Trousseau's Syndrome Associated with Pancreatic Cancer

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Abstract.

Trousseau's syndrome is defined as any unexplained thrombotic event that precedes the diagnosis of an occult visceral malignancy or appears concomitantly with a tumor. The high incidence of thromboembolic disease in patients with advanced pancreatic carcinoma has been well reported. We report a case of Trousseau's syndrome in a 64-year-old man with pancreatic head cancer, presenting with acute ischemic stroke one week following pancreaticoduodenectomy. The patient was promptly treated with low-molecular-weight heparin without recurrence of thromboembolic events during follow-up.

Keywords: ischemic stroke, Trousseau's syndrome, pancreatic cancer, thrombosis

INTRODUCTION

The relationship between venous thromboembolic features and malignancy was first described by Armand Trousseau in 1865 [1]. Two years later, Trousseau himself developed this syndrome as a result of gastric carcinoma [2]. Cancer has increasingly been recognized as a prothrombotic state of the human body. Trousseau's syndrome has been applied to various clinical conditions, ranging from brain infarction to any kind of hypercoagulability associated with any malignant disease [1,2]. The clinical manifestations of malignancy-related thromboembolism include spon-
taneously recurrent migratory venous thrombosis, arterial thrombosis, microangiopathy, nonbacterial thrombotic endocarditis, or acute or chronic disseminated intravascular coagulation [3]. New variants of Trousseau's syndrome have recently been described, including accelerated courses of peripheral vascular disease and ischemic heart disease, both of which are enhanced by concealed cancer [4,5]. Here we have presented an interesting case of Trousseau's syndrome associated with pancreatic adenocarcinoma.

CASE REPORT

A 64-year-old non-smoking male with a history of diabetes mellitus and regularly controlled hypertension presented with anorexia, abdominal pain and tea-colored urine. On physical examination, the patient was apyrexial with jaundice of his skin and sclera, and his abdomen was soft and flat without palpable mass. Abdominal ultrasound demonstrated a mass in the head of the pancreas causing common bile duct dilatation. Computerized tomography (CT) showed a 3.2 cm tumor at the pancreatic head and the uncinate process, with distal narrowing and proximal dilation up to 1.2 cm of the common bile duct (CBD). The tumor was also found to invade the second portion of the duodenum and regional lymphadenopathy was also noted (Figures 1,2). Endoscopic retrograde cholangiopancreatography (ERCP) revealed ulceration in the second and third parts of the duodenum, consistent with malignant infiltration. A subsequent biopsy of the distal CBD wall showed moderate dysplasia. A stent was inserted into the common bile duct to decompress the biliary tree (Figure 3). Blood test showed a carcinoembryonic antigen (CEA) level of 5.9 ng/mL.

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derwent pancreaticoduodenectomy uneventfully. Pathological exam confirmed the diagnosis of pancreatic ductal adenocarcinoma pT3 N1 M0 stage IIIB, with invasion of the duodenal wall, ampulla of Vater and peripancreatic soft tissue. Lymphovascular and perineural invasion was also present. The surgical margin was negative. Postoperative blood test showed CEA of 2.3 ng/mL and CA19-9 at 98.3 U/mL.

One week following pancreaticoduodenectomy, the patient presented with sudden onset of left hemi-plegia. Magnetic resonance imaging (MRI) of the brain demonstrated multiple acute infarcts, predominantly in the right frontal region and left inferior cerebellum (Figures 4, 5, 6). His platelet count, prothrombin time (PT), activated partial thromboplastin time (aPTT), and international normalized ratio (INR) were all within normal ranges. The patient’s D-dimer level was elevated at 2353.5 ng/mL (reference range 0-500), and fibrinogen was mildly elevated at 888 mg/dL (reference range 200-500). Repeated cardiac ultrasound showed normal valve function and contractility without thrombus. The patient did not have atrial fibrillation or arrhythmia throughout the course, which eliminated the possibility of acute brain infarction of cardiac origin. Based upon this accumulated information, a diagnosis of Trousseau’s syndrome was made. Low-molecular-weight heparin (LMWH) was promptly administered. The patient did not develop any other thromboembolic event thereafter, and he was discharged from the hospital two months postoperatively. At the time this article was authored, he was receiving physical therapy and LMWH treatment in combination with chemotherapy.

**DISCUSSION**

Pancreatic carcinoma can be lethal. The median survival duration is 6-10 months with locally advanced disease and 3-6 months in patients with metastases. In addition to the poor overall prognosis, the course of the disease may be complicated by thromboembolic events as illustrated in this case.
In our patient, acute ischemic stroke was the first manifestation of thromboembolism after radical operation for pancreatic carcinoma. The relationship between thromboembolic disease and pancreatic carcinoma was first described by Sproul in 1938 [6], and is now well-documented. The incidence of thromboembolic disease in patients with advanced pancreatic carcinoma has been estimated as being as high as 57% [7]. In an analysis of 66,000 patients with cancer, it was observed that those patients with pancreatic carcinoma had the highest risk of thromboembolic disease [8]. This relationship can be explained by the generation of an intrinsic hypercoagulable state in pancreatic carcinoma, which seems to be related to enhanced tumor growth and angiogenesis [9]. There are many features in common between the pathogenesis of Trousseau's syndrome and factors that appear to facilitate tumor metastases, including roles for tissue factor, selectins, platelets, endothelium, and fibrin [10-12]. Thus, it is likely that the thrombotic processes involved in Trousseau's syndrome also facilitate the spread of tumors. Together with the fact that advanced visceral carcinomas are mostly incurable, this may explain the observation that the search for occult malignancies has not manifested a large impact on the final outcome of cancer survival.

Concerning therapy for Trousseau's syndrome, treatment of the cancer itself is the priority. In addition, thrombolytic therapy and thromboprophylaxis are necessary. Compared with vitamin K antagonist (VKA), heparin is reported to provide a statistically significant reduction in thromboembolic events [13]. This is because heparin has several antithrombotic mechanisms that VKA does not, such as inhibition of the binding of mucin to selectin and release of tissue factor pathway inhibitor from endothelial binding sites [2]. We used LMWH in combination with chemotherapy for this patient and continued it as long as possible, intending the D-dimer and fibrinogen degradation product (FDP) levels to fall adequately within the normal range. According to the results of the latest investigations, LMWH is a promising treatment for patients whose cancer is complicated by thrombosis. It
has recently been reported that there is a trend toward decreased mortality with LMWH as compared with standard heparin. This reduction in mortality appears to be independent of the reduction in thromboembolism and bleeding [14]. The smaller size of LMWH molecules makes entry into tumor cells easier than for standard heparin molecules, and this may be the reason for its benefit.

In summary, our case underscores the importance of early consideration and accurate diagnosis which can lead to appropriate treatment in cancer patients with Trousseau's syndrome.

REFERENCES