-Report on Experiments and Clinical Cases-

Liver Cell Adenoma in a 26-year-old Man

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Abstract

This is a report of a case of liver cell adenoma (LCA) in a 26-year-old man with no prior history of liver disease or glycogen storage disease and no record of hormonal therapy. He was found to have an asymptomatic hepatic mass during a routine medical examination. The physical findings were unremarkable, and the results of routine laboratory studies were all within normal limits. Selective hepatic arteriography showed a hypervascular mass within the right lobe of the liver. Despite the radiological examination, the nature of the mass was unknown, and preoperative biopsy was unadvisable because of the risk of bleeding. Because of the difficulty of determining the malignancy of the hepatic tumor preoperatively, elective laparotomy for diagnosis and hepatectomy as treatment appeared to be the best available approach. Pathological examination of the surgical specimen resulted in a diagnosis of LCA. A review of the literature revealed that LCA unassociated with the use of oral contraceptives is rare.

(J Nippon Med Sch 2001; 68: 516-519)

Key words: liver cell adenoma, hepatectomy, young male

Introduction

Liver cell adenoma (LCA) is considered the rarest benign neoplasm of the liver in young men¹⁻⁵. We recently encountered a patient with LCA who had no prior history of liver disease or glycogen storage disease and had never been on hormonal therapy.

Case Report

A 26-year-old man was found to have a hepatic mass on ultrasonography during a routine voluntarily group medical check-up and was referred to Nippon Medical School Hospital for evaluation. He was asymptomatic. The physical findings were unremarkable. The laboratory data showed serum albumin 4.6g/dI (normal: 3.8~5.5), total bilirubin 0.4mg/dI (normal: 0.2~1.2), GOT 17 IU/I (normal: 10~28), GPT 23 IU/I (normal: 5~33), ALP 176 IU/l (normal: 66~220), γ -GTP 32 IU/I (normal: 8~59), cholinesterase 409 IU/I (normal: 185~431), cholesterol 147 mg/dI (normal: 130~220), blood glucose 91 mg/dI, WBC 4,800/ μ I, RBC 491 × 10⁴/ μ I, Hb 15.2 g/dI, Ht 36.7%, platelet 19.2 × 10⁴/ μ I, α -fetoprotein <10 ng/mI, antibody for hepatitis C virus (-), hepatitis B surface antigen (-).

Ultrasonography showed a 4.5-cm well-defined heterogeneous lesion within the right lobe of the liver. Prior to contrast infusion, Computed tomography (CT) showed a low-density lesion in the right lobe of the liver, that measured 4.5 cm in diameter (**Fig. 1A**). Contrast scan revealed irregular enhancement of the

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mass (**Fig. 1B**). Selective hepatic arteriography showed a hypervascular mass within the right lobe and a homogenous tumor stain was noted during the late phase (**Fig. 2**). Since the nature of the hepatic mass was unknown, anatomical subsegmentectomy of

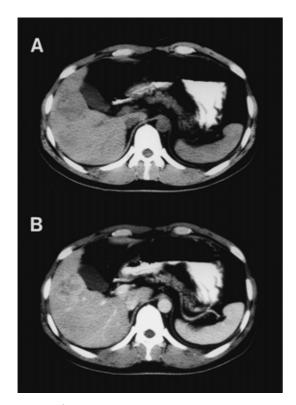


Fig. 1 A) Prior to contrast infusion, CT shows a low-density mass.B) Contrast scan reveals irregular enhancement of the mass.

the right anterior-inferior segment was performed one week after admission. The postoperative course was uncomplicated, and the patient was discharged 2 weeks after operation.

The cut surface of the tumor was well circumscribed, but not encapsulated, and was reddish-tan, and homogeneous, with no central necrosis. Microscopic examination revealed only moderate fatty change in the surrounding parenchyma. Focal hemorrhages were present within the tumor. There were numerous prominent venous outflow channels, occasionally with closely related branching small arterioles. The tumor consisted of large cells of hepatic origin arranged in one-to two-cell-thick cords. Bile ducts were absent. Kupffer cells were markedly reduced in number. The hepatocytes were not atypical and contained uniform nuclei with no mitoses or pleomorphism (**Fig. 3**).

The diagnosis was LCA.

Discussion

LCA is a benign tumor of the liver that was rarely reported before the introduction of oral contraceptives in 1960. Only two cases of LCA were found in a review of 50,000 autopsies performed during the 36 years before 1954⁶. In 1973 Baum was the first to document the relationship between the use of oral contraceptives and LCA⁷. Since that time, many cases

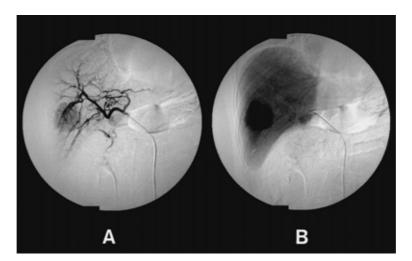


Fig. 2 A) Selective hepatic arteriogram, early arterial phase, showing hypervascular lesion in the right lobe of the liver.

B) Late phase, homogenous capillary staining is evident.

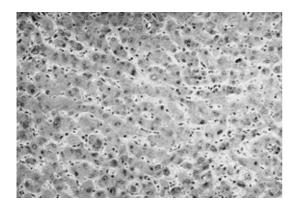


Fig. 3 Microscopic appearance of the tumor. The arrangement of tumor cells shows cord structures (one-to two-cell-thick cords). There are no portal triads. (HE stain × 50)

have been reported⁸⁻¹³, and they have fallen into three relatively distinct categories: LCAs that developed in patients who had taken oral contraceptives or steroids⁸⁻¹¹, LCAs discovered in patients with diabetes mellitus¹², glycogen storage disease¹³ or during pregnancy, and LCAs in patients with adenomatosis. However, a few cases of LCA in young men have been reported in Japan, mostly in the Japanese literature²⁻⁵.

Approximately 90 per cent of benign hepatic tumors are incidental findings. The most common manifestation of LCA is intratumoral or intraperitoneal hemorrhage, which occurs in 50 to 60 per cent of patients^{89,11}. In the present case, the tumor was detected by chance during a routine medical check-up. The clinical presentation was without sudden onset of abdominal pain, and the laboratory studies were all within normal limits.

Routine diagnostic studies have been of little value in the diagnosis of LCA. Liver enzyme changes and bilirubin elevation may occur in association with acute expansion of the neoplasm caused by hemorrhagic necrosis or intrahepatic hemorrhage. Hepatic angiography is considered the most valuable roentgenographic examination¹¹, and even small LCAs are readily detectable¹¹. The procedure is invaluable for localizing the lesion and its blood supply. Focal nodular hyperplasia (FNH) is readily distinguishable from LCA by the absence of a spoke-wheel pattern with central vascular supply and vessels radiating to the periphery. In these benign hepatic lesions, there is usually none of the arterio-venous shunting, vascular puddling, or venous invasion expected in hepatocellular carcinoma (HCC). However, preoperative confirmation of the malignancy of hepatic tumors is difficult by conventional noninvasive and invasive techniques¹⁰, and preoperative percutaneous or laparoscopic biopsy is not recommended because of the risk of bleeding by vascular neoplasms, possible seeding by malignant lesions^{1,14} and the fact that benign and malignant neoplasm may coexist in the same liver¹⁵.

Transcatheter arterial embolization (TAE) is commonly used to treat HCC. However, we thought that if TAE were performed in our patients, it would still be uncertain whether the tumor was benign and whether the prognosis was favorable. Actually, few cases of LCA treated by TAE have been reported. We therefore believe that elective laparotomy for diagnosis and hepatectomy for a treatment may be the best approach.

In most cases, LCA can be distinguished from FNH on the basis of its characteristic pathologic features. LCA tends to be larger than FNH, circumscribed, and occasionally encapsulated and fleshy in appearance. Areas of necrosis and hemorrhage are often visible on the cut surface. The histologic pattern is monotonous with regular proliferation of normal appearing hepatocytes, often in trabeculae with compressed sinusoids in between, but devoid of lobulations, reticular fibers, and bile ducts¹⁶. The pathologic findings in our case were consistent with the features of LCA.

A recent study of 23 patients with LCA found an association with oral contraceptive use in 89% of the cases¹. Our case is exceedingly unusual in two respects: the patient was a healthy young male and the LCA was unassociated with the use of steroid hormones.

References

- Kerlin P, Davis GL, Mcgill DB, Weiland LH, Adson MA, Sheedy PF: Hepatic adenoma and focal nodular hyperplasia: clinical, pathologic and radiologic features. Gastoenterology 1983; 84: 994–1002.
- Sugiyama T, Akahonai Y, Arashi M, Hirane T, Yachi A, Satoh M, Ogawa K:An autopsy case of hepatocellular adenoma and peliosis hepatis considered to be induced by anabolic steroid therapy for aplastic anemia (in Japanese with English abstract). Kanzou (Acta

J Nippon Med Sch 2001; 68(6)

Hepatol Jpn) 1982; 23: 927-933.

- 3. Iwasa R, Sakai K, Kinoshita H, Hirohashi K, Tsuji Y, Okimoto T, Kubo S, Tei N, Fukushima Y, Fujio N, Lee, M, Tanaka H, Nakata K, Oomori K, Kobayashi Y: A case of liver cell adenoma in young male(in Japanese with English abstract). Kanzou (Acta Hepatol Jpn) 1988; 29: 111–116.
- 4. Haba H, Makuuchi M, Watanabe O, Ishikawa M, Nemoto M, Yamasaki S, Hasegawa H, Takayasu K, Moriyama N, Hirohashi S: A case report of liver cell adenoma (HCA) that underwent hepatic resection after 19 months of follow-up (in Japanese with English abstract). Nippon Rinsho Geka Igakkai Zasshi (J Jpn Soc Clin Surg) 1988; 49: 1056–1063.
- Uto H, Shigehira M, Kawano T, Nagatomo H, Kuribayashi T, Taniguchi S, Koga K, Komada N, Kitamura T, Maruyama T, Tsubouchi H: Liver cell adenoma in a young man with elevated serum PIVKA-II level. J Gastoenterol 1996; 31: 441–445.
- Edmondson HA: Tumors of the liver and intrahepatic bile ducts. Atlas of Tumor Pathology, fasc. 25. Washington, D.C.: Armed Forces Institute of Pathology 1958.
- Baum JK, Holtz F, Bookstein JJ, Klein CW: Possible association between benign hepatomas and oral contraceptives. Lancet 1973; 2: 926–929.
- Meissner K: Hemorrhage caused by ruptured liver cell adenoma following long-term oral contraceptives. Hepato-Gastroenterology 1998; 45: 224–225.

- Shortell CK, Schwartz SI: Hepatic adenoma and focal nodular hyperplasia. Surg Gynecol Obstet 1991; 173: 426–431.
- Helling TS, Wood WG: Oral contraceptives and cancer of the liver. Am J Gastroenterology 1982: 77; 504–508.
- Ameriks JA, Thompson NW, Frey CF, Appleman HD, Walter JF: Hepatic cell adenomas, spontaneous liver rupture, and oral contraceptives. Arch Surg 1975; 110: 548–557.
- Foster JH, Donohue TA, Berman MM:Familial liver-cell adenomas and diabetes mellitus. N Engl J Med 1978; 299: 239–241.
- Howell RR, Stevenson RE, Ben-Menachem Y: Hepatic adenoma with type I glycogen storage disease. JAMA 1976; 236: 1481–1484.
- Foster JH, Berman MM: The malignant transformation of liver cell adenomas. Arch Surg 1994; 129: 712–717.
- Davis M, Portmann B, Searle M, Wright R, Williams R: Histological evidence of carcinoma in a hepatic tumour associated with oral contraceptives. Br Med J 1975; 4: 496–498.
- Friedman LS, Gang DL, Hedberg SE, Isselbacher KJ: Simultaneous occurrence of hepatic adenoma and focal nodular hyperplasia. Hepatology 1984; 4: 536–540.

(Received, June 6, 2001) (Accepted, August 23, 2001)