature adipose (10X). (C) Mature adipose tissue infiltrating into pancreatic tissue (4X).