Case Reports in Gastroenterology

Case Rep Gastroenterol 2025;19:43–51
DOI: 10.1159/000543018
Received: November 8, 2023
Accepted: November 29, 2024
Published online: January 24, 2025

Single Case

Rare Encounter: A Case Report of Hepatic Perivascular Epithelioid Cell Tumor – An Uncommon Mesenchymal Tumor in the Liver

Diogo Paula[a, b, c] Maria João Amaral[a, b, c] Joana Madeira[b, d]
João Simões[a, b, c] André Lázaro[a, b, c, e] Nuno Silva[b, f]
José Guilherme Tralhão[a, b, c, e, g]

[a]General Surgery Unit, Centro Hospitalar e Universitário de Coimbra (CHUC), Coimbra, Portugal; [b]Clinical Academic Center of Coimbra, Coimbra, Portugal; [c]Faculty of Medicine, University of Coimbra, FMUC, Coimbra, Portugal; [d]Pathology Unit, Centro Hospitalar e Universitário de Coimbra (CHUC), Coimbra, Portugal; [e]Coimbra Institute for Clinical and Biomedical Research (iCBR) Area of Environment Genetics and Oncobiology (CIMAGO), Faculty of Medicine, University of Coimbra, Coimbra, Portugal; [f]Hepatic Transplantation Unit, Centro Hospitalar e Universitário de Coimbra (CHUC), Coimbra, Portugal; [g]Institute of Biophysics, Faculty of Medicine, University of Coimbra, Coimbra, Portugal

Keywords
Liver tumor · Hepatic perivascular epithelioid cell tumor

Abstract
Introduction: Perivascular epithelioid cell tumor (PEComa) is a rare neoplastic mesenchymal tumor, more frequently found in the uterus, although it can occur in different organs. Hepatic PEComa is extremely rare, with only a few cases described in the literature. ***Case Presentation:*** We present a case report of a 33-year-old female patient with a history of macroprolactinoma. She was initially referred to our Department due to a 9-mm hepatic nodule incidentally diagnosed in an abdominal ultrasound in 2018. She was asymptomatic. Follow-up ultrasound showed a growth from 9 mm to 16 mm in 2019 and 30 mm in a liver magnetic resonance imaging (MRI) scan in 2022. The case was discussed in a multidisciplinary team meeting, and since malignant transformation or hepatocellular carcinoma could not be ruled out, the decision was to undergo hepatic resection. An open hepatic subsegmentectomy of segment 5 was performed, with uneventful postoperative period. The definitive diagnosis was hepatic PEComa. ***Conclusion:*** Hepatic PEComas are rare liver tumors, and their preoperative diagnosis is challenging due to the lack of specific radiological features. In most cases, the diagnosis is only confirmed through histopathological and immunohistochemical studies.

Correspondence to:
Diogo Paula, diogopaula.dp@gmail.com

Case Rep Gastroenterol 2025;19:43–51
DOI: 10.1159/000543018

Resection of the lesion appears to be the curative treatment; however, due to the rarity of the condition, there are no studies comparing surgical treatment with other options. In our case, the hypervascular lesion was initially misdiagnosed as an adenoma. PEComas should be considered as a differential diagnosis in liver nodules with well-defined margins and increased uptake in the arterial phase in computed tomography or MRI scan. Surgical resection was curative, and no recurrence was detected during the patient's follow-up.

Introduction

Perivascular epithelioid cell tumors (PEComas) are rare mesenchymal tumors that can occur in various anatomical regions, such as kidney, uterus, gastrointestinal tract or soft tissues. Perivascular epithelioid cells were first described by Bonetti et al. [1] in 1992, and the term PEComa was introduced in 1996 by Zamboni and colleagues [1, 2]. In 2013, the World Health Organization defined PEComas as mesenchymal tumors composed of distinctive cells showing a focal association with blood vessel walls and usually expressing melanocytic and smooth muscle markers [3]. The PEComa tumor family includes angiomyolipomas (AML), clear cell sugar tumors of the lung (CCST), lymphangioleiomyomatosis (LAM), and a group of rare tumors arising from abdominal organs, soft tissues, and bones, which are immunophenotypically and morphologically similar to AML, CCST, and LAM [4]. This latter group is referred to as "PEComas other than AML, CCST, LAM" or "PEComa NOS (not otherwise specified)." The term "PEComa" is generally used for this group of tumors that cannot be specifically classified as AML, CCST, or LAM.

PEComas show a focal association with blood vessel walls and commonly express melanocytic (HMB-45 or Melan-A) and smooth muscle (SMA) markers [4]. On computed tomography examination, PEComas are usually low-density lesions often containing fat, which are enhanced in the arterial phase and persist during the portal phase [5]. On magnetic resonance imaging (MRI) scan, most patients exhibit a hypointense signal on T1-weighted imaging and a hyperintense signal on T2-weighted imaging. Similar to the computed tomography scan, the lesions show homogeneous enhancement during the arterial phase and it is significantly weakened in the venous phase [6]. Cases of hepatic PEComas are uncommon, and they are difficult to diagnose before resection or biopsy due to the lack of pathognomonic features and a wide range of differential diagnoses [7]. Currently, there are no guidelines concerning diagnostics, treatment, or follow-up, making treatment and follow-up decisions for the patient rely on the experience of the patient's care team or through similar protocols for other liver nodules. Nevertheless, a multidisciplinary approach and discussions among specialists in the field are essential for developing an individualized treatment plan for each case.

Case Report

A 33-year-old woman with a prior history of macroprolactinoma causing amenorrhea and infertility was referred for surgical consultation due to an asymptomatic hepatic nodule. A 2018 abdominal ultrasound showed a hyperechogenic and homogeneous 9-mm nodule in segment 5, suggestive of a hemangioma (Fig. 1a). One year later, the ultrasound showed an increase in size to 16 mm with no change in characteristics (Fig. 1b). In 2022, the follow-up ultrasound revealed a hyperechogenic and heterogeneous nodule measuring 28 mm in

Case Rep Gastroenterol 2025;19:43–51
DOI: 10.1159/000543018

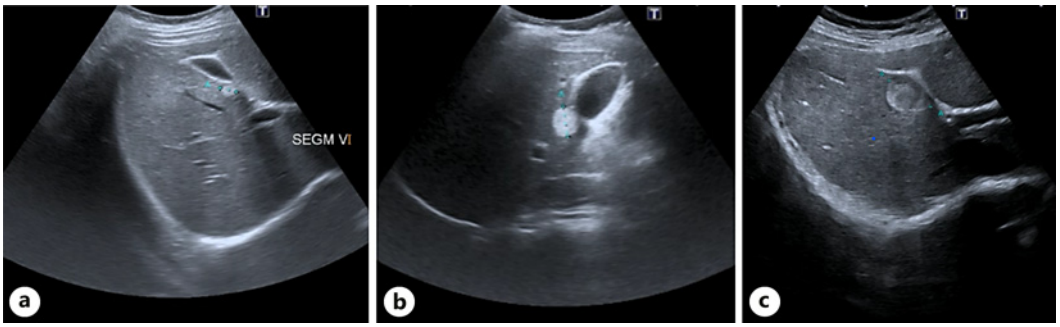

Fig. 1. a 2018 ultrasound: hyperechogenic and homogeneous nodule measuring 9 mm in segment 5. **b** 2019 ultrasound: hyperechogenic and homogeneous nodule measuring 16 mm in segment 5. **c** 2019 ultrasound: hyperechogenic and homogeneous nodule measuring 16 mm in segment 5.

segment 5 (Fig. 1c). Due to the change in characteristics and size increment, an abdominal MRI scan was performed and identified a slightly hyperintense nodule on T2 (Fig. 2a) and hypointense on T1 (Fig. 2b), measuring 30 mm, with an internal nodular area of 17 mm. The dynamic study showed hypervascularity of the lesion, with arterial phase enhancement and washout in the portal phase (Fig. 2c, d). Additionally, alpha-fetoprotein and CA 19.9 levels were within normal limits.

In an oncological multidisciplinary team meeting, the diagnosis of hepatocellular adenoma was considered but due to the aspect "nodule inside nodule" and dynamic features, malignant transformation or hepatocellular carcinoma (HCC) could not be ruled out. Therefore, decision was in favor of surgical resection for definitive diagnosis. The patient underwent open hepatic subsegmentectomy of segment 5 without complications and was discharged home on the second postoperative day.

The resected subsegment weighed 17 g and measured 4.7 × 3.8 × 2.8 cm. It had a pink smooth capsule and, upon sectioning, revealed a subcapsular nodular lesion measuring 2.5 × 1.6 × 1.5 cm. The lesion was well delimited and consisted of brownish and soft tissue. Microscopic examination showed proliferation of bulky and polygonal cells with eosinophilic or clear cytoplasm, sometimes with "spider" reticulation (Fig. 3a, b). The cells were arranged in towels or trabecule and exhibited areas of coagulation necrosis and hemorrhage. The lesion was richly vascularized, with focal adipose tissue, especially at the periphery (Fig. 3c). The growth was expansive, with a distance to the margin of less than 1 mm, and the surrounding liver tissue was normal (Fig. 3d). Immunohistochemical staining revealed intense and diffuse expression of HMB-45, while SOX10, another melanocytic marker, was negative (Fig. 4). The diagnosis was hepatic PEComa, predominantly epithelioid, with focal adipose tissue.

After the diagnosis, the patient was once again discussed in a multidisciplinary meeting, and surgery was considered curative. It was decided to continue follow-up in the surgical consultation and perform a hepatic MRI annually. To date, no recurrence has been detected. The CARE Checklist has been completed by the authors for this case report, attached as supplementary material (for all online suppl. material, see https://doi.org/10.1159/000543018).

Discussion

PEComas are rare tumors that can occur in various parts of the human body, including the uterus, skin, thorax, gastrointestinal tract, and liver, making hepatic PEComas an even rarer condition. Most PEComas are sporadic, but about 10% are associated with tuberous sclerosis

Case Rep Gastroenterol 2025;19:43–51
DOI: 10.1159/000543018

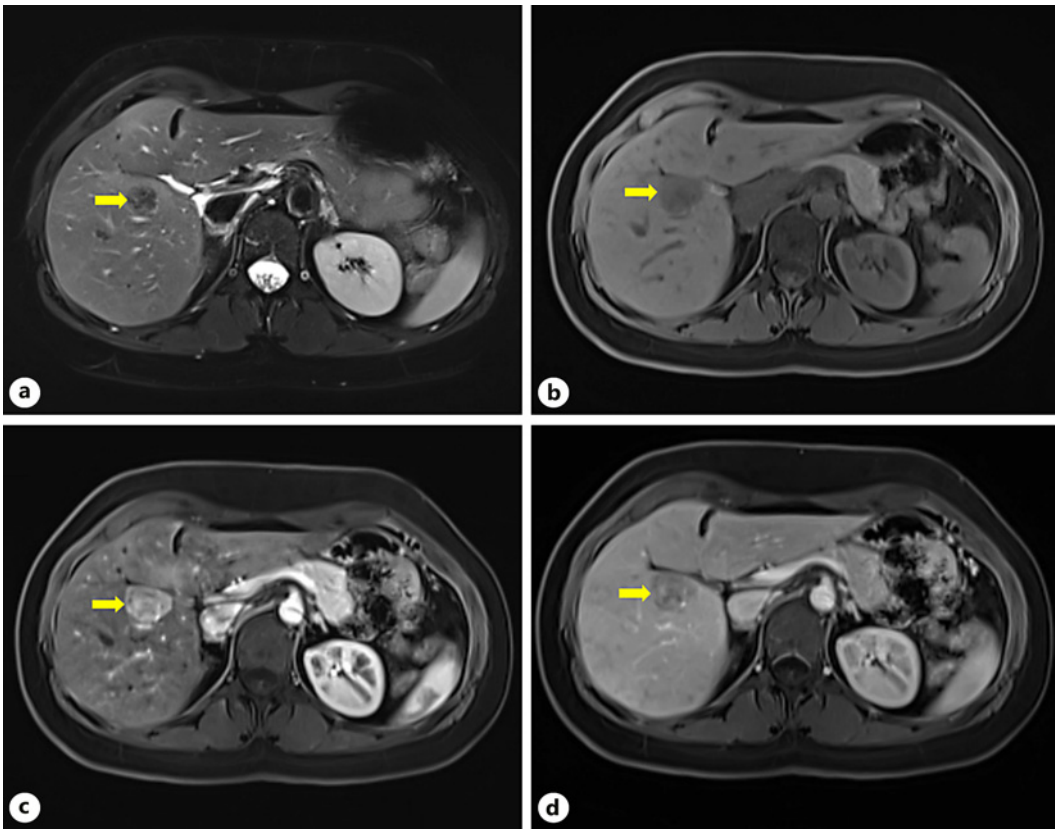

Fig. 2. Hepatic MRI: slightly hyperintense nodule (arrow) on T2 (**a**) and hypointense on T1 (**b**), measuring 30 mm, with an internal nodular area measuring 17 mm. **c**, **d** The dynamic study showed hypervascularity of the lesion, with arterial phase enhancement and washout in the portal phase.

complex (TSC), and its pathogenesis may be related to the deletion of *TSC1* (9q34) or *TSC2* (16p13.3) [8]. Some authors suggest that the mTOR pathway is involved in the tumorigenesis of PEComas [9].

Hepatic PEComas are more commonly found in young and middle-aged females, with a female-to-male ratio of 6:1 [3]. Most of these tumors are asymptomatic and are often discovered incidentally in patients without obvious clinical symptoms. However, when they grow large enough to compress surrounding tissues, patients may experience tenderness in the liver region, upper abdominal pain or discomfort, and accompanying symptoms such as nausea or vomiting [8].

While most PEComas are benign, there have been reported cases of malignant PEComas [10, 11]. Diagnostic criteria proposed by Folpe et al. [12] for potential malignant PEComas include tumor size greater than 5 cm, infiltration into surrounding tissues, vascular necrosis, high nuclear grade, high cellularity, necrosis, and a mitotic rate greater than 1/50 high power. Meeting two or more of these favors potential malignancy. Tumors with only nuclear polymorphisms, multinucleated giant cells, or a size greater than 5 cm are considered to have uncertain malignant potential [12].

Imaging features play a crucial role in diagnosing hepatic PEComa, but their accuracy is often unsatisfactory due to the diverse components and patterns observed in these tumors. Even when combining CT and MRI data, the rate of accurate diagnosis is only around 20% [8]. Typically, PEComas appear as well-delimited hypoechoic lesions on ultrasound [13]. On contrast-enhanced ultrasound, they show early arterial hyperenhancement with preserved

Case Rep Gastroenterol 2025;19:43–51
DOI: 10.1159/000543018

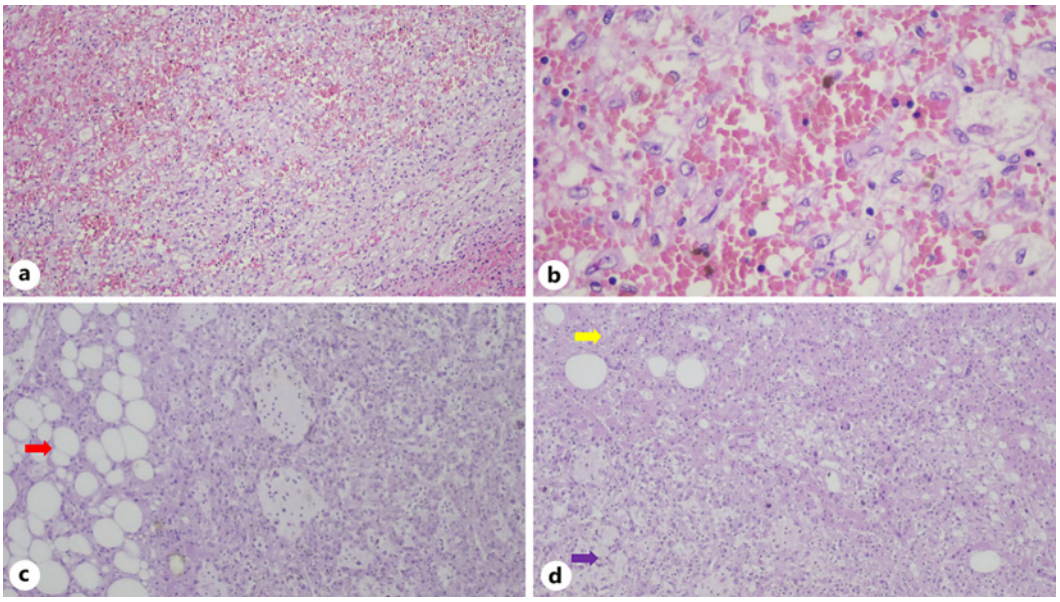

Fig. 3. Histological pictures of the lesion. **a** Histopathology showing proliferation of voluminous and polygonal cells with eosinophilic or clear cytoplasm, arranged in sheets or trabecule (H&E stain. ×100). **b** Cellular detail (H&E stain. ×200). **c** Focal observation of adipose tissue, especially in the periphery. Red arrow: adipose tissue (H&E stain. ×100). **d** Interface between the lesion and hepatic tissue without alterations. Yellow arrow: normal hepatic tissue; purple arrow: lesion (H&E stain. ×100).

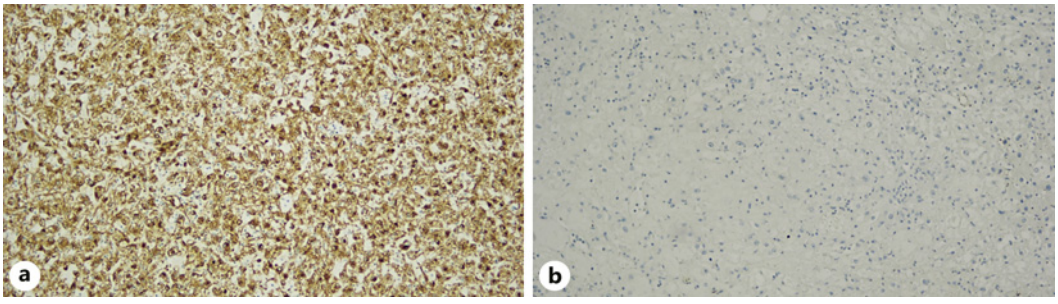

Fig. 4. Immunohistochemical pictures of the lesion. **a** Immunohistochemistry showed that the lesion was positive for HMB-45 (100×). **b** Immunohistochemistry showed that the lesion was negative for SOX10 (100×).

isoenhancement in the portal phase and a mild parenchymal washout [13]. On CT and MRI scans, PEComas present as lesions with circular or quasi-circular inhomogeneous occupancy, low-density, clear boundaries, and expansive growth [6]. Adipose tissue, hemorrhage, necrosis, and cystic degeneration may occasionally be detected. The lesions with features of neovascularization and arteriovenous connections show heterogeneous enhancement in the arterial phase [6]. Another significant characteristic of hepatic PEComas is abnormal enhancement of enlarged blood vessels in the edge or center of the lesion. In the portal phase, the enhancement persists, but it is significantly weakened in the venous phase [6]. If tumors have more fatty elements and fewer blood vessels, they may exhibit features of low-density lesions in the delayed phase. Thus, hepatic PEComas can be misdiagnosed as HCC, focal nodular hyperplasia, lipoma, adenoma, or hamartoma on a CT scan. In particular, the imaging

Case Rep Gastroenterol 2025;19:43–51
DOI: 10.1159/000543018

Table 1. Summary of differential diagnosis of hepatic PEComa

	Clinical characteristics			Imaging appearance						
	age	liver disease	laboratory value	T1W1	T2W1	DWI	arterial phase	portal venous phase	hepatobiliary phase	unique features
Hepatic PEComa	Young and middle-age	–	–	↑	↓	↓	↓	↑	↑	-
FNH-like nodules	42–69	Alcohol-related cirrhosis	–	Varied	Varied	↓/=	↓	↑ with or without a rim-like enhancement	↓/=	≤2 cm
Hepatocellular adenoma	Young	–	–	Varied	Varied	↓	↓	↑	↑	Signal drop in the opposed phased/atoll sign
Hepatic epithelioid angiomyolipoma	Young and middle-age	–	–	↑	↓	↓	↓	↑	↑	The central vessel and the early drainage
Hepatocellular carcinoma	>60	Cirrhosis, hepatitis	Increased AFP	↑	↓	↓	↓	↑	↑	Capsule, nodule in nodule
Intrahepatic cholangiocarcinoma	>40	With or without cirrhosis	Increased CA 19-9 and/or CA 125	↑	↓	↓	↓	↑/↓	↑	NA
Intrahepatic bile duct adenoma	20–70	With or without cirrhosis	–	↑	↓	↓	↓	↑/↓	↑	Single, ≤2 cm, subcapsular/on the surface of the liver

Adapted from Tang et al. [14], hepatic nodules with arterial phase hyperenhancement and washout on enhanced computed tomography/magnetic resonance imaging: how to avoid pitfalls. FNH, focal nodular hyperplasia; DWI, diffusion-weighted imaging; ↓, hyperintensity; ↑, hypointensity; =, isointensity; –, negative.

findings of highly differentiated HCC are very similar to those of fat-poor hepatic PEComas [8]. This diagnosis is radiologically challenging due to the variable enhancement pattern depending on the proportion of different components such as adipose tissue, blood vessels, and smooth muscle cells [5]. In Table 1, there is a summary of the differential diagnosis of hepatic PEComa and their radiologic characteristics. Although combining various imaging examinations may improve the accuracy of diagnosis to a certain extent, the lack of pathognomonic characteristics associated with the extensive list of differential diagnoses and the rarity of hepatic PEComa, make it very difficult to diagnose radiologically.

Hepatic PEComas exhibit mature adipose tissue and are surrounded by thick-walled or thin-walled blood vessels, around which polygonal or round epithelioid tumor cells are radially arranged [11]. Vascular hyalinization and spindle cells resembling smooth muscle cells have been reported. Additionally, the tumor cells can contain other cell types, including vacuolar cells with a transparent cytoplasm and eosinophilic cells with atypical nuclei [8]. Also, abundant dilated hepatic sinusoids and extramedullary hematopoiesis have been observed [11]. They can exhibit positive staining for both myogenic marker (SMA) and melanogenesis markers (HMB-45 and Melan-A) [4], which are key markers for diagnosing hepatic PEComas. However, these three markers are simultaneously positive in only 80% of cases [12]. Additionally, PEComas can exhibit positive staining for vimentin, S-100, Mitf, desmin, CD-31, and CD-34. They are negative for chromogranin A, CK, CD117, CD10, AFP, and EMA [15].

In our case, the PEComa was predominantly epithelioid and showed positive staining for HMB-45 but was negative for both SMA and Melan-A. This can be explained by the fact that HMB-45 is expressed at higher levels than SMA when epithelioid cells are the predominant cell type in tumors, whereas the opposite result is observed when spindle cells are the predominant cell type [12].

Fine-needle biopsy is recommended for the diagnosis of hepatic PEComa due to the challenges associated with radiologic diagnosis [16]. It is important to differentiate PEComas from other diagnoses such as HCC, metastatic clear cell carcinoma, soft tissue clear cell sarcoma, or malignant melanoma. HCC and metastatic clear cell carcinoma may resemble hepatic PEComas morphologically, but they are negative for melanocytic markers (HMB-45 and Melan-A) [16]. Soft tissue clear cell sarcoma and malignant melanoma, which may express HMB-45 and Melan-A, are more atypical and do not express myogenic markers (SMA) [16].

Due to the rarity of this pathology, there are no specific treatment guidelines, but surgical resection appears to yield good results. The goal is to completely remove the tumor and prevent dissemination caused by tumor rupture. The majority of benign PEComas do not recur after surgical resection [8]. However, malignant hepatic PEComas lack effective treatments, and patients who undergo surgery may experience tumor recurrence and distant metastasis [5]. Sirolimus, an mTOR pathway inhibitor, may be effective against malignant hepatic PEComas since tumorigenesis seems to be related to the activation of the mTOR pathway, as previously mentioned. Neoadjuvant sirolimus therapy has been proposed as a treatment for large malignant hepatic PEComa to reduce its size prior to surgery [17]. Stereotactic body radiation therapy has also been used as neoadjuvant therapy by Kirste et al. [18] to reduce the size of unresectable PEComa and enable surgical resection.

Conclusion

Hepatic PEComas are rare liver tumors, and their preoperative diagnosis is challenging due to the lack of specific clinical and radiological characteristics. In most cases, the diagnosis is obtained through histopathological and immunohistochemical studies. In our case, the

lesion was initially misdiagnosed as an adenoma. PEComas should be considered as a differential diagnosis in liver nodules with well-defined margins and increased arterial phase uptake.

Hepatic PEComas are extremely rare, and based on the few reports available in the literature, surgery appears to be the treatment of choice. Further research and case reports are needed to understand the role of other therapies, such as sirolimus or stereotactic body radiation therapy, as alternatives or adjuncts to surgery.

Statement of Ethics

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. Confidentiality and privacy of information were guaranteed in accordance with the Declaration of Helsinki. Ethical approval is not required for this study in accordance with local guidelines.

Conflict of Interest Statement

The authors have no conflicts of interest to disclose.

Funding Sources

This study was not financially supported.

Author Contributions

Conceptualization: D.P., J.S., and A.L.; methodology: D.P., J.S., and N.S.; resources: D.P., M.J.A., and J.M.; writing – original draft preparation: D.P., M.J.A., and J.M.; writing – review and editing: J.S., A.L., N.S., and J.G.T.; and supervision: A.L., N.S., and J.G.T. All authors have read and agreed to the published version of the manuscript.

Data Availability Statement

All data generated or analyzed during this study are included in this article and its online supplementary material. Further inquiries can be directed to the corresponding author.

References

1 Bonetti F, Pea M, Martignoni G, Zamboni G. PEC and sugar. Am J Surg Pathol. 1992:307–8. https://doi.org/10.1097/00000478-199203000-00013.
2 Tang D, Wang J, Tian Y, Li Q, Yan H, Wang B, et al. Hepatic perivascular epithelioid cell tumor: case report and brief literature review. Medicine. 2016;95(51):e5572. https://doi.org/10.1097/MD.0000000000005572
3 Son HJ, Kang DW, Kim JH, Han HY, Lee MK. Hepatic perivascular epithelioid cell tumor (PEComa): a case report with a review of literatures. Clin Mol Hepatol. 2017;23(1):80–6. https://doi.org/10.3350/cmh.2016.0034
4 Machado I, Marhuenda A, Trallero M, Caballero M, Santos J, Cruz J, et al. Hepatic epithelioid angiomyolipoma/PEComa and focal nodular hyperplasia in a patient with a previous history of cutaneous melanoma. Rev Esp Patol. 2019;52(4):250–5. https://doi.org/10.1016/j.patol.2018.05.001

5 Jia J, Luo J, Pan CG, Ge G, Feng M, Zou B, et al. Single-center experience in the diagnosis and treatment of hepatic perivascular epithelioid cell neoplasm. J Clin Transl Hepatol. 2022;10(1):72–9. https://doi.org/10.14218/JCTH.2020.00170
6 Tan Y, Xiao E. Hepatic perivascular epithelioid cell tumor (PEComa): dynamic CT, MRI, ultrasonography, and pathologic features – analysis of 7 cases and review of the literature. Abdom Imaging. 2012;37(5):781–7. https://doi.org/10.1007/s00261-012-9850-1
7 Gu J, Wang W, Wang S. A retrospective case study of 13 uterine perivascular epithelioid cell neoplasm (PEComa) patients. Onco Targets Ther. 2021;14:1783–90. https://doi.org/10.2147/OTT.S300523.
8 Yang X, Wang Q, Zhou X, Zhou H, Jia W, Hu C, et al. Retrospective analysis of hepatic perivascular epithelioid cell tumour (PEComa) in a single centre for clinical diagnosis and treatment clinical diagnosis and treatment of hepatic PEComa. Medicine. 2022;101(25):e29506. https://doi.org/10.1097/MD.0000000000029506
9 Huang SC, Chuang H, Chen T-D, Chi CL, Ng K-F, Yeh T-S, et al. Alterations of the mTOR pathway in hepatic angiomyolipoma with emphasis on the epithelioid variant and loss of heterogeneity of TSC1/TSC2. Histopathology. 2015;66(5):695–705. https://doi.org/10.1111/his.12551
10 Li Z, Zhou Y, Wang C, Yu H, Yang G, Ma Y. Insights into clinical diagnosis and treatment of malignant hepatic perivascular epithelioid cell tumor. Intractable Rare Dis Res. 2022;11(4):202–5. https://doi.org/10.5582/irdr.2022.01111
11 Abhirup B, Kaushal K, Sanket M, Ganesh N. Malignant hepatic perivascular epithelioid cell tumor (PEComa): case report and a brief review. J Egypt Natl Canc Inst. 2015;27(4):239–42. https://doi.org/10.1016/j.jnci.2015.05.004
12 Folpe AL, Mentzel T, Lehr H-A, Fisher C, Balzer BL, Weiss SW. Perivascular epithelioid cell neoplasms of soft tissue and gynecologic origin: a clinicopathologic study of 26 cases and review of the literature. Am J Surg Pathol. 2005;29(12):1558–75. https://doi.org/10.1097/01.pas.0000173232.22117.37
13 Matrood S, Görg C, Safai Zadeh E, Alhyari A. Hepatic perivascular epithelioid cell tumor (PEComa): contrast-enhanced ultrasound (CEUS) characteristics – a case report and literature review. Clin J Gastroenterol. 2023;16(3):444–9. https://doi.org/10.1007/s12328-023-01779-w
14 Tang M, Li Y, Lin Z, Shen B, Huang M, Li ZP, et al. Hepatic nodules with arterial phase hyperenhancement and washout on enhanced computed tomography/magnetic resonance imaging: how to avoid pitfalls. Abdom Radiol. 2020;45(11):3730–42. https://doi.org/10.1007/s00261-020-02560-0
15 Ma Y, Huang P, Gao H, Zhai W. Hepatic perivascular epithelioid cell tumor (PEComa): analyses of 13 cases and review of the literature. Int J Clin Exp Pathol. 2018;11(5):2759–67.
16 Khan HM, Katz SC, Libbey NP, Somasundar PS. Hepatic PEComa: a potential pitfall in the evaluation of hepatic neoplasms. BMJ Case Rep. 2014;2014:bcr2014204122. https://doi.org/10.1136/bcr-2014-204122.
17 Bergamo F, Maruzzo M, Maruzzo M, Basso U, Basso U, Montesco M, et al. Neoadjuvant sirolimus for a large hepatic perivascular epithelioid cell tumor (PEComa). World J Surg Oncol. 2014;12:46. https://doi.org/10.1186/1477-7819-12-46
18 Kirste S, Kayser G, Zipfel A, Grosu AL, Brunner T. Unresectable hepatic PEComa: a rare malignancy treated with stereotactic body radiation therapy (SBRT) followed by complete resection. Radiat Oncol. 2018;13(1):28. https://doi.org/10.1186/s13014-018-0974-5