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Short Communication

Hepatocellular Adenoma and IVF

Michelle Jones-Pauley[1], Lissa Franco[1] and David W Victor III[1,2]*

[1]*Houston Methodist Hospital, United States*

[2]*Sherrie and Alan Conover Center for Liver Disease and Transplantation, Houston Methodist Hospital, USA*

***Corresponding author:** David W Victor III, Hepatology and Transplant Medicine, Houston Methodist Hospital, United States

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Abstract

One to three percent of live births in the US and Europe are currently brought about with assisted reproductive technologies such as in vitro fertilization (IVF). IVF primarily utilizes fertility hormones, such as LH, FSH and Estrogen to promote ovulation and thus fertility. The effect of estrogen on hepatocellular adenoma (HA) growth is well established through many studies analyzing the relationship between oral contraceptives (OCPs) and hepatocellular adenoma since the 1970s. No current guidelines address IVF and screening or follow up of hepatocellular adenomas. We recommend consider ultrasound screening evaluation and follow up ultrasounds for know hepatocellular adenoma for patients undergoing IVF.

Introduction

One to three percent of live births in the US and Europe are currently brought about with assisted reproductive technologies such as in vitro fertilization (IVF) [1]. IVF primarily utilizes fertility hormones, such as LH, FSH and Estrogen to promote ovulation and thus fertility. The effect of estrogen on hepatocellular adenoma (HA) growth is well established through many studies analyzing the relationship between oral contraceptives (OCPs) and hepatocellular adenoma since the 1970s [2-4]. Although they are largely benign, hepatocellular adenomas can have severe consequences such as malignant transformation, rupture, and spontaneous haemorrhage [5]. These neoplasms are associated most commonly with prolonged oral contraceptive use, glycogen storage diseases, and anabolic androgens [6]. However, they can arise in other high-estrogen states, such as pregnancy [7]. Given this association, should women desiring IVF be screened for HA prior to starting IVF treatment?

IVF consists of multiple protocols, one of which includes a course of Gonadotropin Releasing Hormone (GnRH) analogs followed by a course of clomiphene, a selective estrogen receptor modulator (SERM). The mechanism of action for clomiphene takes place in the hypothalamus, where clomiphene binds estrogen receptors for a prolonged amount of time. While bound to the receptor, the drug mimics estrogen and has an amplified effect as compared to the steroid alone [8]. In a letter to the editor of the NEJM, a group of physicians wrote of the apparent association between the treatment of a young woman with clomiphene (who had no previous exposure to OCPs) and a large HA (10cm x 20cm) [9]. While there are no studies directly observing an effect of clomiphene on HA, there is a documented case of tamoxifen, another SERM, inducing growth of HA by an undefined mechanism [10]. One case study from Brazil did find an apparent association between IVF and the presumed progression of HA into Hepatocellular carcinoma [11].

Hepatic adenomas have a known association with oral contraceptives (OCPs) as described in multiple studies since the 1970s [2-4]. The proposed mechanism is based on the increased presence of nuclear estrogen receptors within hepatocellular adenoma cells as compared to normal hepatocytes [10]. This over expression of receptors allows the cells to respond to estrogens growth promoting properties and stimulates growth of the HA as a whole. There are many established associations between OCPs and HA growth, and even a case report establishing a connection between regressions of HA size after removing OCP exposure [12]. However, when it comes to pregnancy there is no predictable pattern of adenoma behaviour. In two cases of hepatic adenoma in pregnancy, the adenomas ruptured and required emergent surgical repair [5].

In a retrospective case review of 17 pregnancies with hepatic adenoma, 2 required caesarean section at 34 and 36 weeks (prior to threatened rupture), 1 underwent radiofrequency ablation and 14 others were simply monitored closely without ill effect [13]. The risk of HA rupture does appear to be associated with the size of the adenoma and also recent hormone exposure [14]. HA's tend to present as either abdominal pain, an incidental imaging finding, or sudden collapse causing hemodynamic instability. There are rarely liver enzyme derangements and some women may not even be

symptomatic with smaller lesions. With these facts in mind, screening women pursuing IVF (particularly those who previously used OCPs) with ultrasound prior to starting IVF should be considered.

Recommendations are somewhat lacking regarding the screening of IVF candidates for hepatic lesions. The American College of Obstetricians and Gynaecologists currently has no guidelines regarding screening for HA prior to IVF commencement. The American College of Gastroenterology currently recommends monitoring of known HA in pregnant women with ultrasound but gives no recommendation for screening prior to starting IVF [15]. Given the known association between estrogen and HA growth, perhaps a screening modality (such as hepatic ultrasound) should be employed to further direct management of HA in women desiring IVF..

References

1. Paulson R (2018) In Vitro Fertilization.
2. Fitz JG (1984) Oral Contraceptives and Benign Tumors of the Liver. West Journal of Medicine 140(2): 260-267.
3. Rooks JB, Ory H (1979) Epidemiology of Hepatocellular Adenoma. Jama 242(7): 644-648.
4. Vana J, Murphy GP, Aronoff BL, Baker HW (1979) Survey of primary liver tumors and oral contraceptive use. Journal of Toxicology and Environmental Health 5(2-3): 255-273.
5. Monks PL, Fryar BG, Biggs WW (1986) Spontaneous Rupture of an Hepatic Adenoma in Pregnancy with Survival of Mother and Fetus. The Australian and New Zealand Journal of Obstetrics and Gynaecology 26(2): 155-157.
6. Curry MP, Afdhal NH (2018) Hepatic Adenoma.
7. Kent DR, Nissen ED, Nissen SE, Ziehm DJ (1978) Effect of Pregnancy on Liver Tumor Associated with Oral Contraceptives. Obstetrics and Gynecology 51(2): 148-151.
8. Clomiphene (2018) Drug Information.
9. Carrasco D, Barrachina M, Prieto M, Berenguer J (1984) Clomiphene Citrate and Liver-Cell Adenoma. New England Journal of Medicine 310(17): 1120-1121.
10. Porter LE, Elm MS, Thiel DH, Eagon PK (1987) Hepatic estrogen receptor in human liver disease. Gastroenterology 92(3): 735-745.
11. Amarante Marcus Paulo Fernandes, Renata D`Alpino Peixoto, Marcos Belotto, Marcelo Rocha de Sousa Cruz (2015) Hepatocellular Carcinoma Related to Attempt of Fertilization: a Case Report. Case Reports in Clinical Pathology 3(1).
12. Sinclair M, Schelleman A, Sandhu D, Angus PW (2017) Regression of hepatocellular adenomas and systemic inflammatory syndrome after cessation of estrogen therapy. Hepatology 66(3): 989-991.
13. Aalten SV, Noels JE, Windt DV, Kok N, Man RD, et al. (2010) Management Of Hepatocellular Adenoma During Pregnancy. Journal of Hepatology 54(3): 553-558.
14. Deneve JL, Pawlik TM, Cunningham S, Clary B, Reddy S, et al. (2009) Liver Cell Adenoma: A Multicenter Analysis of Risk Factors for Rupture and Malignancy. Annals of Surgical Oncology 16(3): 640-648.
15. Tran TT, Ahn J, Reau NS (2016) Corrigendum: ACG Clinical Guideline: Liver Disease and Pregnancy. The American Journal of Gastroenterology 111(11): 1668-1668.

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