Atypical Adenomatous Hyperplasia Indistinguishable From Hepatocellular Carcinoma with Current Imaging Modalities

MEVCUT GÖRÜNTÜLEME YÖNTEMLERİYLE HEPATOSELLÜLER KARSİNOMADAN AYIRDEDİLEMEYEN BİR ATİPİK ADENOMATÖZ HİPERPLAZİ VAKASI

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SUMMARY

A 63 year-old woman with chronic liver disease showed the findings of hepatocellular carcinoma (HCC) with fatty metamorphosis on the examination of ultrasonography, computed tomography (CT), magnetic resonans imaging, CT during arterial portography and infusion hepatic angiography. The nodule was surgically resected. However, the histological examination of the resected specimen revealed an atypical adenomatous hyperplasia with fatty metamorphosis. Although this nodule did not contain HCC foci, morphometry analysis revealed that the nodule was predominantly supplied by arterial blood, and portal venous supply was found to be markedly decreased as in a hepatocellular carcinoma foci.

We present here patient with adenomatous hyperplasia which showed the typical features of HCC on all diagnostic methods. Furthermore, we discuss the clinical importance and difficulties in the differential diagnosis of the adenomatous hyperplasia.

Key Words: Liver neoplasms, Diagnosis, **Blood** supply, Adenomatous hyperplasia

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ÖZET

Kronik karaciğer hastalığı olan 63 yaşındaki bir kadın hastada ultrasonografi, bilgisayarlı tomografi, magnetik rezonans, hepatik anjiografi, arteriyel portografi sırasında bilgisayarlı tomografi muayeneleriyle yağlı metamorfozis gösteren hepatosellüler karsinom tanısı kondu. Kitle cerrahi olarak ameliyat edildi. Ancak, histolojik incelemede lezyonun yağlı metamorfoz gösteren atipik adenomatöz hiperplazi olduğu tesbit edildi. Hepatosellüler karsinom odağı içermemesine rağmen, morfometrik incelemede lezyonun başlıca arteriyel kanla beslendiği, portal venöz akımın tıpkı hepatosellüler karsinomda olduğu gibi belirgin derecede azaldığı görüldü.

Bu makalede, bütün muayene yöntemleri ile hepatosellüler karsinoma bulguları gösteren bir adenomatöz hiperplazi vakası sunulmuş, bu lezyonların önemi ve ayırıcı tanıdaki güçlükler tartışılmıştır.

Anahtar Kelimeler: Karaciğertümörü, Tanı, Kan akımı, Adenomatöz hiperplazi

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It has become possible to detect an increasing number of small nodular lesions of the liver due to recent advances in diagnostic techniques. Among these nodular lesions, adenomatous hyperplasia (AH) and hepatocellular carcinoma (HCC) are two different hepatic masses which frequently develop in the cirrhotic liver (1). AH is divided into ordinary, which Is composed of hepatocytes similar to those of the surrounding liver and shows regularly distributed portal tracts, and atypical forms which consists of hepatocytes showing nuclear atypia and irregular or sparse portal tracts (2,3).

The imaging features of HCC are well-known and the differentiation from other focal lesions has been reported to be possible on the basis of recent advances in various imaging methods in previous reports (4-6). Here, we describe a case of atypical AH with fatty metamorphosis in a precirrhotic liver that simulated the features of HCC in all imaging methods.

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CASE REPORT

A 63 year-old woman was admitted to the hospital because of a high echoic lesion noted on liver ultrasonographic (US) examination. Two years before the admission, she was first found to have abnormal liver function tests. The patient's medical history included noninsulin-dependent diabetes mellitus and previous appendectomy and myomectomy. Alcohol was consumed once or twice a week. There was no history of blood transfusion. The physical examination was unremarkable except for hepatomegaly that extented three flngerbreadths below the right costal margin. Her liver was nontender, dull edged and uneven surfaced. No stigmata of chronic liver disease were present.

Liver function tests were as follows: sGOT 64U, sGPT 47U, ALP 9.5 K-AU, ZTT 14.8 KU, TTT 6.7 SHU, hepaplastin test 130%, ICG retention test In 15 min. 27%, BSP test 9.8%, protrombin time 13.1 sec. Tumor markers including AFP, CA 19-9, CEA, PIVKA II, CA 125 were within normal limits. Serologic tests for hepatitis viruses, including hepatitis C, and autoantibodies were all negative.

At this point, the patient was suspected to have a small HCC developed on the basis of the cryptogenic precirrhotic liver, and other radiologic procedures were performed to identify this lesion.

Computed tomography (CT) showed a low density area about 15 mm in the longest axis in segment 7 of the liver and did not enhance with contrast material. Magnetic resonance imaging (MR) scans demonstrated the lesion that was characterized by a ring-like high intensity on T1 weighted (spin echo) images, and relatively high intensity compared to the surrounding liver tissues on T2 weighted (spin echo) images (Figure 1). Dynamic spin echo imaging with Gd-DTPA showed no enhancement. These MRI findings were compatible with HCC fatty metamorphosis. Infusion hepatic angiography (IHA) showed a small tumor stain in the capillary phase (Figure 2). CT during arterial portography (CTAP) disclosed a perfusion defect in this area of the liver (Figure 3).

We considered that these findings best fitted to the diagnosis of small HCC with fatty metamorphosis and precirrhosis. Surgical resection of the tumor was recommended and partial hepatectomy was performed.

Macroscopically, the tumor was yellowish, sharply demarcated from the surrounding liver tissue and 12x12 mm in diameter. Histological examination of the specimen revealed several portal tracts in the nodule. However, the number of portal tracts was found to be decreased when compared with that of the surrounding liver tissue (Figure 4a). Marked fatty change of the hepatocytes was noted. Some areas of the nodule contained Mallory bodies and hepatocytes with increased nuclear chromatin. However, the whole histological

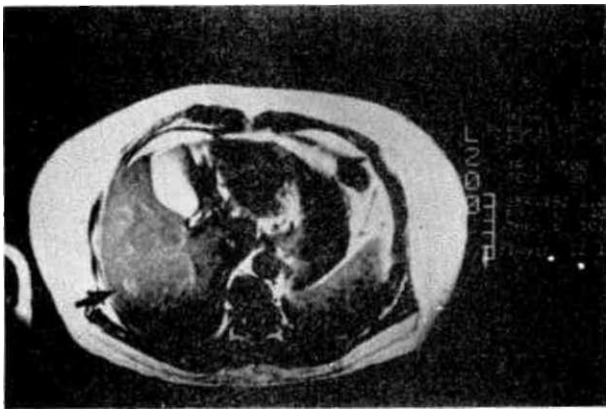

Figure 1. T2-weighted (2500-30) axial MR image displays relatively high intensity (arrow) compared to the background liver tissue.

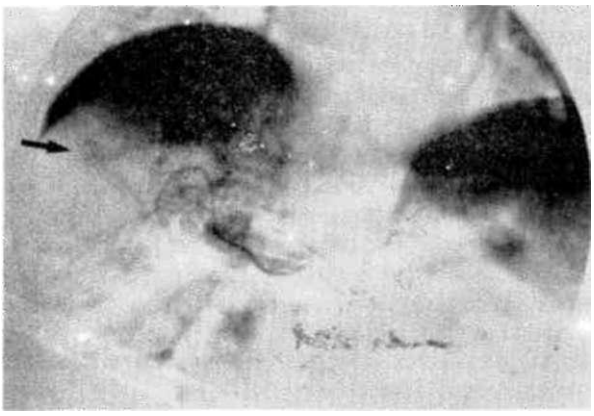

Figure 2. Capillary phase of hepatic angiography showing a tumor (arrow).

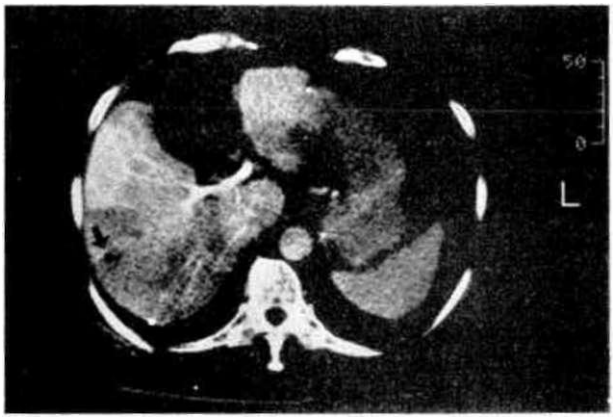

Figure 3. CT during arterial portography image demonstrates the nodule of low-attenuation relative to the surrounding liver (arrow), diagnosed as portal supply negative.

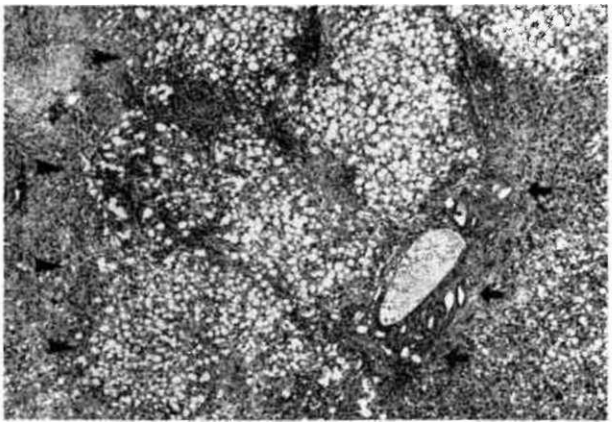

Figure 4a. Low power view of adenomatous hyperplasia. Arrowheads indicate the boundary between adenomatous hyperplastic nodule and surrounding nodule. The adenomatous hyperplasia contains portal tract in which the number of arteries (arrow) is abnormally increased. Hepatocytes of this adenomatous hyperplasia show marked fatty change (magnification x 40).

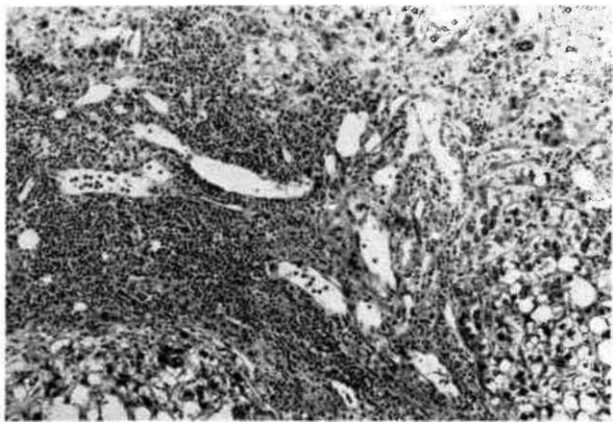

Figure 4b. Higher magnification of the adenomatous hyperplasia. There are many arteries in the nodule (magnification x 100).

examination did not demonstrate any obvious foci of HCC. The histopathological diagnosis of the nodule was an atypical adenomatous hyperplasia with fatty metamorphosis (2). The background liver showed an early stage of liver cirrhosis.

Morphometric examination of the pathologic specimen (3) revealed that the number and approximate cumulative area of hepatic arterial lumen were significantly increased within the nodule, whereas the approximate cumulative area of the portal vein was less than that of the surrounding liver tissue, suggesting that the nodule was supplied predominantly by hepatic arterial blood (Figure 4b).

DISCUSSION

On the spectrum of nodular lesions developing in the cirrhotic liver, AH is described as a sizable and discrete nodular parenchymal lesion containing portal tracts (3). It has been postulated that AH in a cirrhotic liver is a preneoplastic lesion or might play a role in the pathogenesis of HCC. Because it occasionally coexists with obvious HCC foci or may contain well differentiated HCC within the nodule and it could undergo malignant transformation (7-9). Because of the variable manifestations of AH, some distinct forms have been described. Among these forms; ordinary AH is a nodule which shows mild hypercellularity but lacks any structural atypia, whereas atypical AH is composed of hepatocytes showing nuclear atypia compared with the surrounding liver parenchyma. However, its structural and cellular atypia is not sufficient to make a definite diagnosis of malignancy. A third form is AH with malignant foci (2).

Our case fulfilled the criteria for atypical AH and no obvious HCC focus was on the histological evaluation. Examination of the resected specimen revealed the presence of portal tracts with portal vein, hepatic arteries and bile ducts, associated with some features such as fatty degeneration, Mallory bodies, and hepatocytes with hyperchromatic nuclei. Because of these findings the nodule was diagnosed as atypical AH with fatty metamorphosis on the histological examination **(10).**

However, preoperatively we strongly suspected this lesion fitted an HCC profile, taking into consideration not only the CT and MR findings, but also the features of tumor stain on the IHA examination. The diagnosis was also supported by CTAP examination which demonstrated a perfusion defect ir. this area (6).

IHA is one of the most reliable imaging modality which can detect the tumor and its extent. Tumor stain appears as a common and the only angiographic finding in a considerable number of HCCs smaller than 20 mm. This feature is also important, because it reflects the internal structure of the lesion and has been considered almost pathognomonic of HCC **(11).** Matsui et al found in a large series of 84 patients with HCC that almost all HCC nodules showed a tumor stain at IHA associated with a perfusion defect at CTAP (6).

It was very interesting that this nodule found in a liver with chronic liver disease was composed of the nonmalignant hepatocytes with portal tract, whereas the IHA and CTAP features were characteristic of HCC. Therefore, we examined the vasculature of the nodule in the pathological specimen. The morphometric analysis confirmed that the nodule had abundant hepatic arteries, but few portal veins, suggesting that the nodule had been predominantly supplied by hepatic arterial blood. From this morphometric analysis, it was clarified that both the tumor stain on the IHA and the perfusion defect on the CTAP were caused by the alteration of blood supply. However, it is very uncommon for an AAH without HCC foci to have a marked

blood supply from the hepatic arterial system (6,12,13). Ueda et al have reported that the number of hepatic arteries markedly increased, and the number of portal veins markedly decreased in the HCC cases (13).

It is likely that these abundant arteries in the nodule represent the early stages of angiogenesis in the carcinogenesis of HCC, since angiogenesis may precede neoplastic cell occurrence in some hyperplastic lesions (14). On the other hand, considering the stepwise progression in hepatocarcinogenesis and previous reports concerning the transformation of AH to HCC (7,8), it may be assumed that the vascular characteristics of the tumor had changed before histopathologic malignant transformation occurred. Indeed, to know whether this estimation would definitely come true in future is difficult. However, it is possible that the diagnostic information provided by the imaging modalities, particularly IHA and CTAP, facilitated the diagnosis of a lesion which probably would have become malignant in the short term.

This case illustrates possibility of atypical AH which may be principally supplied by hepatic arterial sources and can show entirely HCC-like features on various imaging methods, even in the absence of any HCC foci. Therefore, in differential diagnosis of small hepatic lesions, it would be important to obtain tissue specimens using US-guided biopsy.

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