Case Report

Giant Cell Carcinoma of the Liver: occurrence in a patient with ileal carcinoid, medullary breast carcinoma and pulmonary aspergillosis

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Abstract

Pure giant cell carcinoma of the liver is a rare tumor that is usually associated with cirrhosis. Its occurrence in a young woman without evidence of cirrhosis, and in association with two other uncommon tumors, is described in this report.

A 37-year-old black woman noticed a lump in her right breast in March, 1974. Modified radical mastectomy was performed four weeks later. Pathologic diagnosis was medullary carcinoma (Fig. 1). Seven axillary nodes were free of tumor. Ten months later, intermittent fever developed and hepatomegaly was noted. Liver scan showed large filling defects in both lobes; bone scan and chest roentgenogram were normal. Serum alphafetoprotein and hepatitis-associated antigen were not determined. Percutaneous liver biopsy showed anaplastic carcinoma with giant cells. The clinical impression was metastatic breast cancer. There was no history of alcoholism or liver disease, nor family history of cancer.

Fever persisted despite antibiotic therapy; multiple bacterial cultures of blood, sputum, and urine were negative. An amebic titer of 1:128 (indirect hemagglutination) raised the question of amebic abscess, but ultrasound liver scan showed only solid lesions. Disseminated intravascular coagulation was manifested by a falling hematocrit, schistocytes, a positive protamine test, and a prolonged partial thromboplastin time. Heparin administration was begun. Bone marrow aspirate was normocellular. Chemotherapy was begun with Adriamycin, cyclophosphamide, fluorouracil, and methotrexate. Antibiotics, including cephalotin and gentamicin, were continued because of bilateral rales, although the temperature returned to normal. The patient expired 23 days after admission. A blood culture drawn shortly before death showed Pseudomonas. Fungal cultures were not obtained. The patient never had symptoms of the carcinoid syndrome.

Autopsy Findings

At autopsy, the liver weighed 4840 gm. An ill-defined cystic mass was present in the right lobe of the liver. Several umbilicated, whitish tumor nodules were found primarily in the left lobe. Cut sur-
face (Fig. 2) revealed a 20 x 18 x 10 cm multilocular, cystic tumor mass, which largely replaced the right lobe and contained plasma clots and blood clots. The cysts were lined by light brown or white soft tissue. The liver was not cirrhotic. The common bile duct, pancreatic duct, inferior vena cava, and portal vein were free of both tumor and thrombus. The gallbladder was small and contained numerous sandy stones. Tumor was present in peripancreatic and porta hepatitis nodes and in the right kidney. Both lungs showed multiple, small, thin-walled abscesses, with patchy consolidation and hemorrhage. The pulmonary arteries were free of thrombus. Three nodules measuring 0.2, 0.4, and 0.5 cm were present in the submucosa of the ileum.

Microscopic examination of the tumor in the liver (Fig. 3) disclosed a predominance of bizarre tumor giant cells, often multinucleated. Abnormal mitoses were frequent. Most of the tumor cells were PAS-negative, but some contained PAS-positive, fine, doubly refractile granules, probably representing lipofuscin. Numerous thrombi at various stages of development were present in large hepatic vessels. The adjacent liver was compressed, with marked congestion and hemorrhage. There was also multifocal coagulative necrosis, mainly centriflobular. Some liver cells revealed fatty metamorphosis. There were no bile lakes, bile infarcts, or duct proliferation. Tumor cells infiltrated through the hepatic sinusoids, and had suggestive continuity with cords of hepatocytes in other regions. A minimal inflammatory response was present around the tumor. A similar microscopic picture, characterized by giant cells, was seen in the peripancreatic and porta hepatitis lymph nodes and in the right kidney. Sections through the nodules in the ileum revealed carcinoid tumors.

The lungs were not involved by metastatic tumor, but did contain fungus balls with multiple foci of necrosis. The morphological and histochemical characteristics were those of aspergillus. The remaining lung was also involved by necrotizing pneumonitis and edema; intravascular thrombi were frequent. Focal fibrinoid necrosis and intravascular thrombi were also noted in the glomerular tufts, away from the metastatic tumor in the kidney. There was no evidence of tumor in the remaining breast, chest wall, or axillary lymph nodes. Comparison of the original breast carcinoma (Fig. 1) with the liver carcinoma (Fig. 3) led to the conclusion that they represented different tumors.

Comment

Pure giant cell carcinoma of the liver makes up only 1.8 percent of primary liver carcinomas, although occasional giant cells may be seen in 14 percent. Since 90 percent arise in cirrhotic livers and there is a male preponderance, the occurrence in a young woman with no evidence of cirrhosis or history of alcoholism is quite rare. Giant cells may be present in a variety of other cancers, including medullary carcinoma of the breast, which makes up 4.3 percent of infiltrating breast carcinomas. The source
of diagnostic confusion in this case was the fact that occasional giant cells were indeed seen in the medullary breast carcinoma, which had been resected 10 months earlier. Although there were many more giant cells in the liver biopsy than in the breast carcinoma, it was initially assumed that the liver tumor might have represented a metastatic breast cancer. Militating against this, however, was the knowledge that medullary carcinoma carries a somewhat better prognosis than the average breast carcinoma, and that the resected axillary nodes had been free of tumor. Nevertheless, the patient's rapid downhill course led to the administration of combination chemotherapy aimed at the breast carcinoma. The patient died before the effect of this therapy could be ascertained.

Another source of confusion was the borderline amebic titer in a patient with unexplained fever. Had the ultrasound scan correctly diagnosed the major hepatic lesion as being cystic, amebic abscess would have been a plausible consideration. It is of interest that aflatoxins, the metabolic products of *Aspergillus flavus*, are known to produce liver carcinoma in animals.7-9 Although *Aspergillus fumigatus* is the most frequent etiologic agent in human aspergillosis, *Aspergillus flavus* is found in some cases.10 It is much more likely that this patient's aspergillosis was a terminal event, related to cancer, debility, and possibly chemotherapy, than that the aspergillosis preceded and perhaps produced the liver carcinoma. This fungus can also produce disseminated intravascular coagulation.11 A close association of coagulopathy and cancer is acknowledged.12,13 It is instructive that this patient's intravascular coagulation occurred in the lungs, adjacent to the fungal infection, and in the liver, adjacent to the tumor. Aspergillosis is found predominantly in cancer patients, with over 60 percent localized to the lungs. Antemortem diagnosis is difficult; the organism can be cultured from clinical specimens in fewer than 40 percent of patients, and the chest roentgenogram is normal at the onset in a similar percentage.11 The explanation for the occurrence of three uncommon tumors (giant cell liver carcinoma, ileal carcinoid, and medullary breast carcinoma) in the same patient must remain speculative.
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