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Hepar lobatum carcinomatosum due to metastatic breast carcinoma

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Summary. This is the first clinico-pathological report of hepar lobatum carcinomatosum (HLC), the rarest form of metastatic liver disease. The primary lesion was a scirrhous breast carcinoma. HLC closely resembles its syphilitic counterpart macroscopically, and is characterized by multifocal cancer-bearing scars and compensatory hyperplasia of the spared liver parenchyma. Multifocal carcinomatous obstruction of portal and hepatic venous vessels as well as rather slow progression of the clinical course may determine the development of HLC. In addition to the possible association of portal hypertension, the differential diagnosis from other types of unusual liver metastasis is discussed.

Key words: Liver neoplasms – Neoplasm metastasis – Breast neoplasms

Introduction

Liver metastasis is a common event during the course of neoplastic disease and usually takes the form of multiple nodules scattered throughout the liver. Rarely, it may masquerade as cirrhosis (Craciun et al. 1931; Micologhi et al. 1958) or may be manifest as diffuse intra-sinusoidal metastasis (Ziegler 1919; Herxheimer 1930; Watson 1955; Kettler 1958; Smith 1961; Bolck and Machnik 1978; Schneider and Cohen 1984; Razenberg et al. 1985) or as a grossly distorted liver (Borja et al. 1975). Recently the author found a lobulated liver in a patient with metastatic breast carcinoma. Microscopic examination revealed a peculiar form of metastatic liver disease. The purpose of this paper is to describe the clinico-pathological characteristics of this rarest form of metastatic liver disease, hepar lobatum carcinomatosum (HLC).

Case report

The patient was a 48-year-old Japanese woman. Eleven months before death she was admitted to the Dokkyo University Hospital because of pain in the right hypochondrium. Clinical examination, including abdominal CT suggested multiple liver tumours of metastatic nature associated with moderate liver dysfunction. A poorly defined mass, measuring 5×2 cm, was felt in the right breast just beneath the nipple and biopsy revealed a carcinoma. She received right mastectomy with bilateral oophorectomy. Pathological examination of the right breast revealed invasive duct carcinoma composed of small solid nests of carcinoma cells accompanied by abundant scirrhous stroma (Fig. 1). The carcinoma had already involved the skin at and around the nipple and the underlying pectoral muscles extensively. Metastasis to the axillary lymph nodes and to the right ovary was evident. After cancer chemotherapy which consisted of two courses of intravenous administration of adriamycin and 5-fluorouracil with daily oral endoxan, she was discharged. In spite of cancer chemotherapy, CT revealed gradual enlargement of liver metastases with no evidence of regression. Two weeks prior to death she was readmitted to the hospital with the complaint of anorexia and tremor of the upper extremities. Her general state deteriorated rather rapidly with increasing jaundice and loss of consciousness. Results of laboratory data included serum ammonia, 110 μg/dl; serum GOT, 180 K.U. and polyclonal hypergammaglobulinaemia, 3. lgr/dl, suggesting hepatic failure.

Autopsy findings. The liver, weighing 1,210 g, showed a deeply grooved and coarsely lobulated external aspect. Some of the grooves were closely adjoined by poorly defined, grayish-white nodular tumour deposits. The tumour-free liver showed a smooth-surfaced, coarsely nodular parenchyma of up to 6×4 cm in size. The entire liver closely resembled syphilitic hepar lobatum or "Kartoffelleber" by Kalk (1948; 1954) (Fig. 2). Cut surface of the liver disclosed multiple foci of ill-defined scar-like tumour tissue traversing throughout the liver

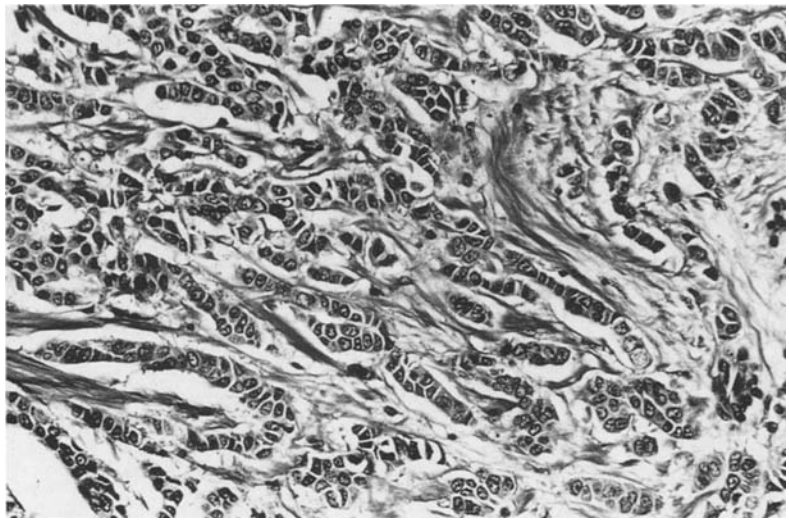

Fig. 1. Histology of right breast carcinoma, showing solid nests of carcinoma cells associated with scirrhous stroma. Haematoxylin-eosin ×66

Fig. 2. Hepar lobatum carcinomatosum, showing a coarsely nodular lobulated liver parenchyma by deeply grooved scars as well as several typical nodular metastatic deposits

as well as several ordinary tumour nodules. The majority of those scar-like areas were closely associated with grooves seen on the external aspect. The remaining nodular liver parenchyma showed prominent lobular markings partly due to marked cholestasis and appeared to be hyperplastic.

The right breast was absent, with no local recurrence of carcinoma. The sites of metastasis other than the liver included lumbar vertebral bodies and lungs, the latter showing carcinomatous lymphangitis and pleuritis. No tumour was found in the left breast. Signs indicating portal hypertension were recognized, including accumulation of clear ascites (4,800 ml), development of oesophageal varices, oedema of the gastrointestinal wall and congestive splenomegaly.

Histology of the liver reveals extensive metastasis of a scirrhous carcinoma identical with the primary breast lesion (Figs. 3 and 4). In addition to several ordinary nodular deposits, ill-defined infiltrating foci of carcinoma are noted, accompanied by exuberant scirrhous stromal reaction (Fig. 3a). These areas frequently show scar-like paucicellular "burned-out" features consisting of a condensed fibro-elastic tissue which obliterates the hepatic lobular architecture with closely packed portal triads and hepatic venous channels (Fig. 3b). Such scar-like areas, containing only sporadic small degenerative nests of carcinoma cells (Fig. 4a), are surrounded by a rim of viable carcinoma. The majority of the affected portal and hepatic venous vessels are occluded by carcinoma and/or fibrous tissue, and not infrequently, the lining epithelium of the small- and medium-sized bile ducts shows in-situ replacement by carcinoma cells (Fig. 4b). The hepatic arterial branches and large intrahepatic bile ducts are patent. The non-neoplastic portion of the liver consists of hyperplastic parenchyma with two-cell thick liver cell plates and hypertrophic lobular architecture (Fig. 5) (Sternberg 1923; Kalk 1948; Scheuer 1973).

The histology of the spleen shows increased reticulin fibers in the splenic red pulp with the finding of sinus hyperplasia, suggesting chronic congestion of the organ.

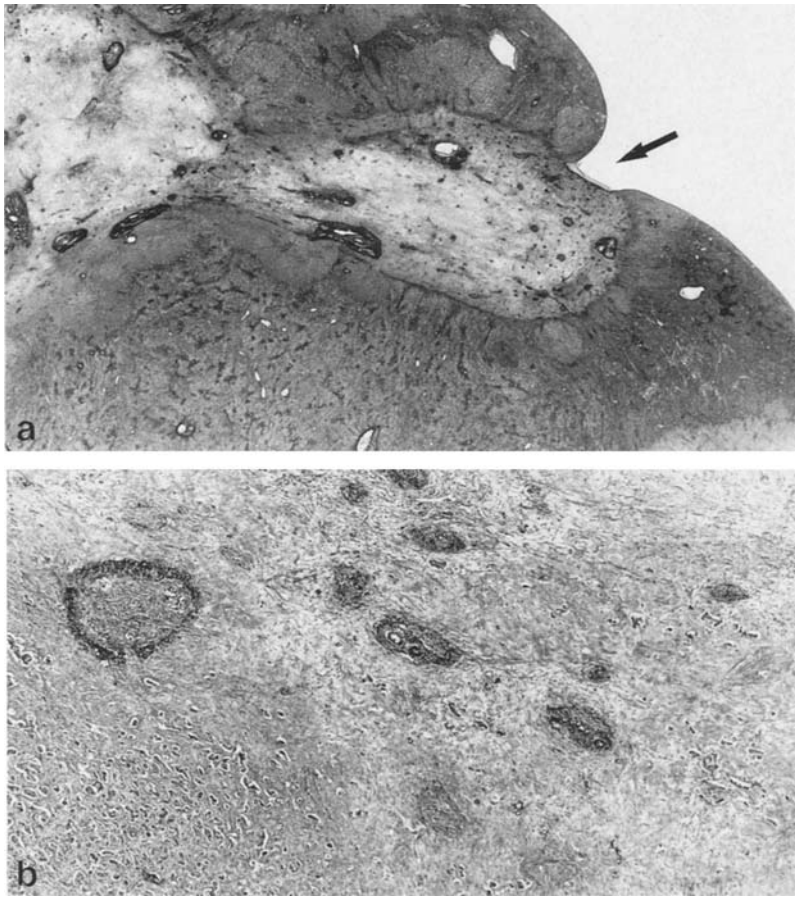

Fig. 3. Histology of hepar lobatum carcinomatosum. **a** Extensive cancer-bearing scar underlying the grooved area (arrow), adjoined by a hyperplastic liver parenchyma. Elastic-haematoxylin-eosin ×0.7; **b** Paucicellular cancer-bearing scar containing closely packed atretic portal triads as well as a medium-sized hepatic venous branch. Elastic-haematoxylin-eosin ×10

Discussion

Hepar lobatum carcinomatosum (HLC) is the rarest form of metastatic liver disease. Review of the literature reveals only one similar case reported by Busni (1924). In his detailed autopsy report of a 37-year-old woman with carcinoma of the breast, he described a specific form of metastatic liver disease which was quite distinct from hepar lobatum syphiliticum complicated by metastatic carcinoma. However, his report contained no clinical presentation or clinico-pathological consideration of HLC.

It is clear that HLC is characterized by the combination of multifocal cancer-bearing scars and compensatory hyperplasia of the spared liver parenchyma similar to that seen in "Kartoffelleber" by Kalk (1954). Macroscopically, HLC may resemble its syphilitic counterpart, but unquestionable tumour tissue can be demonstrated around or independent of those scar-like areas. However, metastatic carcinomatous cirrhosis first described by Craciun (1931) may show a micronodular cirrhosis with no marked regenerative hyperplasia of the liver cells. A grossly distorted liver or "Narbenleber" (Kalk 1954) due to metastatic carcinomatosis (Borja et al. 1975) which may or may not be associated with portal hypertension clinically, seems to be encountered occasionally in autopsy practice, especially in breast cancer. The latter two conditions can be distinguished from HLC by macroscopical appearances.

At least two factors may be responsible for the pathogenesis of multifocal cancer-bearing scars: scirrhous stromal reaction to carcinoma, or vascular impairment due to infiltration. Metastatic liver cancers from the stomach, gallbladder, pancreas etc. may commonly be associated with a scirrhous stroma, but HLC has not been observed with such primaries. It is therefore likely that occlusion of portal and/or hepatic venous branches rather than a scirrhous stromal reaction to metastatic carcinoma may play a major role in the development of HLC. In this respect, further two conditions may be required: non-uniform or diffuse but multifocal distribution of the affected blood vessels and slow progression of the process allowing the spared liver parenchyma to develop compensatory hypertrophy. The pathogenetic mechanism of HLC may,

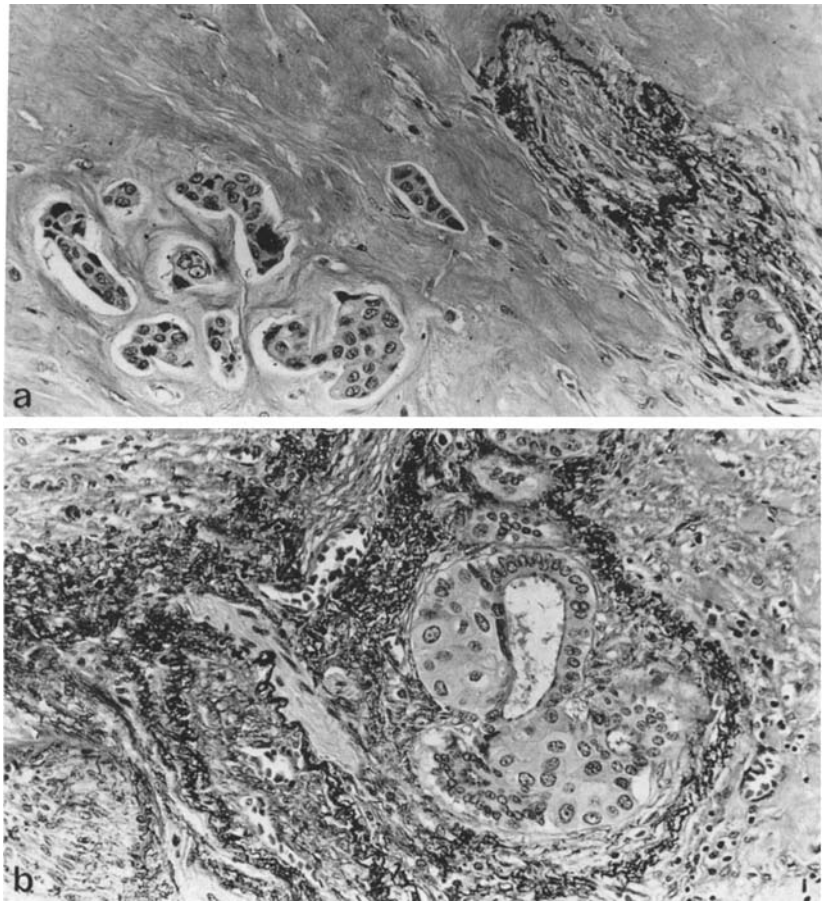

Fig. 4a. Histology of hepar labatum carcinomatosum. High power view of **3b,** showing small nests of carcinoma cells and an atretic portal triad embedded in a hyaline stroma. Elastic-haematoxylin-eosin ×66; **b** Interlobular bile ducts showing in-situ replacement of the ductular epithelium by carcinoma cells. Elastic-haematoxylin-eosin ×66

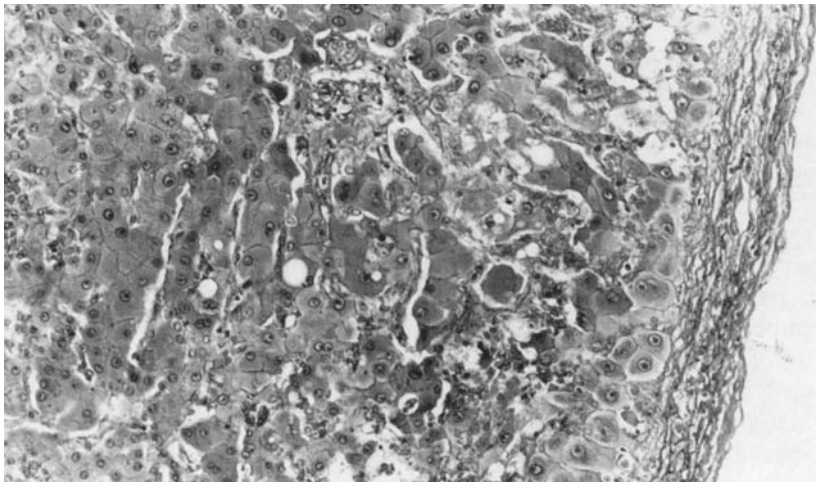

Fig. 5. Hyperplastic liver parenchyma composed of hypertrophic polygonal liver cells forming two-cell thick liver cell plates. Elastic-haematoxylin-eosin ×50

thus be quite similar to that of its syphilitic counterpart (Bolck and Machnik 1978).

Occlusion of portal venous branches may cause Zahn infarcts. Occlusion of hepatic venous branches may superimpose a truely congestive effect upon the damaged liver tissue, leading to its gradual shrinkage with fibrosis. Occlusion of the lymphatic vessels may add a dystrophic effect in terms of lymph stasis. Thus, those paucicellular "burned-out" scars may represent a long-standing shrinkage process following gradual carcinomatous impairment of the venous vessels mentioned above.

It is known that unusual metastatic liver diseases may be associated with portal hypertension, both clinically and morphologically. Some cases show gastrointestinal bleeding from ruptured oesophageal varices (Hyun et al. 1964; Borja et al. 1975). It is probable that in such cases extensive occlusion of portal and hepatic venous vessels within the liver is responsible for the development of portal hypertension (Hyun et al. 1964).

It is possible that therapeutic intervention may modify the natural progression of nodular liver metastasis. Craciun et al. (1931) have referred to the possibility of an effect of radiotherapy upon the development of carcinomatous cirrhosis. In our case, however, the dose of antineoplastic drugs used was within the ordinary range and repeated CT examinations prior to and after their administration demonstrated no regression of liver metastasis. Busni's case with unquestionable HLC (1924) also seems to have received no therapy. Therefore, it is unlikely that HLC represents a specific form of therapeutically modified nodular liver metastasis, rather it should be considered to be a distinct clinico-pathological entity.

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