

High Grade Dysplastic Nodule in a Non-Cirrhotic Liver in the Young

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Received: 08 Sep 2021

Accepted: 18 Sep 2021

Published: 23 Sep 2021

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Keywords:

Hepatocellular Carcinoma; HCC in The Young; Hepatectomy with Caudate Lobectomy; High Grade Dysplastic Nodule

Citation:

Choudry M. High Grade Dysplastic Nodule in a Non-Cirrhotic Liver in the Young. *Ame J Surg Clin Case Rep.* 2021; 3(13): 1-3

1. Abstract

Patients with high grade dysplastic nodule (HGDN) have an increased risk for development of hepatocellular carcinoma. Hepatocellular carcinoma (HCC) in a young patient with no cirrhosis or fibrosis is a relatively rare condition. HCC develops in patients in the setting of liver cirrhosis with established risk factors related to various etiologies including hepatitis virus infection, high alcohol intake or metabolic diseases. This was a case of a 29-year-old male with a 7-month history of intermittent right upper quadrant pain with CT scan findings of caudate lobe mass with malignant features. The patient underwent extended left hepatectomy with caudate lobectomy. Patient was discharged on fifth postoperative day, and was advised for follow-up surveillance on an outpatient basis. Liver cirrhosis is the main risk factor for developing HGDN, although rare cases of HGDN in a non-cirrhotic young patient should not be disregarded. Even though, it difficult to differentiate HGDN from early HCC based on radiologic imaging and histopathological criteria. Early diagnosis accompanied with proper surgical intervention such as anatomic resection and regular surveillance should be considered in the course and management of these patients, despite its rarity.

2. Introduction

Hepatocellular carcinoma (HCC) in a young patient with no cirrhosis or fibrosis is a relatively rare condition [1]. HCC develops in patients in the setting of liver cirrhosis with established risk factors related to various etiologies including hepatitis virus infection, high alcohol intake or metabolic diseases [2]. Worldwide, HCC is the sixth most common cancer [3], and the third most common cause of cancer deaths in 2020 [4]. The incidence was highest in East Asia, at 17.9 per 100,000 population (26.9 in males and 8.9

in females). In the Philippines, chronic Hepatitis B and alcohol as the most common etiologies of HCC, with a prevalence rate of 7.8% [5].

In 80% of cirrhotic livers [3], hepatocarcinogenesis is a multistep process that is characterized by the progression from hyperplastic regenerative nodules to low grade dysplastic nodules (LGDN), high grade dysplastic nodules (HGDN) and to HCC (less than 2 cm) [2]. In the Philippines, there has been no known published documentation of high grade dysplastic hepatic nodule in a non-cirrhotic liver in a young male patient with no known risk factors.

3. Significance of the Study

High grade dysplastic nodule is a risk factor for the development of hepatocellular carcinoma, which is more commonly seen in patients with cirrhotic liver. There has been no report of a case of high grade dysplastic nodule in a non-cirrhotic young male patient in the Philippines. This study can contribute to the medical literature, in addition to, share our experience with this case to the surgical community. This will aid surgeons especially in the low to middle income countries that may encounter this type of dilemma, with regards to the diagnosis, surgical course and management of this case at our local setting.

4. Case Presentation

This was a case of a 29-year-old male with a 7-month history of intermittent right upper quadrant pain. He works as a seafarer, whom undergoes annual medical checkup. Upon routine abdominal ultrasound findings revealed a suspicious caudate lobe mass. Hence advised for further workup, but patient was non-compliant due to fear of possible outcomes. Interim, he noted intermittent right upper quadrant pain, non-radiating, with pain scale of 4/10, with no precipitating and alleviating factors. He consulted a faith healer

and took herbal concoction intermittently for 3 months. After 3 months of self-treatment, he sought consult with a local physician, in which he was diagnosed with extra-pulmonary tuberculosis, and underwent HRZE regimen for a month. Upon follow-up, repeat ultrasound revealed an increase in the size of the caudate mass. He was then apprised for surgical intervention and referred to a hepatobiliary specialist in a tertiary hospital. His past medical and surgical history was unremarkable. He is a social alcoholic beverage drinker, and smoker. He denies illicit drug use, and homosexual encounter.

The patient was of average built with normal systemic examination findings. His abdominal findings was flat, with normoactive bowel sounds, soft, and nontender on all quadrants. No signs of liver cirrhosis and portal hypertension. Tumor marker of the patient revealed normal AFP and CA 19-9. Serology for viral hepatitis including HBsAg, and anti-HCV were negative. The ultrasound findings revealed Suspiciously prominent lobular caudate lobe measuring 6.0 x 4.8cm x 4.5cm with minimal perfusion on Doppler study, with interval increase in mass to 6.4cm x 5.4cm x 4.9cm. The Triphasic CT Scan of the Abdomen showed caudate lobe mass measuring 6.5 x 6.1 x 5 cm with early enhancing slightly hypodense circumscribed mass with rapid washout compatible with Hepatocellular Carcinoma.

Intraoperative findings (Figure 1) revealed 5x6 cm mass at the caudate lobe with involvement of the middle hepatic vein, hence extended left hepatectomy with caudate lobectomy was performed. The liver was smooth, with no signs of liver cirrhosis. Patient was discharged on fifth postoperative day, and was advised for follow-up surveillance on an outpatient basis.

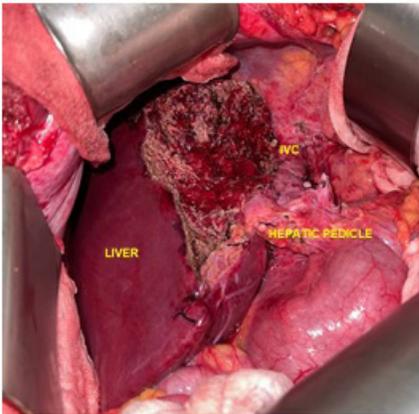


Figure 1: Smooth, noncirrhotic liver

On gross pathologic examination (Figure 2) showed a well-circumscribed ovoid mass at the caudate area, measuring 5x6cm, which grossly does not invade the surrounding liver parenchyma. On microscopic examination (Figure 3) liver sections with mild architectural atypia and hepatocytes arrested in two cells thick. These cells are polygonal with round, centrally located nuclei and abundant eosinophilic cytoplasm. Mild pleomorphism is noted

with some cells having 2 nuclei. Ductular reaction is noted as exhibited by proliferation

with reactive bile ducts lined by cuboidal cells infiltrating the surrounding area with the ducts are mononuclear inflammatory cells. No lymphovascular invasion is noted. There are few mitotic figures seen. The final histopathologic findings revealed high grade dysplastic nodule (5x6 cm) with negative surgical margins, and negative for lymph vascular invasion.



Figure 2: Well-circumscribed ovoid mass at the caudate area, about 5x6cm

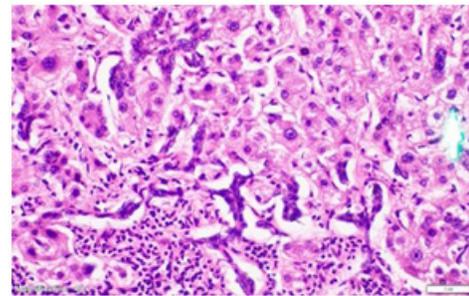


Figure 3: Microscopic features of HGDN

5. Case Discussion

High grade dysplastic nodule (HGDN) shows increased risk for development to HCC [6]. Dysplastic lesions are composed of hepatocytes that show histologic characteristics of abnormal growth caused by a presumed or proved genetic alteration. These lesions are commonly seen in cirrhosis, compared to non-cirrhotic livers [7]. However, approximately 20 to 25% of patients develop HCC with no cirrhosis. Several theories [1] have been proposed regarding the development of HCC in patients with no obvious risk factors. First is the exposure to chemical carcinogens. Second is the malignant transformation of a hepatic adenoma, in the context of exogenous steroid hormone use or hereditary metabolic disorders. Literature [8] have shown that epidemiological differences among patients without cirrhosis is that these patients were more likely to be young women with mean age of 43+9, with normal alpha-fetoprotein, and larger tumor size which would require a more extensive operation. Fortunately, post-operative survival is higher in patients without cirrhosis because they lack the complicating

factors associated with surgery. In contrast to this case, in which the patient is a 29-year old, male, with non-cirrhotic liver, and no established risk factors such as chronic hepatitis infection, alcoholic liver disease, or use of anabolic steroids and androgenic supplements.

The pathological criteria used to distinguish HCC from high-grade dysplastic nodules are not clearly defined. Most small HCCs cannot be distinguished histologically from dysplastic nodules with certainty [7]. The current standard treatment option for HGDN and HCC include anatomic resection and wedge resection of the tumor with possible neo-adjuvant chemotherapy or chemoembolization. When surgery is not an option, treatments including Trans-Arterial Chemoembolization (TACE), radio-embolization, and most recently, external beam radiation have been shown to be effective [1,6].

6. Conclusion

Patients with high grade dysplastic nodule (HGDN) have an increased risk for development of hepatocellular carcinoma. Liver cirrhosis is the main risk factor for developing HGDN, although rare cases of HGDN in a non-cirrhotic young patient should not be disregarded. Even though, it difficult to differentiate HGDN from early HCC based on radiologic imaging and histopathological criteria. Early diagnosis accompanied with proper surgical intervention such as anatomic resection and regular surveillance should be considered in the course and management of these patients, despite its rarity.

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