Portal Vein Thrombosis in a Patient with Breast Carcinoma

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Portal vein thrombosis is a rare thrombotic complication [1]. When patients present with this entity, one should look for factors that predispose for hypercoagulability. Malignancy and certain drugs are known to have prothrombotic effects. We present the case of a woman with a metastatic breast carcinoma treated with aromatase inhibitor (a prothrombotic agent), and rapidly developing ascites due to a portal vein thrombosis.

PATIENT DESCRIPTION

A 78 year old woman was admitted to our department complaining of vomiting, diarrhea and palpitations. There was no blood or pus in the stool. The patient vomited seven times and had three bowel movements. She denied rash, fever or other complaints. Her medical history was significant for hypertension, insulin-dependent diabetes mellitus, paroxysmal atrial fibrillation, and metastatic breast carcinoma. The breast carcinoma was diagnosed in 1992 and treated with lumpectomy and radiation. The patient had a relapse of the carcinoma in 2004 and subsequently underwent mastectomy and chemotherapy. In 2007, bone metastases were found and palliative radiation was offered. Since the mastectomy the patient has been treated with a bisphosphonate (Aredia®) and an aromatase inhibitor (Aromasin®).

The remarkable findings in the physical examination were distended abdomen with mild ascites, soft and nontender, and mild leg edema. Blood tests were remarkable for macrocytic anemia with hemoglobin of 8.3 g/dl, mild neutropenia (1000/mm^3) and hypoalbuminemia of 2.3 g/dl.

Treatment with antibiotics and fluids was begun, leading initially to clinical improvement, but her condition deteriorated on the seventh day of hospitalization with severe tachypnea, dyspnea and rapidly developing ascites. A few relevant options arose in the differential diagnosis of the patient's ascites.

At this stage the carcinomatous disease spread to the bone without liver involvement. The option of liver metastases was considered, but normal liver functions without unusual findings on the abdominal ultrasonography and computed tomography precluded this possibility. Hypoalbuminemia was also considered, but recent albumin levels had been stable and hypoalbuminemia could not be the sole explanation. In the context of metastatic malignancy, a hypercoagulable state, and the rapid course of deterioration, we considered the possibility of an acute thrombotic event. The abdominal Doppler ultrasound demonstrated a complete occlusion of the portal vein. The patient was treated with low molecular weight heparin (Clexane®) without improvement, and she died 5 days later.

COMMENT

HYPERCOAGULABLE STATE AND MALIGNANCY

Cancer is a hypercoagulabale state. The clinical presentation varies from abnormal clotting parameters to fulminant thromboembolism. Several clinical syndromes are described in the literature: Migratory thrombophlebitis (Trousseau's syndrome), idiopathic deep venous thrombosis and other venous thromboses, non-bacterial thrombotic endocarditis, disseminated intravascular coagulation, and thrombotic microangiopathy. Thromboembolism is the second leading cause of death in patients suffering from overt malignancy, with an incidence of 11% among all cancer patients [2]. Other causes of venous thromboembolism in cancer patients are mechanical compression of adjacent vessels and direct invasion, as in renal cell carcinoma.

Multiple factors contribute to hypercoagulability in malignancy. Tumor cells express and secrete procoagulant agents and co-morbidities can enhance the thrombotic tendency in cancer patients. Many procoagulants are described in the literature in association with cancer. These include tissue factor, which is expressed on several tumor cells and initiates the coagulation cascade by activating factor IX and X, and cancer procoagulant, normally found only in malignant and fetal tissue and able to activate factor X without the presence of TF/factor VIIa complex. This factor was found in patients with breast carcinoma.

Different cells change their activity due to the effect of malignant diseases and increase the risk for a major event. Monocytes express TF and other direct factor X activators. Tumor-platelet interaction produces platelet proaggregatory molecules, leading to clot formation. Tumor cells increase the production of adenosine diphosphate by endothelial cells and activate thrombin. Furthermore, tumor necrosis factor

TF = tissue factor

Main etiologies of portal vein thrombosis

Intra-abdominal infection and inflammation
Cirrhosis
Laparotomy
Neoplasm (accounts for 20–24% of all PVT cases)
Hepatocellular carcinoma
Pancreatic cancer
Mucus-producing carcinoma
Congenital and acquired coagulation abnormalities
Primary myoproliferative disorders
Antiphospholipid syndrome
Paroxysmal nocturnal hemoglubinuria
Oral estroprogestative contraceptives

levels are often elevated in patients with cancer, leading to an increased procoagulant state.

The most common cancers associated with thrombotic events are mucus-secreting tumors, mainly of gastrointestinal origin, especially the hepatobiliopancreatic system. In a population study 23,796 autopsies were performed, and in 1% of the cases portal vein thrombosis was found to be the cause of death. Though breast carcinoma is not highly associated with thrombotic complications the study found that within that 1%, there were four patients with breast carcinoma [1].

PORTAL VEIN THROMBOSIS [TABLE]

The incidence of portal vein thrombosis is not precisely stated in the literature but seems to affect between 8% and 11% of patients with known portal hypertension [3]. In 25% of patients with PVT, liver cirrhosis is apparent although the reason for this association is not well established. In a study of patients with PVT without cirrhosis, 34% of the patients underwent prior abdominal surgery, 14% had pancreaticobiliary surgery and 9% had alimentary tract diseases. Another risk factor for PVT is a hypercoagulable state. However, in more than 33% of all the patients, no etiology was found.

PVT AND HORMONE THERAPY FOR BREAST CANCER

Breast cancer places patients at an increased risk for venous thromboembolic events, further aggravated by the use of adjuvant chemotherapeuticals and/or hormonal agents [4]. There are currently five classes of hormonal medications on the market: selective estrogen receptor modulators, progestational agents, selective estrogen receptor down-regulators, aromatase inhibitors and luteinizing hormone-releasing hormone analogues. Aromatase inhibitors are commonly used in postmenopausal patients with breast carcinoma. They prevent hormone production by inhibiting the conversion of androgens to estradiol and estriol [5]. Anostrozole, an aromatase inhibitor, raises the risk for venous thromboembolic events from approximately 0.36% in the healthy population to 1%.

In conclusion, rapid development of ascites should raise the suspicion of portal vein thrombosis; hypoalbuminemia is not acceptable as a sole explanation for rapidly developing ascites; and breast carcinoma and aromatase inhibitors are associated with thrombotic complications.

PVT = portal vein thrombosis

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