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Case Report

Perivascular epithelioid cell tumor of pancreas on the background of chronic liver disease: a case report and review of literature

Rohan N. Umesh*, Saravanan Janakiraman, Selvaraj Thangasamy, Jeswanth Sathyanesan

Institute of Surgical Gastroenterology and Liver Transplantation, Government Stanley Medical College and Hospital Chennai, Tamil Nadu, India

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***Correspondence:**
Dr. Rohan N. Umesh,
E-mail: roni.rohan@gmail.com

ABSTRACT

Perivascular epithelioid cell tumours, known as PEComas, of the pancreas are an extremely rare group of neoplasms. This heterogenous entity includes angiomyolipoma (AML), clear cell sugar tumour (CCST), lymphangioleiomyoma (LAM), and another group of lesions originating from the soft tissues and organs with similar histological and immunophenotype characteristics. To date, only 23 cases have been reported throughout the world with different clinical presentations. We report a 52-year-old lady who presented with a symptomatic mass in the body of the pancreas on the background of hepatitis B virus (HBV)-related chronic liver disease (CLD). She presented with abdominal pain of 2 months' duration. On initial computed tomography (CT) imaging, it revealed a homogenously enhancing lesion in the body of the pancreas. It was T2 isointense on magnetic resonance imaging (MRI), and there was no uptake present in the 68Ga DOTONAC scan. Endoscopic ultrasound with fine needle aspiration (FNA) showed paucicellular material with occasional dysplastic cells. On account of suspicion of a non-functional neuroendocrine tumour, she underwent a distal pancreatosplenectomy. Intra-operatively, the lesion was encapsulated and hard in consistency, and the rest of the pancreas was soft with an undilated MPD. She had a smooth postoperative recovery. Final histopathology revealed benign PEComa of the distal body and tail of the pancreas with HMB 45 and SMA positivity on IHC. Currently, she has been on regular follow up for the last 12 months. PEComas usually present as a histological surprise and are a diagnosis of exclusion. However, knowledge of this exceptionally rare tumour makes diagnosis at the pre-operative level more certain. Resection must be considered, as it leads to a good prognosis and survival.

Keywords: Perivascular epithelioid cell tumour of the pancreas, PEComa of the pancreas, Distal Pancreatosplenectomy, HMB 45, SMA

INTRODUCTION

Perivascular epithelioid cell tumours, known as PEComas, of the pancreas are an extremely rare group of lesions. This heterogenous entity includes angiomyolipoma (AML), clear cell sugar tumour (CCST), lymphangioleiomyoma (LAM), and another group of lesions originating from the soft tissues and organs with similar histological and immunophenotype characteristics.[1] To date, only 23 cases of pancreatic origin of PEComa have been reported throughout the world with different clinical presentations. We report a benign PEComa in a middle aged lady with a background of chronic liver disease.

CASE REPORT

A 52-years lady presented to us with pain abdomen of 2-months duration, dull aching upper abdominal and occasionally radiating to back. There were no other symptoms. She was a known case of hepatitis B virus (HBV) related chronic liver disease (CLD). She had no signs of decompensation of CLD at the time of

presentation. Her general and abdominal examination was essentially normal. Laboratory parameters including tumour and neuroendocrine markers are mentioned in Tables 1-5. Ultrasound of abdomen showed a hypoehoic lesion in pancreas. Further evaluation with computed tomography (CT) imaging it revealed a homogenously enhancing lesion in body of pancreas. It was T2 isointense on magnetic resonance imaging (MRI) (Figure 1a). EUS showed a 3×4 cm round hypoechoic lesion at distal body of pancreas and guided fine needle aspiration (FNA) was paucicellular material with occasional dysplastic cells (Figure 1b).[6,8] Ga DOTONAC scan revealed an isodense lesion with no uptake (Figure 1c). On account of inconclusive EUS-FNA results and suspicion of non-functional neuroendocrine tumour which is symptomatic, she underwent distal pancreatosplenectomy. Intra-operatively the lesion was encapsulated and hard in consistency and rest of pancreas was soft with undilated MPD (Figure 2).

She was started on orals on day one and ambulated the same day. Her post-operative recovery was smooth except for mild surgical site infection. She was discharged on day 7.

Table 1: Hemogram and viral markers.

Parameters	Observation
Hb	10.8 g/dl
Total leucocyte count	2300/cu.mm
Platelet count	43000/cu.mm
HIV I and II	Negative
HBsAg	Positive
HCV	Negative
Serum C-reactive protein	4.1 mg/dl
ESR	15 mm at 1st hour

Final histopathology revealed benign perivascular epithelioid cell tumour of distal body and tail of pancreas, with both spindle and epithelioid and spindle cell components on 40x magnification (Figure 3), size <5 cm, no necrosis, no atypia, mitosis <1/HPF, no lymphovascular invasion. Full panel of IHC markers staining done and revealed HMB-45 and SMA positive staining (Figures 4 and 5). Follow up period was 12 months and she is doing well.

Table 2: Liver function parameters.

Parameters	Observation
Total bilirubin	0.5 mg/dl
Direct bilirubin	0.2 mg/dl
SGOT	40 IU/ml
SGPT	38 IU/ml
ALP	88 IU/ml
Total proteins	7.1 g/dl
Serum albumin	3.7 g/dl

Table 3: Tumour and neuroendocrine markers.

Parameters	Observation
Serum CEA (ng/ml)	1.41 (normal <5)
Serum CA 19-9 (IU/ml)	31.2 (normal <37)
Serum chromogranin (mcg/ml)	57.25 (normal <100)

Table 4: Panel of IHC markers and the inference.

Markers	Positive/negative
HMB 45	Positive
SMA	Positive
S 100	Negative
CD 34	Negative
CD 117	Negative
DOG 1	Negative
VIMENTIN	Negative
DESMIN	Negative
Pan CK	Negative
Ki 67 index	1%

Table 5: Clinical characteristics of PEComas reported in the literature.

Author and year	Age	Sex	Symptomat-ology	Location	Imaging findings	Procedure	Follow up (months)
Zamboni 1996[7]	60	F	Pain abdomen	Body	CT- well-demarcated solid lesion with even texture	DP	3
Heywood 2004[8]	74	F	Pain abdomen	Head	CT- cystic lesion with irregular thick capsules	PPPD	69
Ramuz 2005[9]	31	F	Pain abdomen	Body	CT- round-like solid lesion with bleeding	SPDP	9
Perigny 2005[10]	46	F	Diarrhoea	Body	CT- nodule of 1.7 cm	Enucleation	3
Ferga 2008[11]	33	F	NA	Head, body and tail	USG- hypoechoic cystic lesion	NA	12
Hirabayas -hi 2009[3]	47	F	Pain abdomen	Head	MRI- solid round lesion, with low T1W1 signals	PPPD	12

Continued.

Author and year	Age	Sex	Symptomat-ology	Location	Imaging findings	Procedure	Follow up (months)
Baez 2009[12]	60	F	Mass per abdomen	Body	CT- solid round lesion with bleeding	DP	7
Zemet 2011[13]	49	M	Fever and cough	Head	CT- mass with calcifications, which was 30 × 40 mm in size and located at head, EUS- well-demarcated hyperechoic calcified mass	PPPD	10
Nagata 2011[14]	52	M	Pain abdomen	Head	Imaging revealed a 4cm mass located in the head	PD	27
Xie[15]	58	M	Pain abdomen	Head	MRI- round-like nodule, with slightly high T2W1, adipose inhibition and DWI signals and low T1W1 Signals	NA	5
Finzi 2012[16]	62	F	Asymptomatic	Head	EUS- 2.0 × 2.0 cm solid and well-demarcated mass in the posterior pancreatic head. CT- 2.5 cm round, solid, well-defined, and homogeneous nodule, which was slightly hyperdense without a significant contrast enhancement	Total excision	5
Al-Haddad 2013[17]	38	F	Pain abdomen	Uncinate	CT- hypervascular uncinate lesion, EUS- 18 mm well-circumscribed, hypoechoic, homogenous mass without vascular invasion	PD	NA
Okuwaki 2013[18]	43	F	Pain abdomen	Body and tail	CT- relatively well-demarcated mass 10 cm diameter in body and tail with an intermingling of high signal intensity inside tumor	DP	7
Moura 2013[19]	51	F	Pain abdomen and jaundice	Head	Imaging showed dilatation of CBD and IHBRD related to intrapancreatic mass, consistent with endocrine/ secondary tumor	PD	6
Li 2016[20]	47	F	Asymptomatic	Body	USG- hypoechoic lesion, CT- low density shadow	Surgery (details NA)	8
Petrides 2015[21]	17	F	Melena	Head	CT- mass at the head, 4.2 cm diameter EUS- ulcerating malignant looking mass infiltrating 50% of the wall of D2 in the region of the ampulla	PPPD	18
Yusuke 2015[2]	61	F	Pain abdomen	Body	CT- solid low-density mass of 7 cm diameter, which was circumferentially well-demarcated and located in the body	PD	12
Tan 2016[22]	58	F	Asymptomatic	Body	USG- hyperechoic mass at the body, well-demarcated and 1.8 cm size, MRI- solid round nodule with low T1-weighted signals and no	Middle pancreatect-omy	5

Continued.

Author and year	Age	Sex	Symptomat-ology	Location	Imaging findings	Procedure	Follow up (months)
					dilation/ stenosis of MPD and branch ducts		
Maurizio 2017[23]	68	M	Pain abdomen	Head	CT- hypervascular well-demarcated lesion in head, diameter 28 mm and no relation with neighboring organs	No surgery (follow up only)	13
Wei 2016[24]	58	F	Asymptomatic	Body	USG- slightly hyperechoic body mass, CT- pancreatic body mass	Middle pancreatic-tomy	18
Hui 2016[6]	50	F	Asymptomatic	Head	CT- relatively low-density nodule in head MRI- low T1W1 signal nodule, which had clear contrast with adjacent normal pancreas of a relatively high signal	Surgery (details NA)	14
Christo-pher 2016[1]	31	F	H/o de novo TSC	Body	CT- 8 mm cyst in the body; enlarged to 5.8 cm by 2013, EUS- cystic lesion with no connection to pancreatic ducts, with a solid unilocular cyst	DP	NA
Geng 2018 [1]	40	F	Asymptomatic	Body	CT- moderately progressive enhancement and solid pseudo-papillary tumor, cystic and solid lesion	Laparosco-pic DP	30
Our case 2022	52	F	Pain abdomen	Body and tail	CT- homogenously enhancing lesion in body of pancreas 3.5×4 cm, MRI- T2 isointense lesion, 68Ga DOTONAC – no uptake	DPS	12

NA- Not available, SG- ultrasonography, CT- computed tomography, MRI- magnetic resonance imaging, EUS- endoscopic ultrasound, PD- pancreaticoduodenectomy, PPPD- pylorus preserving pancreaticoduodenectomy, DP- distal pancreatectomy, DPS- distal pancreaticosplenectomy, SPDP- spleen preserving distal pancreatectomy; TSC- tuberous sclerosis.

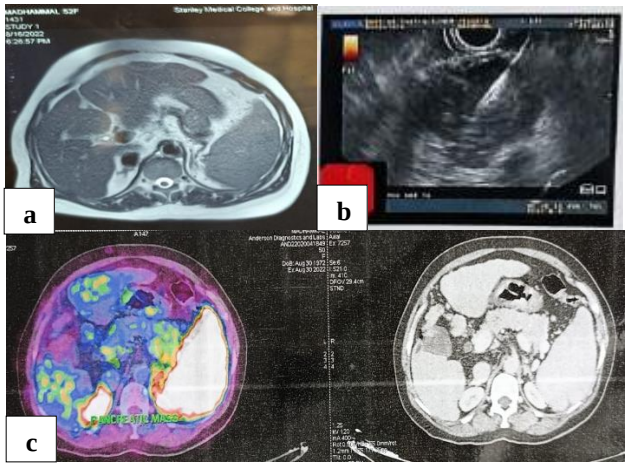

Figure 1: (a) MRI abdomen with a T2 isointense lesion in the body of pancreas; (b) EUS image showing predominantly hypoechoic lesion with minimal vascularity and needle being passed for FNAC; and (c) 68Ga DOTONAC PET-CT with no uptake from the lesion.

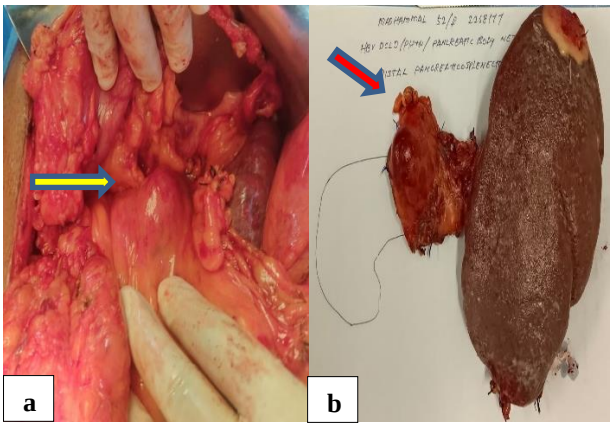

Figure 2: (a) 4×4 cm globular hard mass in distal body region more in upper aspect (solid yellow arrow), rest of pancreas soft in consistency and MPD size was 2 mm, and (b) the distal pancreatosplenectomy specimen with the lesion marked by solid red arrow.

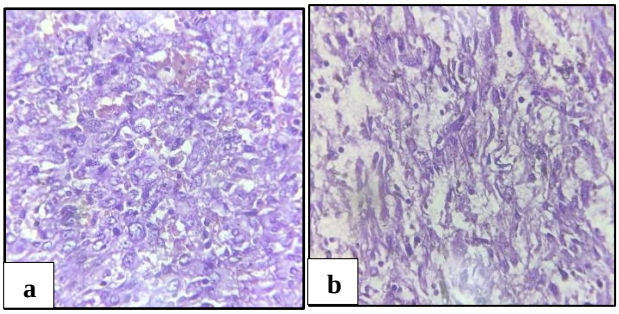

Figure 3: (a) and (b) 40x microscopy images showing epithelioid and spindle components respectively.

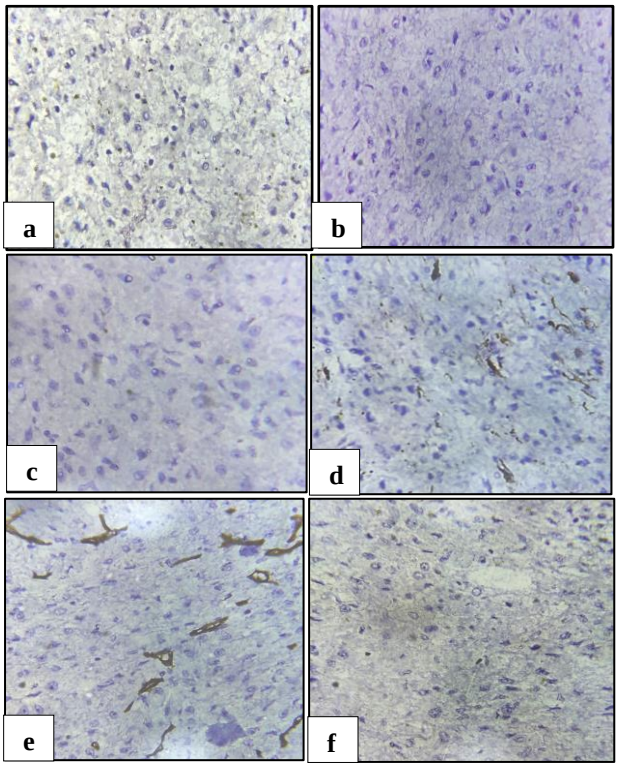

Figure 4: Full panel IHC markers done to identify the type of mesenchymal tumor which included (a) CD117, (b) IHC DOG-1 negative, (c) S 100 negative, (d) CD 34, and (e) Pan CK all of which were negative; (f) shows Ki 67 index of 1%.

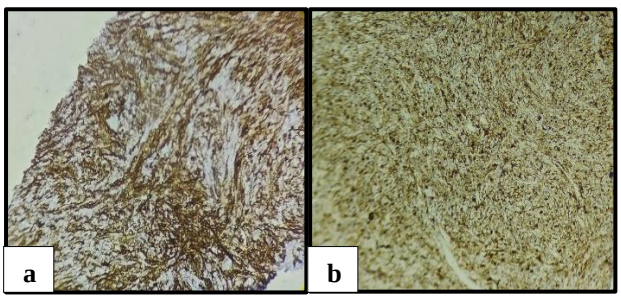

Figure 5: (a) and (b) IHC staining showing HMB 45 as well as SMA strong positivity respectively which points down to epithelioid cell origin of this rare tumor.

DISCUSSION

Perivascular epithelioid cell tumours, also known as PEComas, are a heterogenous group of mesenchymal tumours arising from epithelioid cells of perivascular location arranged in a radial pattern around the blood vessels, which characteristically express melanophore markers and smooth-muscle cell markers.[1] WHO defined the term PEComa as "a class of mesenchymal tumour composed of histologically and immunohistochemically distinctive perivascular epithelioid cells (PECs)".[2] This heterogenous family includes angiomyolipoma (AML), clear cell sugar tumour (CCST), Lymphangioleiomyoma (LAM), and a group of tumours originating from the soft tissues and viscera with similar histology and immunophenotypic characteristics.[1] PEComas are ubiquitous tumours that may arise from any tissue or organ in the body, including the gastrointestinal tract, but their pancreatic origin is extremely rare. [2] The first case of a clear cell sugar tumour arising from the pancreas was reported by Zamboni et al, who came forward with the concept of a perivascular epithelioid cell tumour (PEComa).[1] Since then, about 23 cases have been reported across various parts of the world with different clinical presentations. We have attempted to summarise the important features of all the cases of pancreatic PEComa, including ours, in Table 5. One case of pancreatic PEComa was associated with tuberous sclerosis, as reported by Christopher et al in 2016.

PEComa of the pancreas predominantly occurs in females, with only 4 of the 24 cases reported in males so far, including our middle aged female patient. The head and body of the pancreas are common sites of involvement.[1] Age incidence varies in the reported literature from as young as 17 years to the oldest age incidence of 74 years.[7,21] Most of the pancreatic PEComas presented with pain in the abdomen, with the next common presentation being an asymptomatic pancreatic lesion detected incidentally on imaging. One patient had melena on presentation.[21] The biological and histological behaviour of pancreatic PEComas has been largely unknown in the reported literature so far, though most cases are benign.[6] Two cases have been reported to have malignant behaviour with liver metastasis. One case of pancreatic origin PEComa associated with tuberous sclerosis was also found to be benign on histology.

Ultrasound features include hypo- or isoechoic predominantly solid lesions. Hyperechoic characteristics may be due to the presence of calcifications.[1] CT is the initial investigation of choice, and the lesion is well-defined with a vascular capsule. It is predominantly hypodense with mild uniform contrast enhancement. MRI reveals a T1W hypointense and T2 slight hyperintense lesion with mild enhancement on contrast administration. CT and MRI features may not be diagnostic on initial evaluation, but a high degree of suspicion will make inclusion in the differential diagnosis possible owing to their increasing incidence. EUS guided FNAB will yield a

diagnosis at the pre-operative level. Differential diagnoses include GIST, a non-functional neuroendocrine tumour, or a soft tissue sarcoma.

Histology, in combination with immunohistochemistry, will confirm the diagnosis. Macroscopically, the tumour is predominantly solid, with a few areas of cystic spaces with haemorrhage and rarely necrosis. The tumour cells are large epithelioid or spindle-shaped cells with a nested or patchy distribution.[6] The cytoplasm is transparent, contains eosinophilic granules, and can be stained PAS-positive, indicating that the cytoplasm is rich in glycogen.[1] Nuclei are small, round to oval in shape, with an inconspicuous nucleolus.[1] Adipocytes intermingled within the tumour cells may also be seen sometimes.[6] Mitotic figures may be seen occasionally, and if the count is high per HPF, malignancy must be suspected. Other features of malignant transformation include multinucleated giant cells, nuclear pleomorphism, pronounced heteromorphic nuclei, vascular invasion, infiltration adjacent to normal pancreatic tissues, bleeding, and necrosis within the tumour.[1] The expression of HMB45 as well as SMA on IHC and the demonstration of premelanosomes or melanosomes on electron microscopy are hallmark characteristics of PEComa.[3] They are negative for other IHC markers like epithelial cell markers (CK) and neuroendocrine markers (S-100). The IHC characteristics of pancreatic PEComa are similar to those of other sites.[1,5]

Surgery is the treatment of choice as it leads to complete removal. Pancreaticoduodenectomy for head lesions and spleen preserving distal pancreatectomy for body and tail lesions are advocated. Small lesions in asymptomatic patients may be placed under close follow up after confirming the diagnosis by EUS-FNAB.

CONCLUSION

PEComas of the pancreas are an extremely rare group of heterogenous lesions. They usually present as a histological surprise and as a diagnosis of exclusion. Our patient with PEComa of pancreatic origin is the only 24th such case reported in the world. Knowledge of this lesion makes inclusion in the differential diagnosis of the mass lesion of the pancreas possible. Resection must be considered, as it provides cure leading to a good prognosis and long term survival.

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