

CASE REPORT

Pregnancy complicated by focal nodular hyperplasia: a case report of one woman over two consecutive courses of pregnancy

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Key Clinical Message

We encountered a woman with a preexisting large focal nodular hyperplasia (FNH) of the liver, persisting during two separate pregnancies. FNH size was not affected by either pregnancy. Her elevated serum γ -glutamyltransferase and alkaline phosphatase levels before pregnancy were reduced during both pregnancies, but returned to prepregnancy levels after delivery.

Keywords

Focal nodular hyperplasia, liver enzyme, MRI, pregnancy.

Introduction

Focal nodular hyperplasia (FNH) is a benign lesion of the liver that is not uncommon in adults and is frequently observed in healthy individuals. It is unclear, however, whether pregnancy in women with FNH increases the risks of FNH growth and complications or alters hepatic function in patients. We encountered a woman with a large FNH, who experienced two pregnancies and delivered healthy infants at term uneventfully. The courses of her pregnancies and the effects of pregnancy on FNH, including lesion size and hepatic function were evaluated at the same institution.

Case History

The patient was a 25-year-old, gravida 0, para 0, female, who had been followed up since the age of 18 years at the internal medicine outpatient ward of our institution because of a large FNH. At the age of 13 years, a nodule

measuring 8 cm was observed in the patient, at a medical institution near her residence. A biopsy was performed, and on histological analysis of the specimen, she was diagnosed with FNH. Because the nodule was located near the hepatic hilus, surgical intervention was not performed. At the age of 25 years, the patient married and moved near our hospital. An MRI taken before her first pregnancy showed that the nodule was 11 cm in diameter (Figs. 1A and 2A). A high intensity area was observed at the center of the lesion, a finding compatible with central scar tissue, with a moderately high intensity area observed at the surface of the lesion. Because of lack of symptoms, conservative management was selected by her physician.

Before becoming pregnant, her liver function tests showed that her serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT) concentrations were in the normal ranges, but her γ -glutamyltransferase (GGT) and alkaline phosphatase (ALP) concentrations were elevated, to 651 IU/L and 407 U/L, respectively.

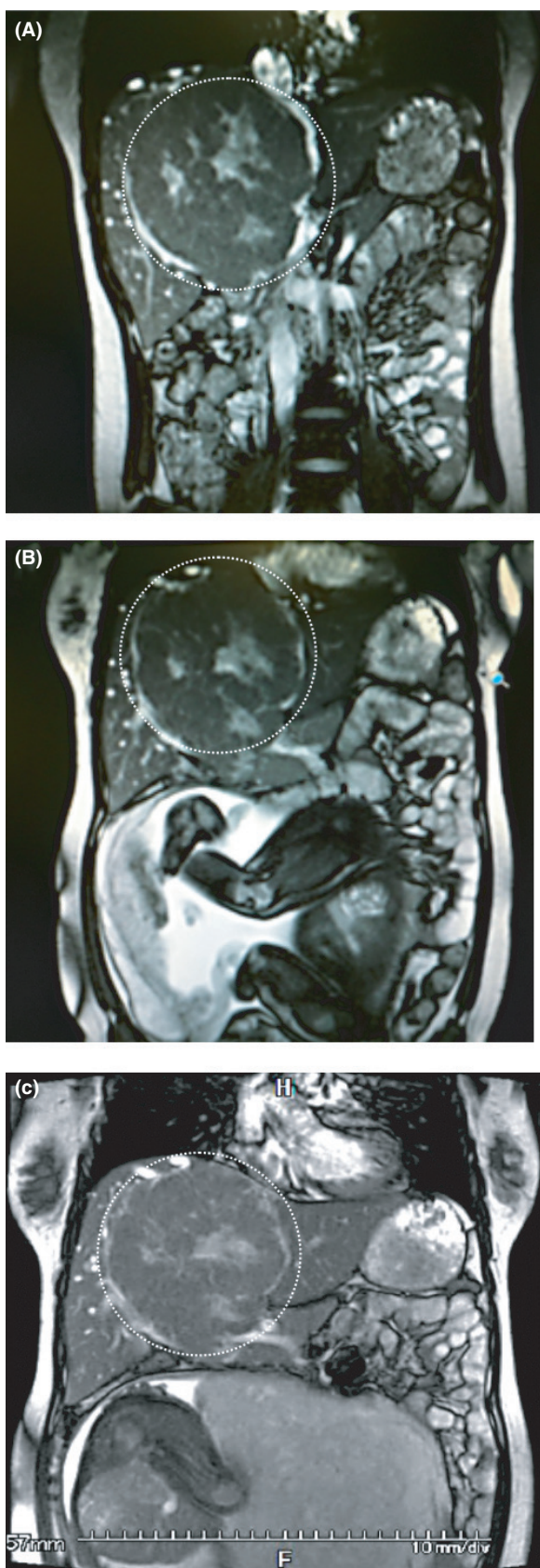


Figure 1. Magnetic resonance images (plain) of T2-weighted coronal sections. Dotted lines in white show the margin of the lesions. (A) Before pregnancy at the age of 23 years. (B) During her first pregnancy at 37 weeks of gestation. (C) During her second pregnancy at 34 weeks of gestation.

Differential diagnosis, investigations, and treatment

After conceiving, she was referred by her physician to our outpatient ward at 9 weeks of gestation. During her first pregnancy, her serum concentrations of liver enzymes decreased to the normal range without any medication (Fig. 3). Magnetic resonance imaging performed at 37 weeks of gestation showed that the size of the FNH was unchanged, with no signs of bleeding or degeneration of the lesion (Figs. 1B and 2B).

Her first course of pregnancy was uneventful. At 39 weeks, she delivered a normal, healthy female infant, weighing 3084 g and with 1 and 5 min Apgar scores of 8 and 9, respectively, by vaginal delivery. Both the mother and child were discharged 5 days after the delivery.

Her postpartum recovery was normal, except that her serum GGT and ALP concentrations became elevated, returning to their prepregnancy levels.

The patient became pregnant again at the age of 27 years. This pregnancy was also uneventful (Figs. 1C, 2C, and 3) and, at 40 weeks of gestation she delivered a normal, healthy male infant, weighing 3130 g and with 1 and 5 min Apgar scores of 9 and 10, respectively, by vaginal delivery. Her postpartum course was again uneventful, and both mother and child were discharged after 5 days.

The size of the FNH remained the same as before her first pregnancy, despite two pregnancies and deliveries. During both pregnancies, her serum concentrations of liver enzymes improved, but returned to prepregnancy levels soon afterwards.

Discussion

Focal nodular hyperplasia is a common type of hepatic mass in adults, with an incidence of approximately 3% [1]. The lesion is caused by a proliferation of normal hepatocytes that are abnormally arranged. Few reports have evaluated FNH during pregnancy and the influence of pregnancy on FNH.

We encountered a woman who had FNH prior to her first pregnancy and followed her throughout two courses of pregnancy. We found that FNH size was not affected by pregnancy. In contrast, the serum concentrations of liver enzymes were decreased during both pregnancies, and returned to their prepregnancy levels soon after the deliveries. A previous study described the effects of 41

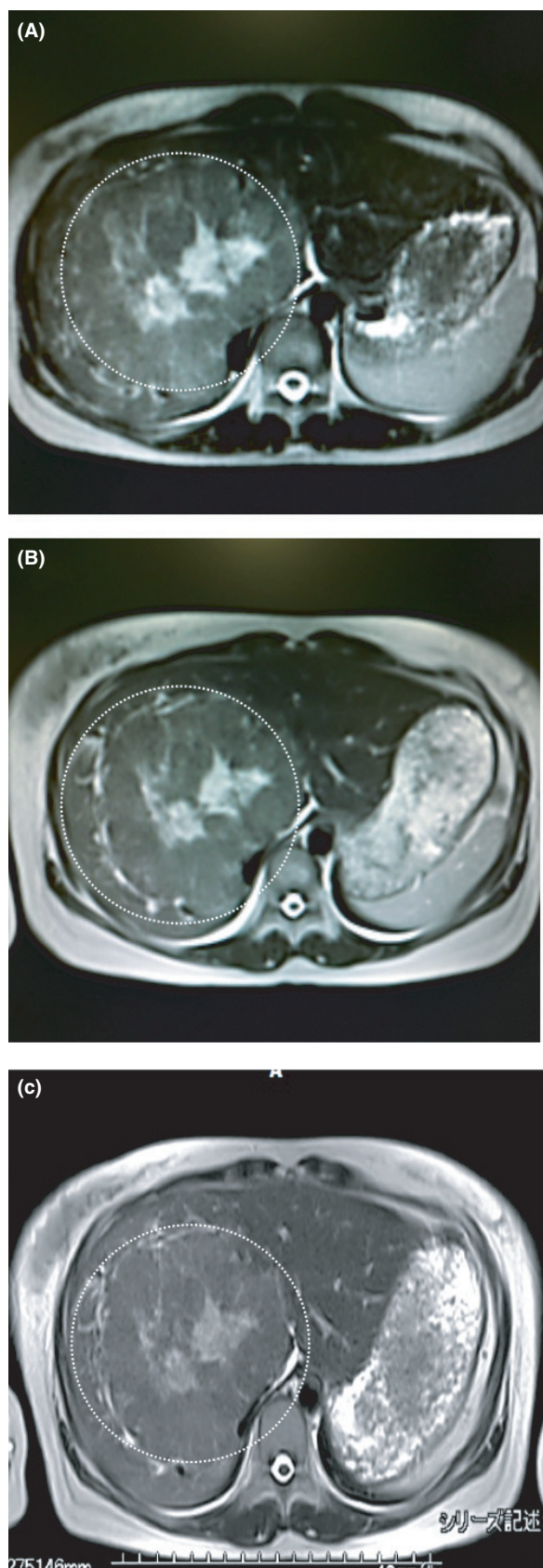


Figure 2. Magnetic resonance images (plain) of T2-weighted horizontal section. Dotted lines in white show the margin of the lesions. (A) Before pregnancy at the age of 23 years. (B) During her first pregnancy at 37 weeks of gestation. (C) During her second pregnancy at 34 weeks of gestation.

pregnancies on FNH in 37 women, finding that the size of the FNH was not affected by pregnancy [2]. Another study [3] evaluating the effects of pregnancy on FNH size in patients found that the mean tumor size before pregnancy was $58.5 \pm 22.7 \text{ mm}^3$. Tumor size remained constant in seven of these 20 patients (35%) and declined in 10 (50%). However, FNH size in multiparous women was assessed using a questionnaire, not by actual measurement. Furthermore, that study evaluated only lesion size, not changes in serum enzyme concentrations. In our patient, the FNH was >11 cm in diameter, the largest FNH reported to date, and its size was not affected by either of her two pregnancies.

There have been no reports on changes in the serum concentrations of liver enzymes during pregnancy in women with FNH. We found that serum AST and ALT concentrations were not altered during pregnancy. In contrast, serum ALP and GGT values, which were elevated before and after her pregnancies, decreased to normal levels during her pregnancies. ALP and GGT are enzymes present in the cell membranes of the bile duct, gall bladder, pancreas, and kidneys. Serum concentrations of ALP elevate by placental origin and GGT are not affected in pregnancies in women without FNH, but were shown to be higher in few pregnant women (<1%) with intrahepatic cholestasis [4]. Pregnancy may alter the results of liver function tests, with placental steroids playing a role. During pregnancy, the production of placental steroids increases the serum estrogen and progesterone concentrations compared with the nonpregnant state. Oral contraceptives can also alter enzyme concentrations. For example, a 9-year study of 216 women in France showed that neither the size nor the numbers of FNH lesions are influenced by oral contraceptive use [5]. Although estrogen receptors were shown to be present in the cytosol and nuclei of hepatic cells including the tissue of FNH [6, 7], few estrogen receptors are present on the cell surface. Estrogen and progesterone affect the mRNA expression and activity of CYPs (cytochrome P450) in primary human hepatic cells, as shown in a recent study [8]. These findings potentially provide a basis to understand the mechanism of altered drug metabolism during pregnancy. However, further studies are needed to investigate the lowering of serum ALP and GGT in FNH.

In conclusion, we have described here a single patient with FNH of the liver complicating pregnancy and post-

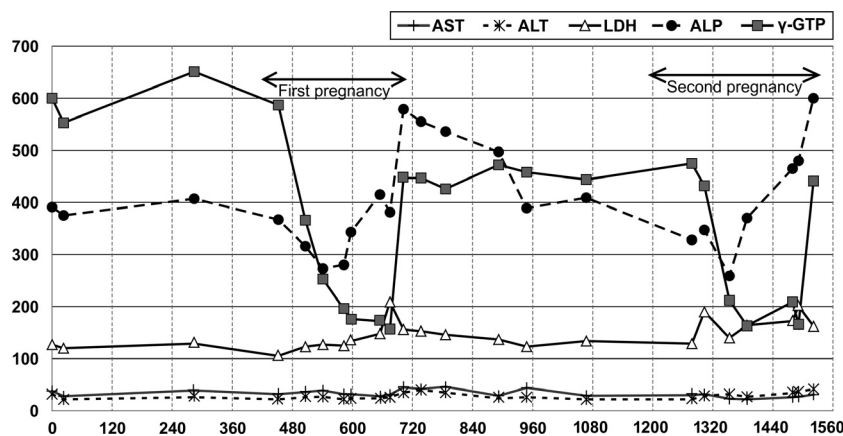


Figure 3. Serum concentrations of liver enzymes over time. The horizontal axis shows days from the initial visit to our institution. The concentrations of aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactate dehydrogenase (LDH), alkaline phosphatase (ALP), and γ -glutamyltransferase (GGT) are shown in U/L.

partum delivery twice over a 4-year observation period. FNH size was not affected by pregnancies, whereas liver function test results improved, allowing these enzymes to return to their prepregnancy levels after deliveries. Lesion size and abnormally elevated serum liver enzyme concentrations are not indicated for surgery in pregnant women with asymptomatic FNH. Our findings indicate that women with large FNH, even those with elevated serum liver enzymes, should not be discouraged from pregnancy.

Conflicts of Interest

None declared.

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