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REVIEW

Hepatocellular adenomas (HCAs) and pregnancy

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INTRODUCTION

Hepatocellular adenomas (HCAs) are benign liver lesions that can present as incidental liver lesions, with abdominal pain, or rarely with bleeding or rupture. The risk of HCA bleeding is related to the size of the lesion with increased risk when >5 cm. Distinct molecular subclassifications result in histologic, radiographic, and clinically distinct groups, including a small subset of HCAs that contain beta-catenin activation on exon 3 that increases the risk of malignant transformation.[1] HCA management is determined by lesion size, growth pattern, patient sex, and the presence of beta-catenin activation. The main risk factor for adenoma development is estrogen exposure by means of the use of combined hormonal contraceptives (CHCs). Pregnancy as a period of high estrogen exposure and hyperdynamic circulation raises concerns regarding HCA growth and the risk of bleeding. Pregnancy-related considerations for HCA management are dependent on lesion size, with lesions <5 cm having low bleeding risk.[2]

HCA BEHAVIOR AND MANAGEMENT PRIOR TO PREGNANCY

Exogenous and endogenous estrogen exposure is the main risk factor for HCA development. There are growing data on the relationship between HCAs and endogenous estrogens from excess adipose tissue in obesity and the beneficial effect of weight loss on HCA regression.[3] Exogenous estrogens, particularly in the form of CHCs, are associated with increased risk of HCA development with a rate of 3–4 per 100,000.[4] Cessation of CHCs can result in regression and resolution of some HCAs.[3]

Two recent studies underscore the relationship between exogenous hormones and HCAs. A retrospective cohort study from 2000 to 2019 of 183 patients with 267 histologically confirmed HCAs assessed outcomes of malignant transformation (6%), symptomatic bleeding (11%), and HCA growth patterns after cessation of CHCs.[3] The growth pattern was monitored in 120 patients who discontinued CHCs and were followed for a median of 5 years: 22% had progressive disease, 47% had stable disease, and 31% had partial or complete resolution. The authors developed an estrogen exposure score to predict HCA regression that accounted for duration of estrogen use and BMI. Of the 13 women who had HCAs after transitioning to progestin-only contraception, 10 women had stability, 2 had regression, and 1 had progression. Additional data regarding progestin-only contraception were outlined in a cohort of 27 patients accounting for 34 discrete time periods of hormone exposure between 2003 and 2021. This study showed the median percent change of HCAs in those on progestin-only contraception was −15% which was similar to those with no exogenous hormonal exposure at −7.4%, whereas it was 29.4% in periods of exogenous estrogen exposure.[5]

These studies support the recommendation to discontinue estrogen-containing CHCs in patients with HCAs; however, progestin-only containing contraceptives may be considered while awaiting further study. Expert opinion recommends women be monitored off CHCs for 6–12 months prior to pregnancy to establish baseline HCA size. Assessment of baseline HCA size prior to pregnancy is important to stratify for management. Up to three-fourths of women know of their HCA diagnosis prior to pregnancy.[2] American Association for the Study of Liver Diseases (AASLD) guidelines (Figure 1) recommend treatment of HCA larger than 5 cm prior to pregnancy, whereas women with lesions

Abbreviations: CHCs, combined hormonal contraceptives; HCA, hepatocellular adenomas.

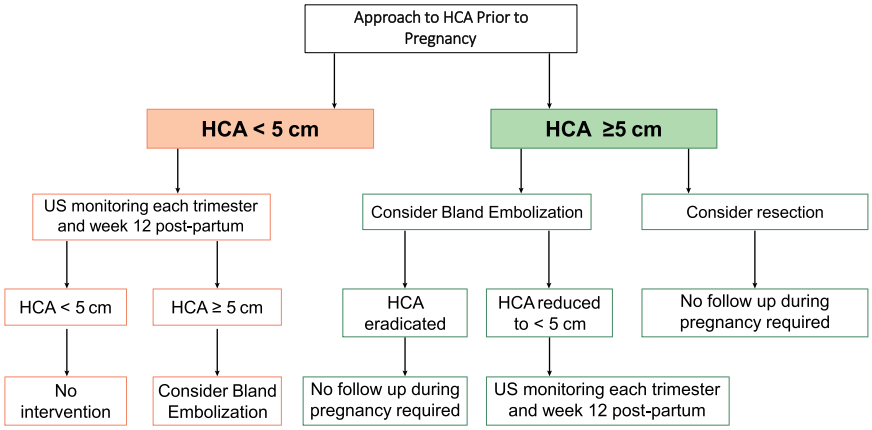

FIGURE 1 Approach to hepatocellular adenoma prior to and during pregnancy. Reprinted with permission from Sarkar et al. Reproductive Health and Liver Disease: Practice Guidance by the American Association for the Study of Liver Diseases. Hepatology 73(1):318-365, January 2021.[6] Abbreviations: HCA, hepatocellular adenomas; US, ultrasound.

<5 cm may proceed with pregnancy with close observation.[6]

HCA BEHAVIOR AND MANAGEMENT DURING PREGNANCY

Pregnancy is characterized by high estrogen levels and hyperdynamic circulation, which raises concern about HCA growth and possible bleeding. The largest prospective study to assess for growth patterns during pregnancy included 48 women during 51 pregnancies enrolled from 2011 to 2019 with lesions <5 cm.[2] The authors followed women throughout pregnancy with ultrasound at 14 +/−3, 20, 26, 32, and 38 weeks and 6–12 weeks postpartum. The median HCA size was 2.3 cm prior to pregnancy, and 25% had growth (defined as 20% increase in lesion size), 53% remained stable, and 22% regressed (defined as a decrease of 30%). Growth occurred between 14 and 32 weeks. One patient who had growth of a lesion to over 5 cm (from 4.9 to 7.6 cm) was treated with prophylactic embolization at 26 weeks. Similar predictions of HCA behavior were shown in a systematic review of 73 pregnancies including those of the aforementioned prospective cohort: 32% progressed, 53% were stable, 15% regressed.[7] If growth is suspected on ultrasound, confirmation of lesion size can be assessed with a noncontrast MRI (gadolinium is contraindicated in pregnancy).

Our understanding of the risk of HCA bleeding during pregnancy has evolved since early studies in the 1970s and 1980s that suggested high bleeding rates and maternal and fetal mortality[8] to more contemporary analyses that show a much lower bleeding risk that is dependent on lesion size.[2,7,9] There were no bleeding events in a 2011 prospective study of 17 pregnancies with 5 patients having HCAs over 5 cm.[9] One patient was prophylactically treated with ablation in the first trimester to prevent growth. Likewise, there were no bleeding events in the prospective study of 51 pregnancies of lesions <5 cm.[2] In a systematic review of 99 pregnancies, 15 HCA-related bleeds were reported all in lesions >6.5 cm: 8 during pregnancy (7 in the third trimester), 2 during labor, and 5 postpartum (4 within the first 2 weeks).[7] The risk of bleeding postpartum may be related to the estrogen withdrawal and its effects on lesion behavior.

Taken together, these data support the AASLD guideline recommendation that women with HCAs <5 cm can proceed with pregnancy.[6] For patients with lesions over 5 cm, intervention is considered carefully based on the risk-benefit profile to the mother and fetus. Embolization is a potential treatment option prophylactically for large HCAs over 5 cm or in the case of bleeding HCA. The optimal timing for embolization is after 26 weeks gestation given the risk of radiation exposure to the fetus. Resection is rarely indicated, but if required it should be considered in the early second trimester. Case series and reviews include outcomes for intervention for bleeding HCA during pregnancy with resection or embolization,[7] though many of the cases occurred prior to the 2000s and do not reflect modern advances in interventional radiology, surgical, and intensive care management. A key to optimizing maternal and fetal outcomes is early recognition of HCA bleeding as a potential cause of abdominal pain and/or shock in pregnant patients.

CONFLICTS OF INTEREST

The author has no conflicts to report.

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