Radiology Case Reports 16 (2021) 84–89

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/radcr

Case Report

Giant pedunculated hepatocellular adenoma masquerading as a subdiaphragmatic mass: Diagnostic challenges of a rare tumor ☆,☆☆

Zahra Shafaee, MD, MBA[a,*], *Shaojun Liu, MD, PhD*[b], *Maria Isabel Fiel, MD*[c], *Robert Blue, MD*[d]

[a] *Department of Surgery, NYC Health + Hospitals/Elmhurst, 79-01 Broadway, Elmhurst, NY 11373, USA*
[b] *Department of Pathology, NYC Health + Hospitals/Elmhurst, 79-01 Broadway, Elmhurst, NY 11373, USA*
[c] *Department of Pathology, Icahn School of Medicine at Mount Sinai, One Gustave L Levy Pl, New York, NY 10029, USA*
[d] *Department of Radiology, NYC Health + Hospitals/Elmhurst, 79-01 Broadway, Elmhurst, NY 11373, USA*

ARTICLE INFO

Article history:
Received 3 September 2020
Revised 20 October 2020
Accepted 23 October 2020

Keywords:
Hepatocellular adenoma
Pedunculated liver mass
Subdiaphragmatic mass

ABSTRACT

Giant pedunculated hepatocellular adenomas are extremely rare tumors and often detected incidentally on cross-sectional imaging studies. We report the case of a 34-year-old woman who underwent cross-sectional imaging for staging evaluation of a uterine tumor. A large left subdiaphragmatic mass, without clear connection to the liver, was seen prompting diagnostic laparoscopy; during which a large pedunculated mass attached to the left lobe of the liver was found and resected. This case report highlights the challenges and pitfalls in the imaging diagnosis of pedunculated hepatocellular adenomas, such as difficulty in characterizing the mass or inability to identify the vascular attachment to the liver. Image-guided biopsy and diagnostic laparoscopy are valuable tools to establish diagnosis; most of these lesions are amenable to laparoscopic resection.

Introduction

Pedunculated liver masses are rare and often detected incidentally on cross-sectional imaging studies. Patients with larger masses may present with abdominal pain, early satiety, and a palpable mass on physical examination. There have been reports of acute abdomen due to the torsion of a narrow vascular pedicle and strangulation of the tumor, causing pain and intra-abdominal hemorrhage [1,2].

Hepatocellular adenoma (HCA) is an umbrella term for benign liver neoplasms with distinct genotypical and pheno-

☆ Competing Interests: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.
☆☆ Acknowledgments: The authors would like to thank Armaan Ahmed for the literature search and editorial assistance.
* Corresponding author.
E-mail address: shafaeez1@nychhc.org (Z. Shafaee).
https://doi.org/10.1016/j.radcr.2020.10.047

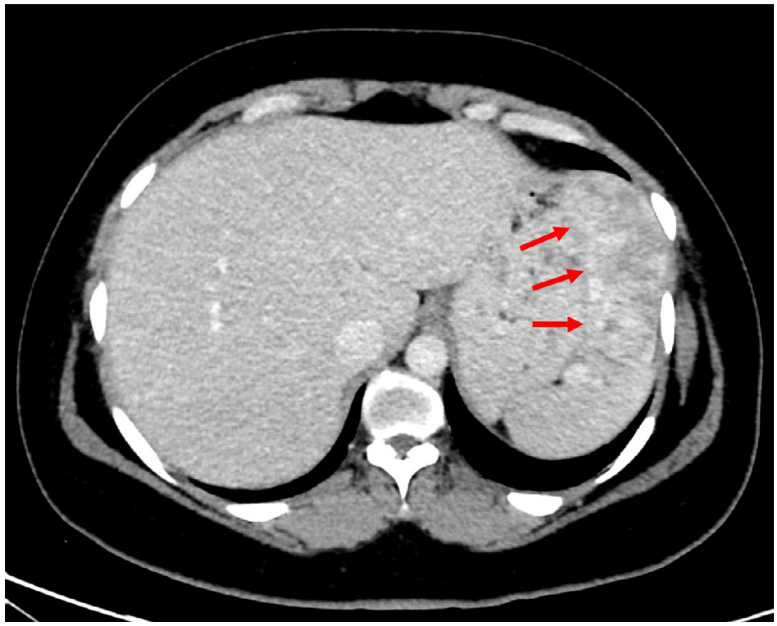

Fig. 1 – Axial CT scan with contrast. Well-circumscribed heterogeneously enhancing mass in the left upper quadrant (arrows), is situated between the liver, spleen, and stomach

typical characteristics. These tumors are more common in women of childbearing age. The reported incidence is 13 per 10,000,000 in women and 2 per 10,000,000 in men [3]. Pedunculated hepatocellular adenomas are extremely rare. In our PubMed and Google Scholar search, we have found 17 reported cases in the past 25 years [1,2,4–13].

Here, we report the case of a young woman with a left subdiaphragmatic mass detected on abdominal computed tomography (CT scan) performed for preoperative evaluation of a uterine tumor. The mass was found to be a pedunculated hepatocellular adenoma, inflammatory subtype.

Case report

Our patient is a 34-year-old multiparous woman, who presented to the emergency room with symptomatic anemia due to abnormal uterine bleeding. She was otherwise healthy with no pertinent medical problems except for being overweight with a body mass index of 29.8 Kg/m^2. She denied oral contraceptives use. Hysteroscopy, dilatation, and curettage were performed. Multiple endometrial polyps and submucosal fibroids were found and biopsied. The pathology report was a uterine smooth muscle tumor of uncertain malignant potential (STUMP). A CT scan of the chest, abdomen, and pelvis with intravenous contrast was obtained to survey for metastatic lesions. In addition to multiple uterine tumors, a large left subdiaphragmatic mass, 9 cm x 6 cm x 4 cm in diameter, was seen. The tumor appeared heterogeneous in character and separate from the spleen, liver, and stomach (Fig. 1). The patient underwent a robotic-assisted hysterectomy and bilateral salpingectomy. After recovering from surgery, she was referred to the surgical oncology service for the management of the left subdiaphragmatic mass. When presented to our service, she was asymptomatic and physical exam as well as laboratory findings, including white blood cell count and hepatic function panel, were unrevealing. To further characterize the tumor a magnetic resonance imaging (MRI) without and with contrast was obtained. MRI showed a well-circumscribed enhancing mass in the left upper quadrant. There was no clear connection to the liver or spleen. The mass was adjacent to the greater curvature of the stomach (Fig. 2).

She underwent diagnostic laparoscopy. A well-circumscribed brownish mass was found. The mass was 9 cm in the greatest dimension, connected to the segment II of the liver with a vascular pedicle, and attached to the diaphragm by the left coronary ligament. Laparoscopic resection was performed. The tumor was separated from the diaphragm with the use of a bipolar sealer/divider device. A surgical stapler was used to ligate and transect the vascular pedicle. The specimen was placed in a retrieval bag and extracted by extending one of the trocar sites. The patient did well postoperatively and was discharged home the next day.

The final pathology result was hepatocellular adenoma inflammatory subtype (I-HCA), without aberrant β-catenin nuclear staining (Figs. 3 and 4).

Discussion

Pedunculated liver masses pose diagnostic dilemmas due to their extra-hepatic location, difficulties in identifying the vascular attachments to the liver, and variable imaging characteristics. This entity includes tumors with different histological features such as hemangioma, hepatocellular adenoma,

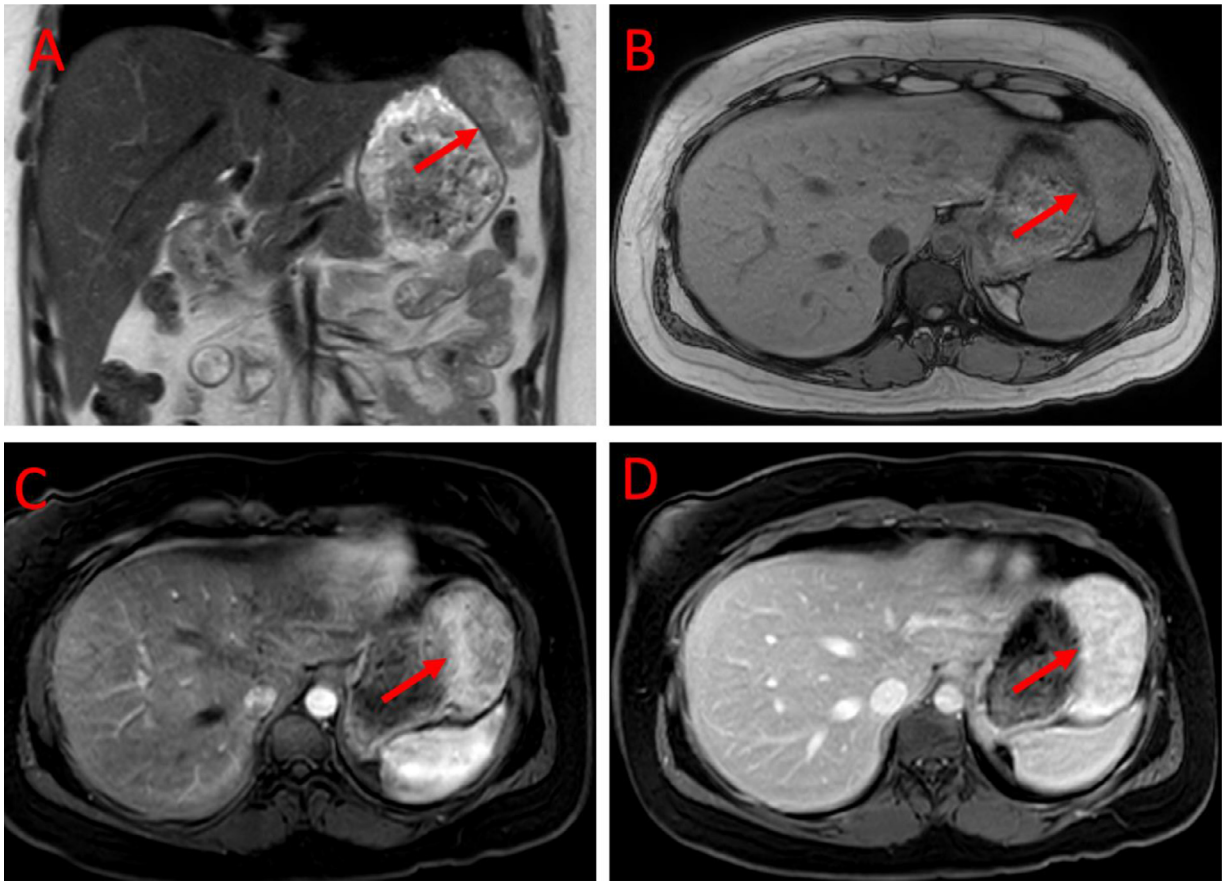

Fig. 2 – MRI of the abdomen with and without contrast. (A) T2 coronal sequence demonstrates an ovoid mass in the left upper quadrant with heterogenous T2 hyperintensity. (B) The opposed-phase axial sequence demonstrates no drop of the signal within the mass to suggest the presence of intralesional fat. (C) T1 axial fat-saturated sequence in the arterial phase demonstrates brisk heterogeneous enhancement, hyperintense to the liver, and hypointense to the adjacent spleen. (D) The delayed post-contrast sequence demonstrates persistent hyperintensity to the liver

follicular nodular hyperplasia, hepatocellular carcinoma, and other rare conditions [14].

Hepatocellular adenomas are more common in women of childbearing age. Estrogen exposure is a risk factor. There is a strong association between high dose first-generation oral contraceptives use and the development of hepatocellular adenomas [15]. Case-control studies on women taking modern low dose oral contraceptives have shown a minimal increase in risk of developing hepatocellular adenoma (hazard ratio: 1.25) [16]. Androgenic hormones in males, such as anabolic steroids used by bodybuilders, have been linked to hepatocellular adenoma and malignant transformation to hepatocellular carcinoma [17]. Glycogen storage diseases [18] and metabolic syndromes, such as diabetes mellitus and dyslipidemia, are also considered risk factors for the development and progression of hepatocellular adenoma [19,20].

There are 4 subtypes based on the presence of inactivating mutation (variation) in the hepatocyte nuclear factor1 gene, activating mutation in the β-catenin gene, or activation of inflammatory signaling pathways [20,21]. Hepatocyte nuclear factor1 gene-inactivated HCA constitutes 35%-40% of hepatocellular adenomas. The histological features are steatosis, cellular atypia, and lack of inflammation. β-catenin-activated adenomas constitute 15%-20% of cases. This subtype is more common in patients with glycogen storage disease and males on androgenic hormones. Tumors with β-catenin exon 3 mutation have a higher risk for malignant transformation to hepatocellular carcinoma [22]. Histological features are similar to Hepatocyte nuclear factor1 gene-inactivated HCA with additional findings of pseudo acinar formation. The immunohistochemistry profile is notable for strong glutamine synthase positivity and increased nuclear beta-catenin expression. The inflammatory (I-HCA) subtype constitutes 30%-35% of cases [21] and was previously known as telangiectatic follicular nodular hyperplasia [23]. This subtype is an example of inflammation-induced hepatobiliary tumors. The inflammatory subtype is more common in patients with heavy alcohol intake and higher body mass index [20,22]. Histologically, I-HCA is characterized by significant sinusoidal dilatation, polymorphous inflammatory infiltrates, areas of peliosis, and thickened tortuous arteries. These features were seen in our case. Immunohistochemistry profile is notable for diffuse strong serum amyloid protein A and C expressions and CD34 reactivity around pseudo portal tracts. The

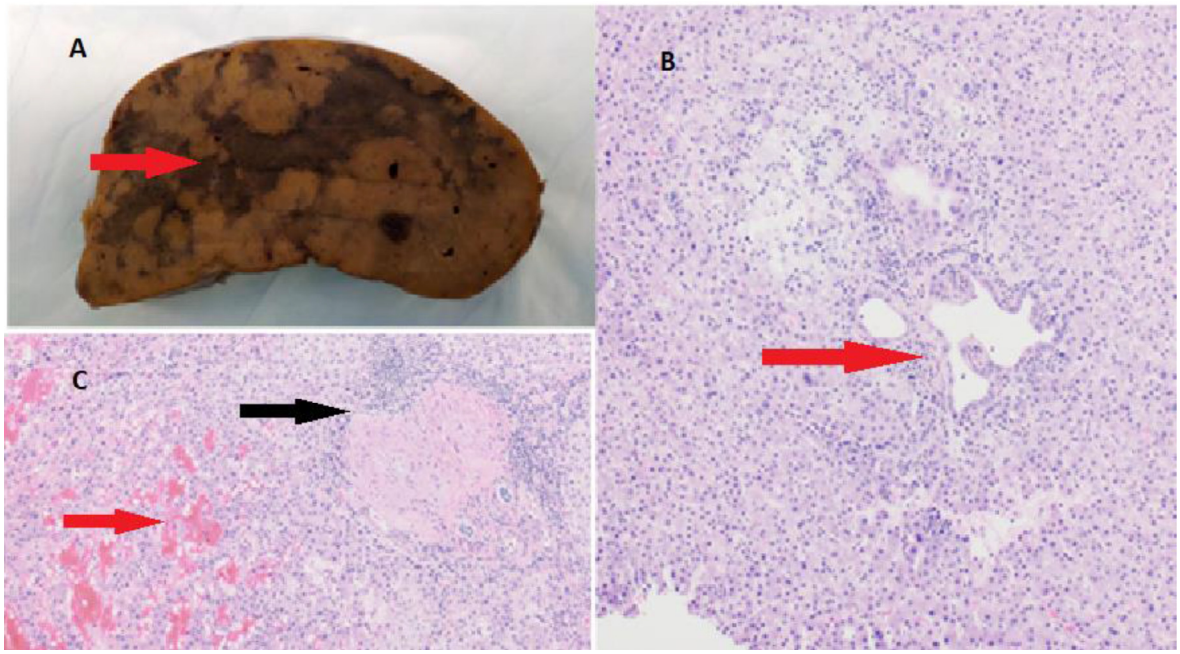

Fig. 3 – Gross and microscopic hematoxylin and eosin staining appearances. (A) Cross-section of the tumor appearing as alternating pale and dark red foci are shown. Arrow points to the area of hemorrhage. (B) The arrow shows an area of telangiectasia. (C) HCA is composed of one to 2 plate liver cells. Red arrow: Dilated sinusoids. Black arrow: Area of chronic inflammatory infiltration with arterialized blood vessels.

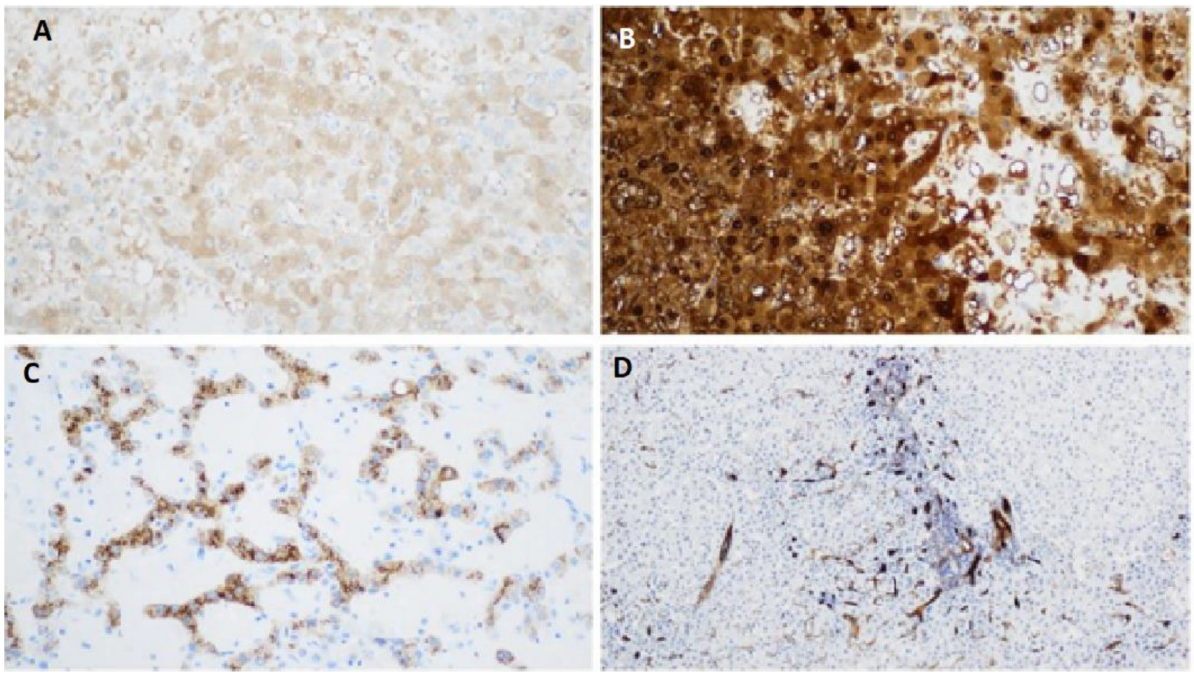

Fig. 4 – IHC staining. (A) Scattered large foci of positive cytoplasmic staining for C reactive protein (CRP). (B) liver fatty acid binding protein (LFABP) is retained in the hepatocytes. (C) Negative staining for Serum Amyloid A (SAA) in the hepatocytes is shown. (D) Increased vascularity and arterialized blood vessels are confirmed by CD34

unclassified subtype accounts for 10% of hepatocellular adenomas. There are no specific genetic alterations or unique morphologic features. The sonic hedgehog pathway is activated in 1/3 of unclassified hepatocellular adenomas [22], which is referred to as Sonic Hedgehog HCA. The activation of this pathway is associated with an increased risk of tumor hemorrhage.

Hepatocellular adenomas are often found incidentally on cross-sectional imaging and present diagnostic challenges due to similarities to hepatocellular carcinomas. CT and MRI characteristics are significant for enhancement following intravenous contrast administration with a return to background liver signal intensity on delayed sequences. The presence of diffuse intratumoral fat is a helpful distinguishing factor and is readily identifiable on opposed-phase MRI sequences in most cases, however, this feature is seen in only 17% of I-HCAs [24].

Hepatocellular adenomas are usually hypoattenuating on noncontrast CT but may appear iso- or hyperattenuating based on the extent of fatty infiltration of the background liver parenchyma. Hepatocellular adenomas are commonly heterogeneous on nonenhanced and contrast-enhanced CT. This feature is more prominent in larger tumors and was observed in our case. Intra-tumoral hemorrhage is seen as an area of hyper-attenuation. On contrast-enhanced CT, the lesions are mostly hypervascular and heterogeneous in the arterial phase and become iso- to hypoattenuating in the portal venous phase. Our case demonstrated heterogeneous hyperenhancement on the venous-phase CT performed during the workup of the uterine STUMP, appearing as a well-circumscribed mass in the left upper quadrant (Fig. 1). The vascular pedicle connecting the mass to the liver was not easily identifiable on cross-sectional imaging, and the close association of the tumor to the diaphragm and greater curvature of the stomach raised the possibility of a metastatic lesion from uterine STUMP. MRI is the preferred imaging modality to differentiate hepatocellular adenomas from other liver lesions and distinguish between various subtypes. Hepatocellular adenomas are most often hyperintense to background liver on T2 sequence, a feature that was visualized in this case (Fig. 2A). The “atoll sign” is considered characteristic of the inflammatory subtype and consists of a rim of T2 hyperintensity and central hypo-intensity, but this was not observed in this case. No intratumoral fat was noted on the opposed-phase sequence (Fig. 2B). Brisk arterial enhancement is characteristic and was observed in this mass, but a return to background liver enhancement was not noted on the delayed sequence (Fig. 2C and D).

The management plan is based on clinical presentation and risk stratification. Sex, molecular subtype, number, and size of the tumors should be considered. Malignant transformation and hemorrhage are 2 main complications. Overall, the malignant transformation of hepatocellular adenoma is a rare phenomenon and, even in men with metabolic syndrome, is seen in less than 5% of cases [25]. Underlying risk factors such as obesity, intake of oral contraceptives, or anabolic steroids should be identified and mitigated. An image-guided biopsy will provide tissue for histological diagnosis and molecular subtyping. In men, surgical resection of any hepatocellular adenoma is recommended due to the higher risk for malignant degeneration. In women, molecular subtype and size should be considered. Surgery is offered for tumors 5 cm or larger and for any tumor with mutations in β-catenin exon 3 or alterations of sonic hedgehog pathway regardless of size. For hepatocellular adenomas without high-risk features, discontinuation of oral contraceptives and a 6-12-month period of observation could be offered to evaluate for regression of the mass [26]. Most of the pedunculated hepatocellular adenomas are amenable to laparoscopic resection with a favorable outcome.

Conclusion

Our report highlights the diagnostic pitfalls when dealing with pedunculated liver masses, especially hepatocellular adenomas. These tumors are rare and often found incidentally during abdominal imaging. Radiologic findings depend on the underlying histology, intratumoral hemorrhage, and relation of the mass to the surrounding structures. Hepatocellular adenomas appear as well-circumscribed lesions with heterogeneity on cross-sectional imaging. Radiologic appearance is nonspecific in many cases, varies in different subtypes, and may be indistinguishable from hepatocellular carcinoma. When encountering a perihepatic mass, pedunculated liver tumors should be considered in the differential diagnosis even if a vascular connection to the liver is not identified. Image-guided biopsy establishes the histological diagnosis and allows for genomic analysis of the tumor. This is of the utmost importance when considering conservative management in women of childbearing age with smaller tumors.

REFERENCES

[1] Portinari M, Liboni A, Feo CV. Strangulated adenoma of the liver: a unique cause of acute abdomen. Ann Ital Chir 2014;85(ePub) S2239253X14022439.
[2] Grieser C, Denecke T, Schmidt S. An unusual cause of recurrent acute abdominal pain. Gastroenterology 2012;142(4):E5–6. doi:10.1053/j.gastro.2011.09.008.
[3] Bossen L, Grønbaek H, Lykke Eriksen P, Jepsen P. Men with biopsy-confirmed hepatocellular adenoma have a high risk of progression to hepatocellular carcinoma: A nationwide population-based study. Liver Int 2017;37(7):1042–6. doi:10.1111/liv.13423.
[4] Kawabe N, Higashiguchi T, Yasuoka H, Kawai T, Kamio K, Ochi T, et al. A case of hepatocellular adenoma with pedunculated development and difficulty in diagnosis. Fujita Med J 2020;6(1):21–6. doi:10.20407/fmj.2019-005.
[5] Khiro FI, Jasim HA. Pedunculated hepatocellular adenoma: a presentation of a rare disease. Iraqi Med J 2019;65(2):178–81. http://imj.edu.iq/index.php/imj/article/view/420 Accessed June 29, 2020.
[6] Dokmak S, Aussilhou B, Rasoaherinomenjanahary F, Ronot M, Dahdouh R, Ftériche F, et al. Hemorrhage of hepatocellular adenoma: a complication that can be treated by conservative management without surgery. HPB (Oxford) 2018;20(12):1198–205. doi:10.1016/j.hpb.2018.06.1796.
[7] Vargas-Flores E, Pérez-Aguilar F, Valdez-Mendieta Y. Adenoma hepático extracapsular. Reporte de un caso y

revisión de la bibliografía [Extracapsular hepatic adenoma. Case report and literature review]. Cir 2017;85(2):175–80. doi:10.1016/j.circir.2015.12.006.
[8] Patil RS, Andola SK, Gupta N, et al. Pedunculated hepatocellular adenoma in an accessory lobe of liver presenting as mesenteric mass: a rare case report. Int J Res Health Sci 2013;1(3):227–30. http://ijrhs.org/article/2013/1/3-15 Accessed June 29, 2020.
[9] Abdulkader I, Suárez-Peñaranda M, Pérez-Becerra E, Baltar J, Pazos G, Forteza J. Liver-cell adenomas with heavy iron deposition. Int J Surg Pathol 2004;12(3):245–50. doi:10.1177/106689690401200305.
[10] Lazaridis C, Papaziogas B, Brauer RB, Alexandrakis A, Papaziogas T. Gestiltes adenoma der leber [Pedunculated adenoma of the liver]. Viszeralchirurgie 2000;35(5):342–4. doi:10.1055/s-2000-8046.
[11] Bader TR, Braga L, Semelka RC. Exophytic benign tumors of the liver: appearance on MRI. Magn Reson Imaging 2001;19(5):623–8. doi:10.1016/s0730-725x(01)00384-8.
[12] Ye MQ, Suriawinata A, Haim MB, Parsons R, Schwartz ME. A 42-year-old woman with liver masses and long-term use of oral contraceptives. Semin Liver Dis 1999;19(3):339–44. doi:10.1055/s-2007-1007123.
[13] Grazioli L, Federle MP, Brancatelli G, Ichikawa T, Olivetti L, Blachar A. Hepatic adenomas: imaging and pathological findings. Radiographics 2001;21(4):877–92. doi:10.1148/radiographics.21.4.g01jl04877.
[14] Kim HJ, Lee DH, Lim JW, Ko YT, Kim KW. Exophytic benign and malignant hepatic tumors: CT imaging features. Korean J Radiol 2008;9(1):67–75. doi:10.3348/kjr.2008.9.1.67.
[15] Edmondson HA, Henderson B, Benton B. Liver-cell adenomas associated with use of oral contraceptives. N Engl J Med 1976;294:470–2. doi:10.1056/NEJM197602262940904.
[16] Heinemann LA, Weimann A, Gerken G, Thiel C, Schlaud M, DoMinh T. Modern oral contraceptive use and benign liver tumors: the German benign liver tumor case-control study. Eur J Contracept Reprod Health Care 1998;3(4):194–200. doi:10.3109/13625189809167253.
[17] Velazquez I, Alter BP. Androgens and liver tumors: Fanconi's anemia and non-Fanconi's conditions. Am J Hematol 2004;77(3):257–67. doi:10.1002/ajh.20183.
[18] Labrune P, Trioche P, Duvaltier I, Chevalier P, Odièvre M. Hepatocellular adenomas in glycogen storage disease type I and III: a series of 43 patients and review of the literature. J Pediatr Gastroenterol Nutr 1997;24(3):276–9. doi:10.1097/00005176-199703000-00008.
[19] Zucman-Rossi J, Jeannot E, Van Nhieu JT, Scoazec JY, Guettier C, Rebouissou S, et al. Genotype-phenotype correlation in hepatocellular adenoma: new classification and relationship with HCC. Hepatology 2006;43(3):515–24. doi:10.1002/hep.21068.
[20] Bioulac-Sage P, Rebouissou S, Thomas C, Blanc JF, Saric J, Sa Cunha A, et al. Hepatocellular adenoma subtype classification using molecular markers and immunohistochemistry. Hepatology 2007;46(3):740–8. doi:10.1002/hep.21743.
[21] Dhingra S, Fiel MI. Update on the new classification of hepatic adenomas: clinical, molecular, and pathologic characteristics. Arch Pathol Lab Med 2014;138(8):1090–7. doi:10.5858/arpa.2013-0183-RA.
[22] Nault J, Couchy G, Balabaud C, Morcrette G, Caruso S, Blanc JF, et al. Molecular classification of hepatocellular adenoma associates with risk factors, bleeding, and malignant transformation. Gastroenterology 2017;152(4):880–94. doi:10.1053/j.gastro.2016.11.042.
[23] Bioulac-Sage P, Rebouissou S, Sa Cunha A, Jeanot E, Blanc J, Blanché H, et al. Clinical, morphologic, and molecular features defining so-called telangiectatic focal nodular hyperplasias of the liver. Gastroenterology 2005;128(5):1211–18. doi:10.1053/j.gastro.2005.02.004.
[24] van Aalten SM, Thomeer MG, Terkivatan T, Dwarkasing RS, Verheij J, de Man RA, et al. Hepatocellular adenomas: correlation of MR imaging findings with pathologic subtype classification. Radiology 2011;261(1):172–81. doi:10.1148/radiol.11110023.
[25] Farges O, Dokmak S. Malignant transformation of liver adenoma: an analysis of the literature. Dig Surg 2010;27(1):32–8. doi:10.1159/000268405.
[26] Védie AL, Sutter O, Ziol M, Nault JC. Molecular classification of hepatocellular adenomas: impact on clinical practice. Hepat Oncol 2018;5(1) HEP04. doi:10.2217/hep-2017-0023.