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Cholangiocarcinoma with Metastasis to the Male Breast: Report of a Case with Autopsy Findings

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Abstract A 52-year-old male, with a clinical diagnosis of liver cirrhosis, liver tumor and gynecomastia, developed a hard mass in the left breast. Although the breast lesion at biopsy was considered to be primary breast cancer, postmortem examination revealed metastatic breast lesion originating from cholangiocarcinoma in the liver. The metastatic spread to the mammary gland was likely to have been encouraged by the presence of gynecomastia.

Key Words: Cancer; metastasis, gynecomastia, cholangiocarcinoma

Introduction

Metastatic tumors to the breast are unusual, representing 0.5% to 2% of all breast tumors. About 200 such cases have been reported in the English literature[1-4]. Their most common sources are malignant melanoma and leukemia-lymphoma group. In males, the prostate is relatively frequent as their extramammary origin, and the metastases to the breast occur chiefly in patients receiving estrogen therapy[3]. The liver as a primary site of metastatic breast tumor was described only once in the literature[2]. This paper presents a male patient with cholangiocarcinoma with breast metastasis and gynecomastia. Necropsy findings will be presented.

Case Report

Clinical Course

A 52-year-old male, a heavy drinker, was admitted to Kokura Memorial Hospital because of full-sensation of the upper abdomen. He was moderately-nourished, measuring 162 cm and weighing 54kg. Physical examination revealed ascites, hepatomegaly, splenomegaly, and vascular spider. Jaundice was not present. Laboratory data were: RBC 336×10^4/ml, Ht 37%, WBC 7,300/ml, serum total protein 7.7g/dl, albumin 3.2g/dl, globulin 4.5g/dl, icterus index 5, GOT 26U, GPT 18U and alkaline phosphatase 8.1U. The HBs antigen was positive, but alpha-fetoprotein was negative. His chest X-ray films revealed elevation of the right hemidiaphragm. An upper gastrointestinal series demonstrated esophageal varices. Hepatic scintigrams revealed a space-occupying lesion in the right lobe. Selective celiac angiograms showed an abnormal vascularity of the right lobe. These findings indicated liver tumor with cirrhosis. A needle biopsy of the liver,

however, failed to reveal the tumor. Bilateral gynecomastia developed two months after admission. A hard, painful tumor then developed in the left breast. An excisional biopsy was interpreted as "probable medullary tubular carcinoma" of mammary origin. His general condition gradually deteriorated and he died six months after admission.

Biopsy Finding of the Breast Lesion

The left breast tumor was finger-tip sized, elastic hard, and well circumscribed. Histologically, the tumor consisted of oval to round cells with large vesicular nuclei and abundant, light cytoplasm. The tumor cells contained much glycogen but little mucin. They were arranged in sheet-like fashion around preserved mammary ducts (Fig. 1a). The tissue surrounding the tumor showed ductal hyperplasia and periductal myxomatous stroma (Fig. 1b).

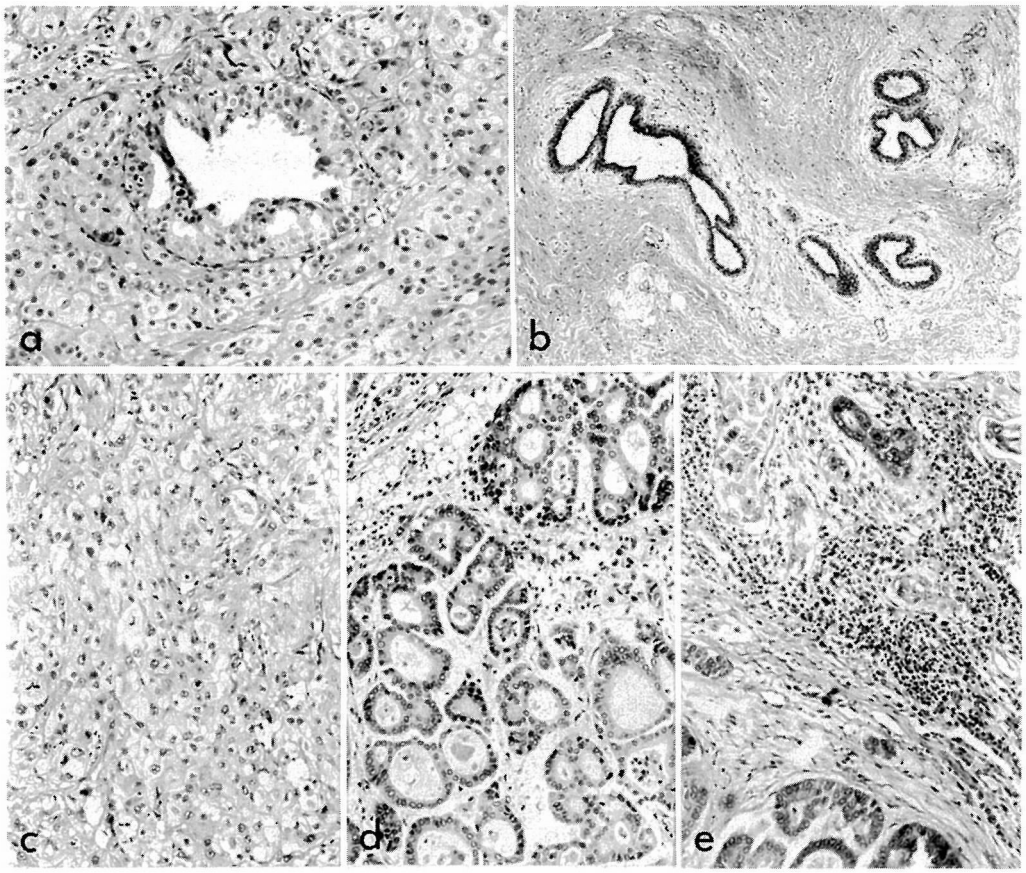

Fig. 1 a; The breast tumor cells arranged in sheet-like fashion around a preserved duct of the breast. (HE stain, original magnification ×100).
b; The breast tissue surrounding the tumor. Note ducta hyperplasia and periductal myxomatous stroma. (HE stain, original magnification ×40).
c; Liver tumor cells show a solid proliferation pattern. (HE stain, original magnification ×100).
d; Tumor cells form a tubular pattern in the liver. (HE stain, original magnification ×100).
e; The area of the liver with both solid and tubular patterns. (HE stain, original magnification ×100).

Autopsy Findings

Autopsy was carried out four hours after death. The patient was icteric. An excisional wound in the left breast was seen and no remaining breast mass was recognized. The abdominal cavity was filled with 5,300 ml of yellowish fluid. The liver was cirrhotic and weighed 1,860 g including the major omentum adhered to its surface. Its right lobe was largely replaced by a massive tumor measuring 10 cm in the diameter. The tumor was elastic hard, its cut surface was grayish white and fibrous with partial necrosis and hemorrhage. The right lung was adherent to the diaphragm. Metastatic lesions were found in the lungs, kidneys, adrenals, major pectoral muscle, diaphragm, ribs, and hepatic hilar, parapancreatic, paraortic, and axillary lymph nodes.

Microscopically, the liver tumors had two distinct features. One was a solid proliferation of tumor cells with moderate anaplasia (Fig. 1c). It resembled the breast tumor of the biopsy specimen. Alcian blue or mucicarmine positive substances were demonstrable within the cytoplasm of some tumor cells. The other was a tubular pattern (mucin-producing adenocarcinoma) composed of cuboidal or columnar cells with hyperchromatic nuclei and eosinophilic cytoplasm (Fig. 1d). The stroma was connective tissue, frequently hyalinized. Bile production was observed in neither of them. These two patterns were intermingled in some part of the liver tumor (Fig. 1e). Intraductal proliferation of adenocarcinoma could be seen in the bile duct near the hilus. The tumor was diagnosed as cholangiocarcinoma with anaplastic component. The noncancerous areas of the liver showed B-type cirrhosis. Orcein stain demonstrated HBs antigen in the cytoplasm of liver cells.

Metastatic lesions of the lungs and paraortic lymph nodes had the tubular pattern. An anaplastic pattern was observed in the metastases of the kidneys, adrenal glands, muscle, bones, and hepatic hilar and axillary lymph nodes. In the parapancreatic lymph nodes, both tubular and anaplastic patterns could be found. Microscopic gynecomastia was also recognized in the right breast. The remaining left breast tissue contained no tumor cells.

Other microscopic findings included pulmonary edema, congestion and anemic infarction of the spleen, atrophy of the testes, and thrombosis of the portal vein.

Discussion

It was difficult to determine whether the breast tumor was primary or secondary. The breast lesion in retrospect was regarded as a metastasis from the liver cancer, although it at biopsy had been mistaken for a primary breast cancer. The breast tumor resembled the areas with anaplastic pattern of the liver cancer and the breast tumor cells proliferated in periductal areas. The ductal epithelium appeared hyperplastic but not neoplastic. The breast tissue surrounding the tumor showed microscopic gynecomastia. Previous reports on breast metastases have stressed these findings described above, such as resemblance of the histological patterns of the metastatic tumor to those of the original tumor, proliferation of metastatic tumor cells in periductal areas and presence of gynecomastia, as features helpful in the diagnosis of metastasis[3,5].

Toombs and Kalisher[2] summarized 152 patients with malignancies metastatic to the breast, 21 males and 131 females. Of these, 72 patients had cancers originating from the lung, stomach, prostate, ovary, kidney, uterine cervix, mouth, thyroid, colon, endometrium, and other organs, in this order of frequency. The liver as the original site of malignancy has been reported only once[2].

Metastases to the breast are more likely to occur in young women. Deeley[6] suggested that the tendency depends on the greater blood supply and different cellular pattern

of their breast compared with elder patients. In males, the prostate was relatively frequent as a primary site. Most patients with metastases to the breast had received estrogen therapy for prostatic cancer[3]. Long-term estrogen therapy may cause histologic changes in the mammary tissue, including increase of vascularity, increase of loose connective tissue, and hyperplasia of ductal epithelium. All these findings could be interpreted as microscopic gynecomastia. Our case patient received no hormonal therapy. The metastatic spread to his breast might be related to the presence of gynecomastia that was probably caused by the disturbance due to liver cirrhosis of inactivation of circulating estrogen.

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