

# Late Recurrence of Metastatic Pancreatic Angiomyolipoma in Tuberous Sclerosis Following Bilateral Nephrectomy and Transplant

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## ABSTRACT

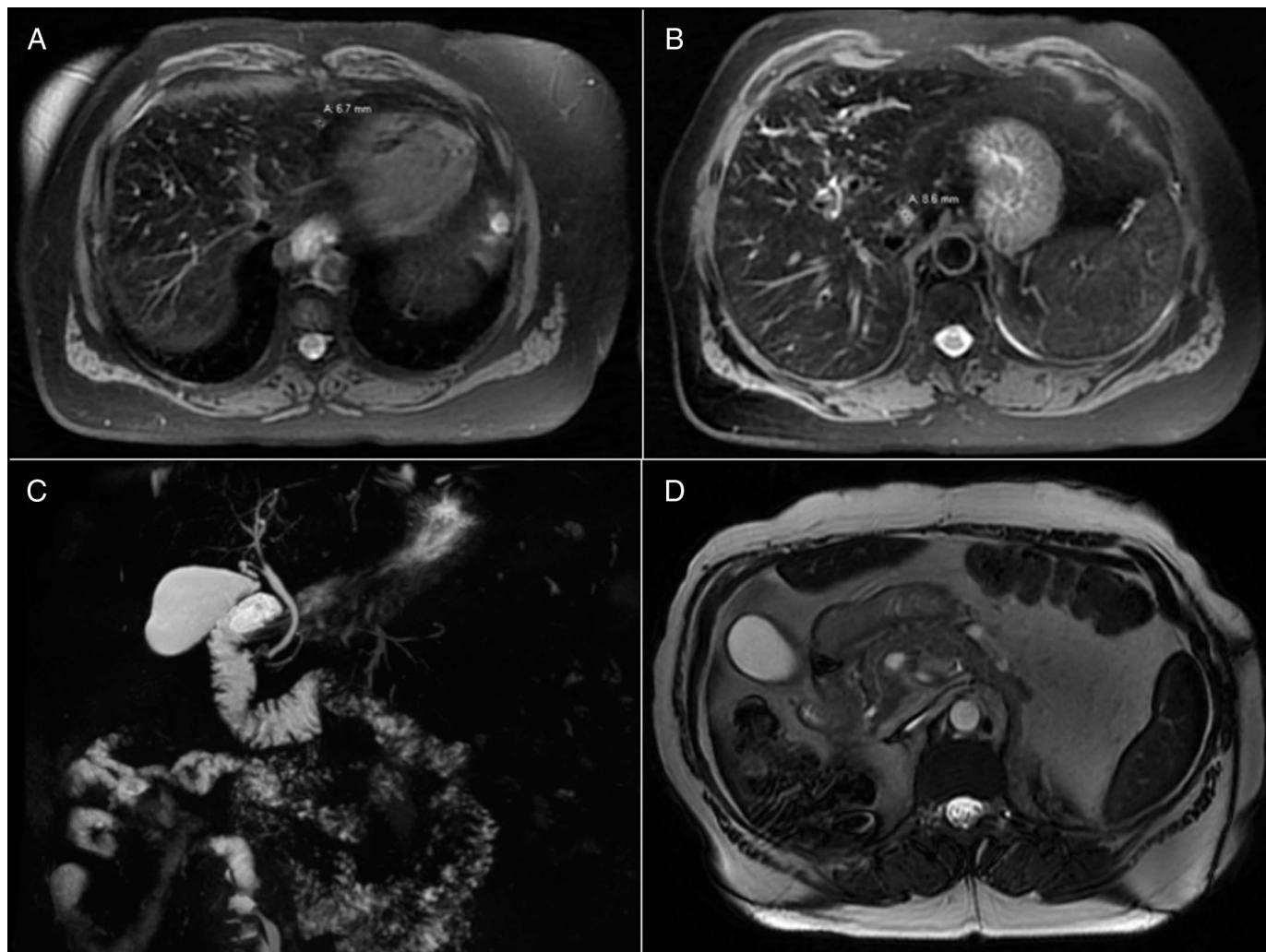
Recurrent angiomyolipomas are rare, particularly in the pancreas of patients with tuberous sclerosis (TSC). We report a 59-year-old woman with TSC who underwent bilateral nephrectomy for malignant, hemorrhagic angiomyolipomas with subsequent renal transplant. Almost 10 years after initial discovery of renal angiomyolipoma, the patient was found to have a pancreatic tail angiomyolipoma on endoscopic ultrasound performed for the evaluation of abnormal liver enzymes. The mass was not visualized on previous imaging. This case highlights the possible role of endoscopic ultrasound in continued surveillance for recurrent angiomyolipoma after nephrectomy in patients with TSC.

## INTRODUCTION

A perivascular epithelioid cell tumor (PEComa) represents a group of mesenchymal tumors with epithelioid or spindle shape cells with abundant clear cytoplasm, a central nucleus, and an inconspicuous nucleolus in a perivascular location.<sup>1</sup> Angiomyolipomas (AML) are a type of PEComa commonly associated with tuberous sclerosis (TSC), which is an autosomal dominant disease associated with mutations in the TSC1 and TSC2 genes.<sup>1,2</sup> AML is most commonly found in the kidney, followed by the liver.<sup>3</sup> These tumors have less often been described in the pancreas, the first reported case in 1996 with less than 24 reported cases to date.<sup>1,4</sup> Even more rare is the association of TSC with pancreatic angiomyolipoma. The first and only case of a pancreatic AML in a patient with TSC was reported by Hartley et al in 2016. The pancreatic mass was identified on radiographic surveillance for bilateral renal AML in a 31-year-old woman, but the diagnosis was made after surgical resection following a failed endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA). The genetic analysis determined the association of the pancreatic mass with a deletion in TSC2, solidifying the association with TSC.<sup>5</sup> We report a unique case of a patient with TSC with bilateral nephrectomy secondary to renal AML and subsequent renal transplant with an incidental finding of pancreatic AML diagnosed by EUS-FNA.

## CASE REPORT

Our patient is a 59-year-old woman with clinical diagnosis of TSC. In 2008, the patient was found to have bilateral renal angiomyolipoma during an emergency department visit for nausea and vomiting. During that admission, she underwent a total right renal nephrectomy secondary to refractory bleeding. In 2014, a total left nephrectomy was performed secondary to worsening renal failure with appropriate medical management while awaiting renal transplant. After years on dialysis, the patient received a deceased donor renal transplant in 2017. During a routine transplant clinic visit, she was found to have mildly elevated liver enzymes with aspartate transaminase 63 U/L, alanine transaminase 73 U/L, alkaline phosphatase 130 U/L, and total bilirubin 1.1 mg/dL. Liver ultrasound showed multiple echogenic liver lesions representing hemangiomas and magnetic resonance imaging (MRI) with contrast-confirmed small nonspecific mildly hyperintense lesions in the caudate and lateral segments of left hepatic lobe representing hemangiomas vs regenerative nodules (Figure 1).



**Figure 1.** Magnetic resonance imaging showing (A) a 6.7-mm liver lesion, (B) 8.6-mm liver lesion, (C) biliary tree, and (D) pancreas.

The patient was then referred to gastroenterology for EUS-guided liver biopsy (EUS-LB) to evaluate for hemangioma or hemosiderosis and rule out biliary obstruction. EUS showed a normal non-dilated common bile duct without evidence of obstruction. EUS-LB was performed using a 19 G core biopsy needle to rule out parenchymal disease. Incidentally, she was found to have a pancreatic tail mass which measured 13 mm in diameter, not visualized on her previous ultrasound or MRI (Figure 2). EUS-FNA was performed on the pancreatic tail mass with a 25 G needle. The LB showed mild iron overload and minimal macrovesicular steatosis. The cytology from the pancreatic lesion was reported as an angiomyolipoma (Figure 3). The patient was subsequently referred to a surgical oncology for the evaluation of distal pancreatectomy. The family and patient decided not to pursue pancreatectomy unless symptomatic or enlarging and has been placed on surveillance imaging.

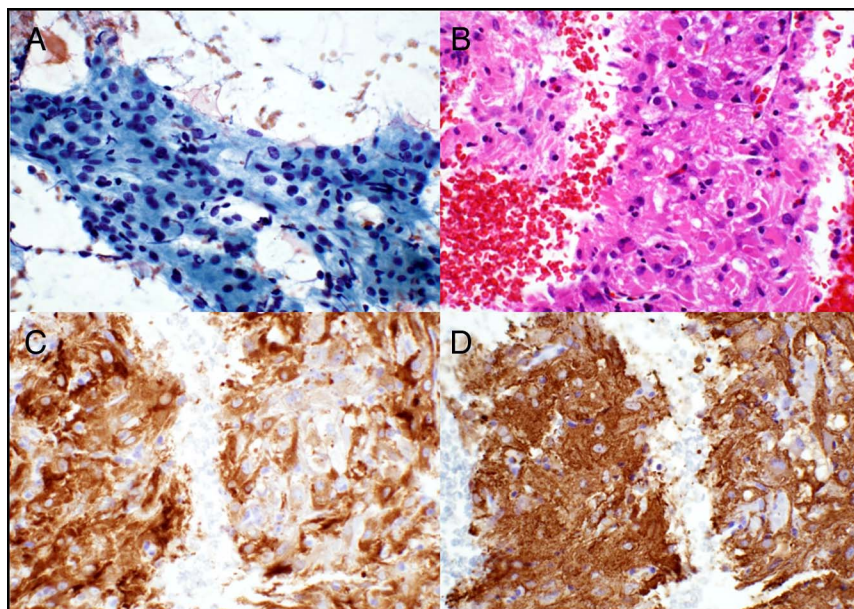
## DISCUSSION

Pancreatic PEComas or AMLs are tumors with an epithelioid appearance in a nest or sheet pattern with eosinophilic granular

cytoplasm, round to oval nucleus with a prominent nucleolus. They are predominantly reported in women between ages 17 and 74. These tumors have most often been reported in the pancreatic head, and only 12.5% (3/24 cases) have been reported in the tail. Clinically, patients with AML present with nonspecific signs and symptoms dependent on size, location,



**Figure 2.** Endoscopic ultrasound image of the pancreatic tail mass.



**Figure 3.** Histopathological slides of pancreatic tail mass consistent with angiomyolipoma (A) HMB-45 stain, (B) hematoxylin-eosin stain, (C) MART-1 stain, and (D) smooth muscle actin stain.

and spread. In a review of the literature of pancreatic PEComa by Zizzo et al, the most common presenting symptom associated with pancreatic PEComa is abdominal pain (60.9%, 14/23).

Interestingly, the second most common clinical presentation (21.7%, 5/23) is asymptomatic with incidental diagnosis after imaging for different clinical reasons, as was the case in our patient.<sup>1</sup> Similarly, imaging of the lesion also does not allow for differentiation from other pancreatic lesions; well-circumscribed lesions may present as heterogeneous and hypodense in studies without contrast and hyperdense when imaged with contrast. Thus, diagnosis requires histopathological analysis, which also has proven to be a challenge.

Of the 24 cases of reported pancreatic PEComas, FNA was performed in 14 cases, only half of these yield diagnostic results, with surgical resection and biopsy determining diagnosis in the rest.<sup>1</sup> It is unclear why FNA biopsies were nondiagnostic in these studies. Nevertheless, treatment for pancreatic PEComa is surgical resection given the malignant potential. Timing and screening for PEComas, particularly in patients with TSC, remains unclear.<sup>1</sup>

TSC is an autosomal dominant disease resulting in tumors in virtually all organs in the body that can appear throughout the patient's lifetime. One of the clinical diagnostic criteria includes the presence of AMLs.<sup>2</sup> The most recent guidelines on surveillance and management published in 2012 have recommendations on screening of renal AMLs but not pancreatic AML, which is not surprising because the only reported case of a pancreatic AML in a patient with TSC who was reported in 2016.<sup>5,6</sup> Screening for renal AML is recommended every 1–3 years with abdominal MRI for AML.<sup>6</sup> In addition, although

nephrectomy is not the recommended form of management, recurrence in another organ, after complete resection of the tumor is possible, as seen in our patient, for which there are no surveillance recommendations. One would expect pancreatic lesions to be detected on MRI; however, as mentioned above, radiologic descriptions of pancreatic AML are nonspecific.

In addition, our patient underwent an abdominal MRI which failed to identify a pancreatic lesion. EUS was the first form of imaging showing the pancreatic lesion in our patient performed for an unrelated indication and incidentally found the pancreatic AML. In conclusion, pancreatic AMLs can occur after resection from another organ in patients with TSC, thus requiring continued surveillance. As pancreatic AMLs are commonly found incidentally and can be missed on imaging, EUS may play a role as a screening modality.

## DISCLOSURES

**Author contributions:** A. Sinha wrote the manuscript and reviewed the literature. K. Tufail, AS Johal, and HS Khara edited the manuscript. AS Johal is the article guarantor.

**Financial disclosure:** None to report.

**Previous presentation:** This case was presented at the American College of Gastroenterology Annual Scientific Meeting; October 25–30, 2019; San Antonio, Texas.

**Informed consent** was obtained for this case report.

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