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Spontaneous Regression of Focal Nodular Hyperplasia in a Male Patient using 3D Liver Volumetric Evaluation and Surgical Planning: A Case Report

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Case Report

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ABSTRACT

Background: The incidence of symptomatic focal nodular hyperplasia (FNH) is 0.03%. FNH has female predominance that accounts for 90% of cases. It is a hypervascular benign liver tumor and is sometimes difficult to diagnose if there is a lack of typical findings on imaging. In the management of FNH, guidelines recommend conservative treatment rather than surgical resection.
Case report: An elderly male presented with abdominal fullness, anorexia, and weight loss with absence of jaundice and fever. The patient underwent percutaneous biopsy that was inconclusive. Subsequent imaging showed regression of tumor demonstrated by 3D liver volumetric assessment with a 92.3% decrease in tumor volume. The patient underwent extended right hepatectomy with total caudate lobectomy. The postoperative period was uneventful and the patient was discharged on postoperative day 8. Histopathological examination of the surgical specimen confirmed the diagnosis of FNH.
Conclusion: Spontaneous regression of FNH in male patients over a 3-month period is rare. The

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injury due to the core needle biopsy was possibly the mechanism that resulted in vascular thrombosis with subsequent regression and secondary immune reaction. To the best of our knowledge, this is the first case report using a 3D liver volumetric regression evaluation, which demonstrated its feasibility and usefulness in the planning of complex liver surgery.

Keywords: 3D Liver; focal nodular hyperplasia; hepatectomy; spontaneous regression; surgical resection; surgical planning.

1. INTRODUCTION

The incidence of symptomatic focal nodular hyperplasia (FNH) is 0.03% [1]. FNH is found most commonly in female patients who represent 90% of the cases [1]. FNH is a hypervascular benign liver tumor that is sometimes difficult to diagnose in the absence of typical imaging findings. However, if the typical findings from contrast-enhanced computed tomography (CT) or magnetic resonance imaging (MRI) of the liver are found, the diagnosis can be made without a tumor biopsy [2]. In addition, the treatment of a typical FNH is conservative treatment [3]. The imaging used for follow-up includes ultrasonography, CT, and MRI of the liver. There is no documented case report of spontaneous regression of FNH in a male patient using 3D liver volumetric assessment along with surgical planning.

2. CASE REPORT

A 72-year-old male presented with abdominal fullness, decreased intake, and weight loss of 2 kg over 2 months with absence of jaundice and fever. The physical examination showed no signs of chronic liver disease. Initial blood chemistries and serology showed twofold elevations of liver enzymes and alkaline phosphatase (ALP), and positive results for hepatitis B surface antigen and hepatitis B core antibody, while serum albumin and carcinoembryonic antigen levels were within normal limits. The alpha-fetoprotein (AFP) level was 1.7 ng/ml. The triphasic-CT scan of the liver revealed a tumor size of 12.0 x 11.6 x 9.9 cm, heterogeneous enhancement on arterial phase with venous washout and a central necrotic area. Since the liver had no cirrhosis with a normal AFP level, ultrasound-guided core needle biopsy was done. A histopathological examination (HPE) showed a vascular tumor with suspected cavernous hemangioma with an old hemorrhage, severe chronic inflammation, and fibrosis. Although the pathological results revealed hemangioma, it was inconsistent with the clinical and imaging findings. Therefore, surgical resection was considered to be reasonable due to the possibility of a misdiagnosis of malignant liver tumor, especially hepatocellular carcinoma (HCC). The patient was reevaluated using both CT scan and MRI of the liver with gadolinium. At the 3-month follow-up visit, the MRI of the liver showed a significant decrease in tumor size to 5.3 x 6.6 x 5.4 cm, T1 weight/T2 weight heterogeneous hypo-hyper-signal intensity with subtle arterial enhancement, and hypo-signal intensity on venous phase. The 3D liver volumetric analysis using Synapse® 3D software calculated the percentage of volume regression of the tumor. From the initial 3D liver reconstruction, the tumor volume was calculated and compared to the previous imaging study. The tumor volume had decreased from 661 ml to 51 ml, which was a 92.3% decrease over the 3-month period. Furthermore, the 3D liver reconstruction also delineated the intrahepatic vascular structures related to the tumor and also calculated the future liver remnant volume (FLR) (51%) (Fig. 1). The preoperative indocyanine green retention test at 15 min (ICGR15) was 9.5%, which indicated that extended right hepatectomy with total caudate lobectomy was a safe and suitable operation in this patient according to the above data. The preoperative planning in our institution is based on the principles of liver surgery; therefore; the FLR is only functional when it has complete inflow and outflow blood supply with adequate biliary drainage, the so called adequate non-congestive FLR volume (Fig. 2). The operation was performed accurately due to the preoperative 3D liver analysis for surgical planning. The patient had an uneventful postoperative course and was discharged on postoperative day 8. The final pathological diagnosis was focal nodular hyperplasia of the liver (Fig. 3). There was no evidence of recurrence after 34 months of follow-up.

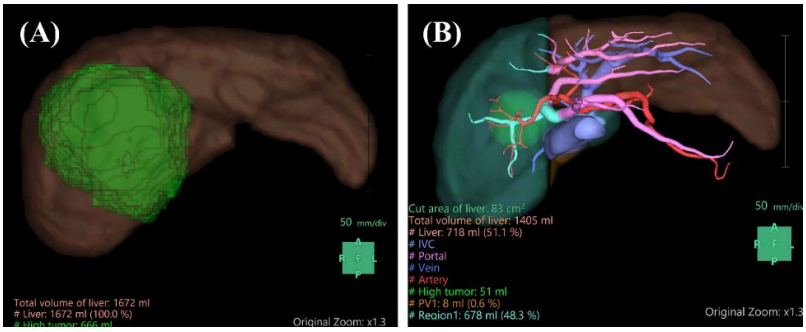

Fig. 1. The 3D-liver volumetric evaluation: (A) initial tumor volume 666 ml or 39.8% compared to total liver volume, the green area represented the tumor. (B) The preoperative 3D-liver reconstruction showed decreased tumor volume to 51 ml or 92.3% compared to initial imaging. The 3D reconstruction image clearly demonstrated the spatial relationship of tumor and internal structures, portal vein (pink), hepatic artery (red), and hepatic vein (blue)

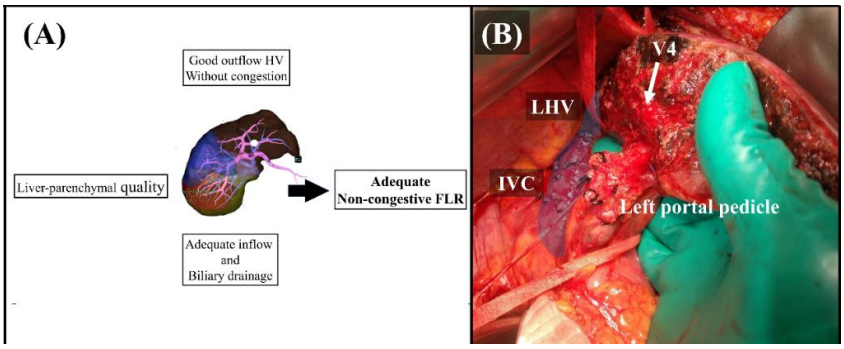

Fig. 2. The surgical planning based on the principle of liver surgery. (A) The future liver remnant is considered functional when adequate inflow, outflow, and biliary drainage were ensured. (B) The left hemiliver was the remnant, demonstrated complete structures that are required for function according to the principles of liver surgery

Abbreviation: FLR= future liver remnant, IVC = inferior vena cava, LHV = left hepatic vein, V4 = vein of segment 4

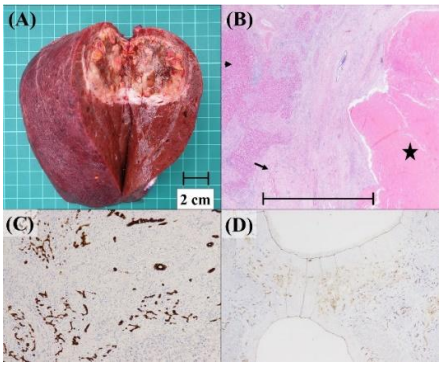

Fig. 3. Pathological findings of focal nodular hyperplasia (FNH) in the patient. (A) Specimen of extended right hepatectomy with caudate lobectomy showed white yellow irregular rubbery mass 5.8 x 4.5 x 4 cm in diameter. (B) Histopathology showed normal liver cells with a large area of fibrosis and bile duct proliferation, diffuse necrosis and hemorrhage (star), a large area of fibrosis (bracket) with bile duct proliferation (arrow), and some areas of normal liver cells (arrow head). (C) and (D) Immunohistochemistry staining: positive for cytokeratin 19 and CD34, respectively. Additional smooth muscle actin staining positive in fibrotic area with negative S100 and the detection of desmin confirmed the diagnosis of FNH

3. DISCUSSION

We presented a rare case of spontaneous regression of FNH in a male patient over a 3-month period with diagnostic difficulty that required surgical resection. Regression of the hypervascular liver tumor was assessed by a 3D qualitative analysis of the liver that showed 92.3% regression of the absolute contrast-enhanced volume. To perform a safe hepatectomy, the 3D liver reconstruction was incorporated into the surgical planning.

A diagnosis of FNH is based on imaging findings that include precontrast CT or MRI scans and the lesion is homogeneous except for a central scar. In the arterial phase, the lesion has strong homogeneous enhancement relative to the background liver; In the venous and delayed phases, the lesion is similar to the adjacent liver [2]. However, in our patient, the lesion had hypodensity and hyposignal intensity of the liver in the venous phase, which raised the possibility of HCC in a hepatitis B infected patient [4]. Although, the imaging characteristics were compatible with HCC, it was argued that there were no documented signs of chronic liver disease or cirrhosis [5]. In this circumstance, both guidelines of the European and American Associations for the Study of the Liver recommends tumor biopsy for a definite diagnosis [4,5]. The initial pathological diagnosis from core needle biopsy was cavernous hemangioma. The possible reason was the cellular component of the FNH indicated the presence of a vascular core inside the tumor [6]. Sampling might have included only the vascular component of the tumor with limited amount of tissue; therefore, a definite diagnosis was not possible. The discordant clinicopathologic features with the possibility of HCC was the key indication for surgical resection in this patient. However, the final diagnosis of regression of FNH was made based on the histopathological and immunohistochemistry examination, which was compatible with a previous report [7]. Although the diagnosis was benign liver tumor, the relatively large tumor size possibly accounted for the presenting symptoms of the patient.

Previous reports of spontaneous regression are limited. The reported incidence ranged from 8% to 50% [8,9]. A study of 34 FNH cases followed by ultrasonography with a mean follow-up time of 42 months showed stable, progressed, and regressed tumor in 70.6%, 2.9%, and 26.5%, respectively. The independent factors for complete regression were older age and longer follow-up time. The tumors regressed over a mean time of 59 months (range, 20-95 months) [10]. In our 72-year-old male patient, the tumor regressed over a 3-month period, which was much less than the low end of the range of the cited study. Even though the authors claimed that the low level of female hormones in older women could explain the link between the loss of FNH and old age, it was not the case. Typically, FNH contains dystrophic arterial vessels within the central fibrous scar [11]. We hypothesized that injury from the core needle biopsy caused endothelial injury and intratumoral hemorrhage that resulted in increased amounts of procoagulants and induced vasospasm that possibly contributed to vascular thrombosis [12]. Intratumoral vascular thrombosis results in tumor necrosis and fibrosis as was seen on HPE. Complete regression of FNH was reported in an infant after tumor biopsy [13]. However, the authors did not explain the association between tumor regression and the biopsy procedure. In addition, the mechanism of regression might be explained by two factors: (1) tissue hypoxia and (2) systemic immune-activation [14]. The initial tumor necrosis led to secondary regression of the tumor caused by activation of a systemic immune response.

Assessment of tumor regression has been demonstrated by multiple imaging modalities of the liver that include ultrasonography and CT and MRI scans [15,16]. Nevertheless, a report using 3D liver volumetry for the assessment of FNH regression could not be found. The assessment tools have been used to evaluate the treatment response in malignant liver tumor. The conventional criteria to evaluate response is based on size [17]. However, in the past decade Choi et al. [18]. reported criteria that adopted tumor density in combination with the size criteria and claimed to be sensitive and specific to evaluate response in gastrointestinal tumors. The inadequacy of one- and two-dimensional assessments prompted the creation of new, quantitative 3D assessment tools. Furthermore, there is strong evidence for a favorable radiological–pathological relationship between a supposedly live tumor reported as contrast enhancement on 3D quantitative MRI and pathologically estimated necrosis in tumor explants [19,20]. Mentioned above was evidence for evaluation of HCC, thus with the hypervascular nature of the FNH. Therefore, it might be possible to adapt those criteria to assess regression. However, the Synapse® 3D

software could not incorporate the MRI data. Instead of using MRI, we selected contrast enhancement on CT scan of the liver for the 3D liver volumetric assessment. As a result, we were able to calculate the volumetric regression of 92.3% in this FNH tumor.

Technological improvements in the healthcare system have led to the evolution of preoperative surgical planning especially for liver surgery [21]. The 3D liver reconstruction allowed for an accurate prediction of the FLR volume. The percentage of FLR volume was specific in predicting post-hepatectomy liver failure (PHLF). Shoup et al. [22]. reported that FLR volume less than 25% tripled the risk of PHLF. In our case, the patient had 51% FLR volume from the 3D liver volumetric assessment. Furthermore, a combination of volume and function evaluation using the ICGR15 test assured the safety regarding PHLF. The 3D liver reconstruction also highlighted the spatial interconnections between the liver organ and the internal structures including the tumor and blood vessels [23]. The evidence suggested that incorporating 3D technology in surgical planning was useful in complex hepatectomy. Although more radical, it was safer [24]. In addition, the benefit of the 3D technology in training centers was shown to improve the understanding of surgical plans proposed by a 3D model [25].

4. CONCLUSION

Spontaneous regression of FNH in a male patient over a 3-month period is rare. The possible mechanism that induced regression was injury that resulted in vascular thrombosis with subsequent regression. To the best of our knowledge, this is the first case report that demonstrated two important uses of a 3D liver volumetric evaluation: (1) the feasibility to evaluate liver tumor regression and (2) its usefulness in preoperative planning of complex liver surgery.

CONSENT

All authors declare that written informed consent was obtained from the patient for publication of this case report and accompanying images.

ETHICAL APPROVAL

All authors hereby declare that this case report was approved by the Human Research Ethical Committee (number REC.64-289-10-1).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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