

CASE REPORT

A case of extensive hepatic adenomatosis in a renal transplant patient

Ming-Jim Yang¹, David Hernandez-Gonzalo², and Elizabeth M. Thomas^{3,*}

¹Department of Family Medicine, University of Florida, 1600 SW Archer Rd, Gainesville, FL 32605, USA,

²Department of Pathology, University of Florida, 1600 SW Archer Rd, Gainesville, FL 32605, USA, and

³Department of Surgery, University of Florida, 1600 SW Archer Rd, Gainesville, FL 32605, USA

*Correspondence address. Department of Surgery, University of Florida, 1600 SW Archer Rd, Gainesville, FL 32605, USA. Tel: +1-352-265-0606; Fax: +1-352-265-0678; E-mail: Elizabeth.Thomas@surgery.ufl.edu

Abstract

Hepatic adenomatosis (HA) is a rare condition that is traditionally associated with oral contraceptive use, glycogen storage diseases or metabolic syndrome. Here we present a renal transplant recipient that was diagnosed with HA and has none of the traditional risk factors. We review the literature on diagnosing and managing HA.

INTRODUCTION

Hepatocellular adenomas (HCA) are primary epithelial neoplasms of the liver that are mostly benign and have been traditionally associated with oral contraceptive (OCP) or steroid use, and more recently, obesity and metabolic syndrome. Hepatic adenomatosis (HA) is a rare condition in which >10 adenomas are found throughout the liver. Here, we present a renal transplant recipient with no traditional risk factors, who presents with an incidental finding of HA.

CASE PRESENTATION

The patient is a 41-year-old female with a past medical history of a living-unrelated renal transplant for end-stage renal disease due to focal glomerulosclerosis. During evaluation for pyelonephritis, a CT scan found multiple non-cystic liver lesions in both lobes. Her medications were significant for maintenance immunosuppression, consisting of tacrolimus 1 mg, cellcept 500 mg, prednisone 5 mg. She denied any history of hepatitis, OCP use or diabetes. Her BMI was 26. She was referred to the hepatobiliary clinic where her initial work-up consisted of lab work, colonoscopy, ultrasound and MRI. Her AFP and CEA were

normal at 2.3 and 0.8, respectively. Her colonoscopy was normal. An ultrasound revealed multiple echogenic round lesions in both lobes with no ductal dilatation. An MRI showed ~50 hyperintense lesions measuring up to 1 cm in both right and left lobes (Fig. 1). A percutaneous liver biopsy was found to be normal hepatic parenchyma. She was managed expectantly for a year until a follow-up MRI showed an increase in size and number of her liver lesions, some of which contained a fatty component.

Given the sheer number of her lesions, a multidisciplinary group at our institution decided that a tissue type and specifically a genetic type diagnosis was required to rule out her risk of malignant transformation. A laparoscopic left lateral wedge resection was thus performed in order to obtain adequate tissue for diagnosis. The patient tolerated the procedure well and was discharged from the hospital after a 3-day hospital stay.

Pathological analysis showed well circumscribed, but non-encapsulated liver lesions, comprised of cords of benign hepatocytes (Fig. 2a). The hepatocytes had regular, uniform nuclei and a low nuclear to cytoplasmic ratio. The lesions lacked portal structures and had evidence of unpaired arteries. Moderate microvesicular steatosis was noted within the lesions but none within the uninvolved liver parenchyma. Mitoses or pseudoacinar changes

Received: June 17, 2018. Accepted: July 25, 2018

Published by Oxford University Press and JSCR Publishing Ltd. All rights reserved. © The Author(s) 2018.

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/4.0/>), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited. For commercial re-use, please contact journals.permissions@oup.com

were not identified (Fig. 2b). Immunohistological analysis showed no liver fatty acid binding protein (LFABP) staining (Fig. 2c) and had no nuclear localization of β -catenin (Fig. 2d). These characteristics were consistent with hepatocellular adenoma, HNF1A type.

DISCUSSION

Here, we present a unique case of HA in a renal transplant recipient without any other risk factors. Only one other case of HA in a renal transplant recipient has been described in the literature. Liao et al. described a young man with idiopathic end-stage renal disease who underwent a cadaveric renal transplant. A little more than 3 years after his transplantation, he was found to have multiple lesions in his liver during a routine ultrasound. Just as with our patient, he had no history of hepatitis, diabetes or androgenic steroid use. Per the case report, because there was

a concern for possible ‘dysplasia’ on a biopsy, he underwent resection of his tumors. His pathology showed a non-mutated, non-inflammatory hepatocellular adenoma [1].

HA was first described by Flejou et al. in 1985. In their case series, they described five patients who presented with ‘numerous benign adenomas in an otherwise normal hepatic parenchyma’ [2]. At the time, they believed that HA was a distinct entity from singular HCA because it seemed to occur in both men and women, and was less strongly associated with OCPs [2]. Once we were able to molecularly classify the individual tumors, the way we approach and think of HA has changed. Four common genetic subtypes are commonly accepted: (i) HNF1 α mutations, (ii) β -catenin mutations, (iii) no mutations but with inflammatory infiltration and (iv) no mutation and no inflammation. Malignant transformation is known to occur in any subtype but most often in the beta-catenin and inflammatory subtypes.

Management of HA now revolves around the molecular phenotype of the individual tumors [3]. Historically, any HCA >5 cm would be considered for resection due to an increased risk for hemorrhage [4, 5]. More recently, Nault et al. has proposed a more personalized approach towards treating HCA’s. Because of the new classification scheme, they proposed treating HCA’s based on their genotype. They recommended surgical resection for high risk lesions such as β -catenin—type HCA’s and/or any HCA >5 cm. Other studies have suggested routinely resecting all male patients with HA [6]. The other types of HCA’s (classes 1, 3, 4) can be managed conservatively with MRI surveillance and by stopping causative agents such as OCPs or androgenic steroids [6]. Because our patient did not have any of the known risk factors or prognostic indicators of HA but her subtype turned out to be an HNF1a subtype, we opted for conservative monitoring with MRI’s annually.

We have thus presented a unique situation in which a patient with a renal transplant on immunosuppression and who has no

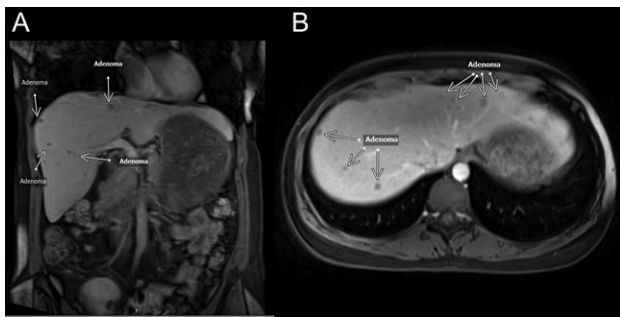


Figure 1: MRI—coronal (A) and transverse (B) MRI sections showing multiple lesions within both lobes of the liver. White arrows mark lesion locations. Per radiology notes, each lesion measured from 0.5 to 1.5 cm in diameter. There were at least 50 lesions in total.

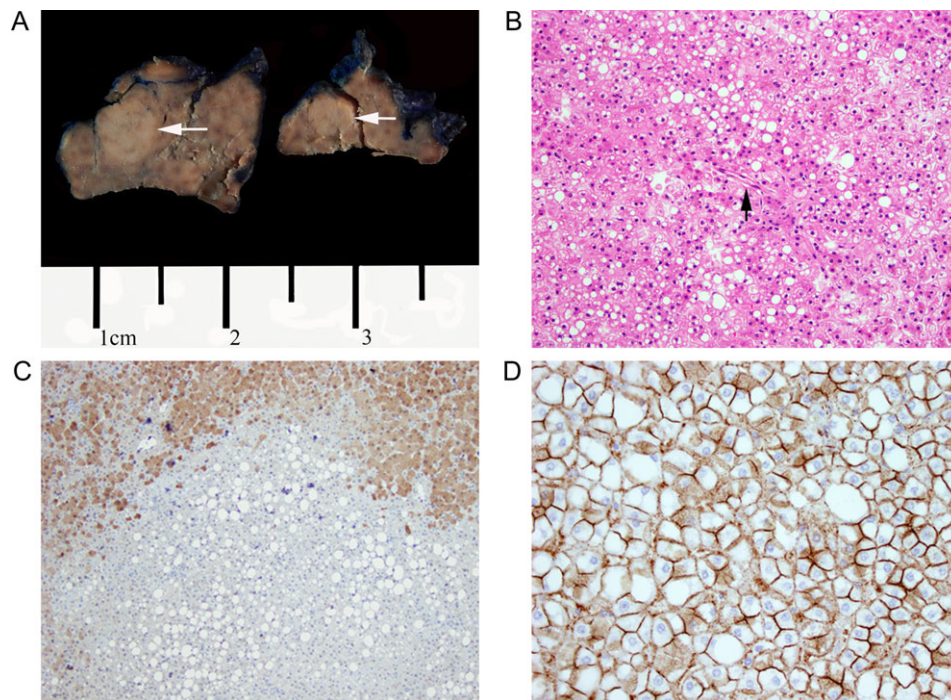


Figure 2: (A) Gross section of left lateral segment showing hepatic adenoma. White arrows indicate adenoma location. (B) H&E stain of hepatic adenoma section. Note diffuse lipid deposition within the adenoma itself and an unpaired artery without other portal structures. Magnification at $\times 20$. (C) LFABP stain. Diffuse LFABP staining was noted within the surrounding liver parenchyma. No staining was seen within the adenoma itself. Magnification at $\times 10$. (D) Beta-catenin staining. Immunochemical stain for beta-catenin showed no nuclear localization. Magnification at $\times 40$.

other traditional risk factors presents with HA. Her case along with the one other case in the literature indicates a possible role that immunosuppression may play in contributing towards adenoma formation. This event is most likely very rare as there are only two case studies at this time. The fact that this occurs though may guide us in understanding the molecular pathogenesis of HCA's and further elucidate this interesting clinical process.

CONFLICT OF INTEREST STATEMENT

None declared.

REFERENCES

1. Liao YT, Jeng YM, Lee YH, Tsai MK, Hu RH, Ho MC. The occurrence of primary hepatic adenoma in deceased donor renal transplant recipient. *Int Braz J Urol* 2014;**40**:118–22.
2. Flejou JF, Barge J, Menu Y, Degott C, Bismuth H, Potet F, et al. Liver adenomatosis. An entity distinct from liver adenoma? *Gastroenterology* 1985;**89**:1132–8.
3. Veteläinen R, Erdogan D, de Graaf W, ten Kate F, Jansen PL, Gouma DJ, et al. Liver adenomatosis: re-evaluation of aetiology and management. *Liver Int* 2008;**28**:499–508.
4. Deneve JL, Pawlik TM, Cunningham S, Clary B, Reddy S, Scoggins CR, et al. Liver cell adenoma: a multicenter analysis of risk factors for rupture and malignancy. *Ann Surg Oncol* 2009;**16**:640–8.
5. Agrawal S, Agarwal S, Amason T, Saini S, Belghiti J. Management of hepatocellular adenoma: recent advances. *Clin Gastroenterol Hepatol* 2014;**13**:1221–30.
6. Nault JC, Bioulac-Sage P, Zucman-Rossi J. Hepatocellular benign tumors—from molecular classification to personalized clinical care. *Gastroenterology* 2013;**144**:888–902.