Metastatic Breast Carcinoma Mimicking Macronodular Cirrhosis

To the Editor: Although breast cancer often metastasizes to the liver, associated hepatic failure with cirrhosis is rare. We report an unusual case of metastatic breast cancer mimicking macronodular cirrhosis with portal hypertension, varices, and fulminant hepatic failure.

Report of a Case.— A 42-year-old woman presented to our facility with new-onset ascites, hepatic failure, and evolving hepatic encephalopathy. Invasive lobular breast carcinoma had been diagnosed 1 year previously, and the patient had received 4 cycles of adjuvant doxorubicin and cyclophosphamide, 4 cycles of paclitaxel, 8 weeks of radiation therapy, and adjuvant hormonal therapy with tamoxifen citrate. She had done well until 3 weeks before the current admission, when she developed general malaise, fatigue, progressive jaundice, and marked abdominal distention.

Computed tomography (CT) of the abdomen showed extensive ascites and a small, hypoperfused liver. Although metastatic breast carcinoma was strongly suspected, cytologic examination of the ascitic fluid and CT findings did not support this diagnosis. Ultrasonography of the abdomen revealed a small liver with relative sparing of the left hepatic and caudate lobes, consistent with macronodular cirrhosis. Blood flow within the main portal vein was hepatofugal, suggesting portal hypertension. Multiplanar magnetic resonance imaging showed a small, cirrhotic-appearing liver with esophageal and gastric varices but no evidence of a focal mass. Together, these findings suggested cirrhosis, not metastatic breast cancer. Therefore, we performed a liver biopsy, which showed portal hypertension and varices. The tissue obtained was histologically compatible with metastatic breast carcinoma. Small foci of residual hepatocytes were evident, with nearly complete replacement of the liver by metastatic adenocarcinoma. The patient returned to her home medical facility, where she died of her illness.

Discussion.— Metastatic carcinomatous cirrhosis is a rare syndrome. Although the liver is a frequent site of metastasis, hepatic failure with cirrhosis is rare, and the associated portal hypertension and esophageal varices seen in our patient are even more unusual. A 20-year retrospective study of the development of esophageal varices secondary to primary and metastatic liver tumors identified 72 patients with radiological, endoscopic, or postmortem evidence of esophageal varices.[1] Liver metastasis was believed to be the cause of portal hypertension and esophageal varices in 17 cases, 8 due to metastatic breast cancer.

Young et al[2] examined CT patterns mimicking cirrhosis in patients with breast cancer metastatic to the liver who underwent chemotherapy. In their prospective study, all 22 patients had pseudocirrhosis, 12 had portal hypertension, and only 2 had esophageal varices. Liver biopsies showed residual tumor with no evidence of cirrhosis. Shirkhoda and Baird[3] reported severe cirrhotic changes on CT in 4 of 32 patients with breast carcinoma metastatic to the liver. The morphologic CT criteria included irregular border, decreased size, and presence of ascites. The 4 patients with cirrhosis had no common pattern of chemotherapy administration. Ogawa et al[4] reported that 36.4% of patients given tamoxifen had fatty liver on annual CT examinations. We were unable to determine whether chemotherapy or tamoxifen played a role in the development of cirrhotic changes in our patient. The pathologic findings suggested pseudocirrhosis due to almost complete replacement of hepatocytes with adenocarcinoma.

Comment.— Breast cancer with liver metastasis has a grave prognosis, and early detection may have clinical importance, although therapy is limited. In our patient, the diagnosis of metastasis was needed to redirect her therapy. She was not a candidate for cytotoxic therapy, but she was a candidate for trastuzumab, a monoclonal antibody targeted against the HER-2/*neu* oncoprotein that was overexpressed in her breast cancer. Unfortunately, the patient died before treatment could be initiated.

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The opinions or assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the Department of the Army or the Department of Defense.

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Acute Myocarditis Associated With Tetanus Vaccination

To the Editor: Millions of people undergo vaccination each year; thus, it is perhaps not surprising that a fraction develop adverse effects because of immunologic responses to the target antigen and to other nonspecific antigens contained within the vaccine. These immunologic reactions can result in aberrations in systemic physiology or direct injury to tissues and organs. Hypersensitivity myocarditis is an inflammatory disease of the myocardium, usually related to drug allergy. Many drugs have been reported as possible etiologic agents.[1,2] We report a case of hypersensitivity myocarditis apparently related to a tetanus vaccination.

Report of a Case.— A previously healthy 14-year-old boy presented with fever and intermittent (lasting a few minutes)

Table 1. **Serial Laboratory Measurements in Patient With Hypersensitivity Myocarditis**

Enzyme	Hospital day 1	Hospital day 2	Hospital day 3	Follow-up (day 6)
Troponin T (ng/mL)	1.04	0.93	0.89	0.18
Myoglobin (μg/L)	83.00	41.13	25.09	31.05
CK-MB fraction (ng/mL)	80.86	57.13	6.42	1.31
Alanine aminotransferase (U/L)	28	27	18	17
Aspartate aminotransferase (U/L)	117	110	41	35
Creatine kinase (U/L)	1218	1095	851	…

chest pain. The symptoms developed 3 days after he had received a vaccination for tetanus (Tetavax, Aventis Pasteur SA, Lyon, France). His medical history was unremarkable except for a severe skin eruption that occurred after trimethoprim-sulfamethoxazole treatment when he was 8 years of age. He had no history of adverse reactions to tetanus or other vaccinations. Findings on physical examination were normal except for fever (38.3°C) that was recorded on 4 occasions. Heart sounds were normal, and no precordial friction rub was detected. On admission, laboratory investigations yielded the following results (reference ranges shown parenthetically): white blood cell count, 10.6×10^9/L with 3% eosinophils; erythrocyte sedimentation rate, 42 mm/h; IgE, 72 kU/L (<10 kU/L); troponin T, 1.04 ng/mL (<0.1 ng/mL); myoglobin, 83 μg/L (<72 μg/L); creatine kinase, 1218 U/L (<190 U/L); CK-MB fraction, 80.86 ng/mL (<5 ng/mL); alanine aminotranserase, 28 U/L; and aspartate aminotransferase, 117 U/L (Table 1). Chest radiography revealed normal findings, and echocardiography showed normal left ventricular function and no pericardial effusion. The initial electrocardiogram (ECG) showed mild ST-segment elevation in the inferior leads and a notable ST-segment elevation in precordial leads V_4, V_5, and V_6. The patient's intermittent chest pain persisted throughout the day. On the second day of hospitalization, repeated ECG revealed diffuse ST-segment elevation, especially in leads V_4, V_5, and V_6, and inverted T waves in the left precordial leads (Figure 1). Findings on repeated echocardiography were again normal. Urgent angiography showed normal coronary arteries. On the third hospital day, ECG disclosed slight ST-segment elevation and inverted T waves in the left precordial leads. The patient's course was uneventful, and he was discharged on hospital day 4. Three days later, the patient was symptom-free, and his ECG was completely normal. Cardiac enzyme levels had decreased to nearly normal levels.

Discussion.— The clinical features of hypersensitivity myocarditis include nonspecific findings such as rash and fever as well as cardiac manifestations.[3] Cardiac involvement can manifest within hours or months after the initial exposure to the drug. Sinus tachycardia, mild cardiomegaly, conduction delays, and nonspecific ST-T changes are common, whereas pseudoinfarction patterns are seen less frequently.[1,2] Cardiac enzyme levels are usually mildly elevated, rarely more than twice the normal value.[3] The mechanism of action has been postulated to be a delayed hypersensitivity reaction.[2] Our patient's symptoms, ECG, and laboratory findings were consistent with myocardial involvement.

Although hypersensitivity myocarditis has been reported in association with a variety of drugs,[1,2] cardiovascular complications due to vaccination are rare,[4-6] and only a few cases of myocarditis after vaccination have been reported. One recent report[5] described a case of myopericarditis after triple vaccination against diphtheria, tetanus, and poliovirus. The patient had symptoms similar to our patient's, with slightly elevated cardiac

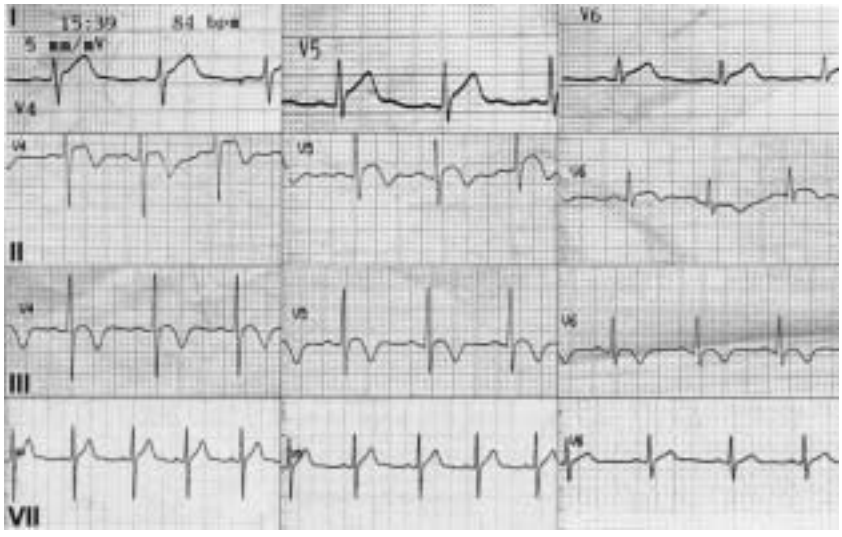

Figure 1. Electrocardiographic tracings recorded on hospital day 1 (I), 2 (II), and 3 (III) and 7 days (VII) after hospitalization, showing ST-segment and T-wave changes in left precordial leads. bpm = beats per minute.

enzymes and normal findings on echocardiography and coronary angiography. The vaccination was the suspected cause in view of the chronology of the symptoms. Performing a provocative test that would confirm the causal relationship between the vaccination and the cardiac anomalies would be unethical.

Our patient's illness had a pseudoinfarction pattern that is seen infrequently in hypersensitivity myocarditis.[7,8] The acute chest pain, ST-segment elevation and T-wave inversion on ECG, and slight increase in cardiac enzyme levels were consistent with myocardial involvement. However, echocardiography revealed normal left ventricular function, and angiography showed normal coronary arteries, findings that suggest the ECG abnormalities were due to myocarditis and not to ischemia.

Hypersensitivity myocarditis should be considered when new ECG changes occur in association with acute-onset chest pain, mildly elevated cardiac enzyme levels, and eosinophilia due to drugs and vaccination.

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Urinothorax: Unexpected Cause of a Pleural Effusion

To the Editor: Urinothorax is a rare type of pleural effusion, defined as urine in the pleural space. We report a case of urinothorax after a surgical ileal conduit and placement of bilateral percutaneous nephrostomy tubes.

Report of a Case.— A 53-year-old man with a history of metastatic bladder cancer was admitted to our hospital. Three months previously, he had undergone radical cystoprostatectomy with formation of an ileal conduit and urinary diversion to an ostomy; subsequently, cellulitis occurred in the abdominal area. Because of the severity of the cellulitis, bilateral percutaneous nephrostomy tubes were placed in attempt to divert urine away from the stoma site and promote healing. However, the patient experienced ileal conduit leakage and required surgical revision to reposition the ileal conduit. During this surgery the nephrostomy tubes were removed.

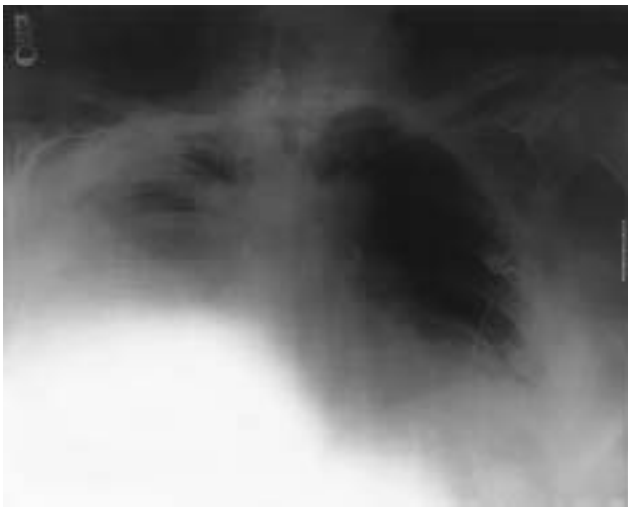

Figure 1. Chest radiograph showing a new large right-sided pleural effusion.

The next day, the patient developed rapidly worsening dyspnea and had a marked decrease in urinary output from the ileostomy. A chest x-ray film showed a new large right-sided pleural effusion (Figure 1). Therapeutic and diagnostic thoracentesis resulted in withdrawal of 3 L of straw-colored pleural fluid. Pleural fluid analysis revealed a transudative effusion with a pH of 7.24, protein level of 0.2 g/dL, and lactate dehydrogenase (LDH) level of 47 U/L. Simultaneous measurement of the serum protein and LDH revealed levels of 6.7 g/dL and 1179 U/L, respectively. The pleural fluid creatinine level was 12.2 mg/dL, and the serum creatinine level was 4.0 mg/dL. Cytologic studies, Gram stain, and cultures of the pleural fluid were negative.

We suspected that this patient had urinothorax due to the sudden onset of respiratory distress, decrease in urinary output, and development of a large pleural effusion after removal of the nephrostomy tubes. To confirm urinothorax, it was necessary to perform thoracentesis so that the retrieved fluid could be evaluated for 3 critical diagnostic criteria[1]: (1) the pleural fluid must be a transudate, (2) the pleural fluid-serum creatinine ratio must be greater than 1.0, and (3) the pH must be less than 7.3. On the basis of criteria of Light et al,[2] pleural fluid is considered a transudate if 1 or more of the following are present: pleural fluid protein divided by serum protein is less than 0.5, pleural fluid LDH divided by serum LDH is less than 0.6, or pleural fluid LDH is less than two thirds of the upper limit of normal for the serum LDH.

Usually, pleural fluid with a low pH is an exudate. However, with urinothorax, acidic urine migrates into the pleural