PANCREAS, BILIARY TRACT, AND LIVER

Portosplenomesenteric Venous Thrombosis in Patients With Acute Pancreatitis Is Associated With Pancreatic Necrosis and Usually Has a Benign Course

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BACKGROUND & AIMS: **Although there are some data on prevalence of portosplenomesenteric venous thrombosis (PSMVT) in patients with acute pancreatitis (AP), the progression of PSMVT in patients who have and have not received anticoagulants has not been studied systematically. We evaluated the prevalence and natural history of PSMVT in a well-defined cohort of individuals with AP.**

METHODS: **In a retrospective study, we analyzed data from the University of Pittsburgh Medical Center on 162 patients with a sentinel attack of AP from 2003–2010. Data were collected on patient demographics, clinical presentation, etiology, clinical course, and outcomes. One hundred twenty-two patients underwent contrast-enhanced computed tomography; the scans were reviewed to identify thromboses and/or narrowing of splanchnic veins (splenic, superior mesenteric, and portal).**

RESULTS: **PSMVT was detected in 22 patients overall (14%; 18% among patients who underwent contrast-enhanced computed tomography). Median time to detection of PSMVT was 17 days (interquartile range, 11–40 days). PSMVT formed most frequently in the splenic vein (19 of 22, 86%), followed by portal (8 of 22, 36%) and superior mesenteric (6/22, 27%) veins. Development of PSMVT was associated with presence (21 of 22, 95%), location, and extent of pancreatic necrosis. Fifty-three percent of patients (21 of 40) with necrosis developed PSMVT. Anticoagulants were administered infrequently (6 of 22, 27%) and always for indications unrelated to PSMVT. Most patients with PSMVT developed collateral veins (19 of 22, 86%), and 27% (6 of 22) were found to have varices during endoscopic evaluation, but clot resolution was infrequent (2 of 22, 9%). No patient developed complications directly related to PSMVT.**

CONCLUSIONS: **PSMVT develops in about half of patients with necrotizing AP and is rare in the absence of necrosis. Despite infrequent administration of anticoagulants, complications directly related to PSMVT are rare.**

Keywords: Pancreas; Inflammation; Clot; Risk; Necrosis.

Acute pancreatitis (AP) is the leading gastrointestinal cause of hospital admissions in the United States and continues to rise in incidence.[1] Most AP patients have a mild course with complete recovery days after disease onset.[2,3] However, a variable fraction develop severe disease. Complications of severe AP can be broadly categorized as systemic (organ failure) or local (pancreatic necrosis and/or fluid collections),[4–6] which are associated with prolonged hospital course, significant morbidity, and mortality.[7]

Peripancreatic vascular involvement in AP is often detected incidentally on imaging studies performed for evaluation of symptoms or complications. Although the pathogenesis is unclear, it is believed that local extension of inflammatory process can involve vessels in the vicinity of the pancreas, which, along with the action of proteolytic enzymes, weakens vessel walls and causes stasis of blood flow.[8,9] Venous involvement is manifested by splanchnic (portal/splenic/mesenteric) venous

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Abbreviations used in this study: AP, acute pancreatitis; CECT, contrast-enhanced computed tomography; CP, chronic pancreatitis; CT, computed tomography; EGD, esophagogastroduodenoscopy; ERCP, endoscopic retrograde cholangiopancreatography; IQR, interquartile range; PFC, peripancreatic fluid collection; PSMVT, portosplenomesenteric venous thrombosis; PV, portal vein; SAPS, severe acute pancreatitis study; SMV, superior mesenteric vein; SV, splenic vein.

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thrombosis (PSMVT) and arterial involvement by pseudoaneurysms from direct erosion of the vessel wall. Complications resulting from vascular involvement include bleeding, organ ischemia, or necrosis.[8,9]

Pancreatitis is an uncommon cause of PSMVT. In 832 patients treated at the Mayo Clinic, only 13% of cases were related to pancreatitis.[10] A fairly large body of literature exists on PSMVT in chronic pancreatitis (CP). Most studies have evaluated the natural history of splenic vein (SV) thrombosis in CP,[11–16] with few directly measuring its prevalence.[11,15–17] Although no formal recommendations exist, anticoagulation is generally not used for PSMVT in CP patients.

There are few data on the prevalence[17–19] and natural course of PSMVT[19] in AP. In contrast to CP where the timing of PSMVT development is often uncertain, the onset of pancreatic injury in AP is known, and thrombus formation is acute/subacute. Therefore, systematic studies are needed to better understand the risk and determinants of PSMVT and the utility of anticoagulation in AP. In this study of a well-phenotyped cohort of AP patients,[4,20] we found the prevalence of PSMVT to be closely linked to pancreatic necrosis. We report the risk of PSMVT and compare the clinical course of patients with necrosis who did/did not develop PSMVT. Finally, we report on the use of anticoagulation and complications in patients with PSMVT and the prevalence of arterial pseudoaneurysms in our cohort.

Methods

Patient Cohort

Severe acute pancreatitis study (SAPS) at the University of Pittsburgh Medical Center prospectively enrolled 256 AP patients from 2 tertiary care hospitals (University of Pittsburgh Medical Center-Presbyterian, University of Pittsburgh Medical Center-Shadyside) in three 1-year periods between June 2003 and April 2010 after obtaining informed consent and by using standardized criteria.[4,20] The study protocol was approved by the Institutional Review Board of the University of Pittsburgh. For the present study, we included SAPS patients who were admitted with their first AP attack and excluded patients with a history of AP or CP.

Data Collection and Disease Severity

As previously described,[4,20] data collection in the SAPS study included detailed information on demographic, clinical, laboratory, and radiographic parameters. Organ failure was defined by the presence of shock (systolic blood pressure $<$90 mm Hg), pulmonary insufficiency (arterial PO_2 $<$60 mm Hg at room air or the need for mechanical ventilation), or renal failure (serum creatinine level $>$2 mg/dL after rehydration or hemodialysis).[4,20] Treatment and interventions (endoscopic, radiologic, or surgical) for either pancreatic necrosis or peripancreatic fluid collections (PFCs) were noted.

Although information on the clinical course during the index admission was collected prospectively, information on specific clinical (eg, use of anticoagulation, development of complications including gastrointestinal bleeding, interventions, etc) and radiologic data on subsequent admissions or during outpatient care as applicable was collected retrospectively. Clinical care including laboratory testing, performance of radiology tests and endoscopy during index admission, and follow-up was based on patients' clinical course.

Evaluation of Portosplenomesenteric Venous Thrombosis and Venous Narrowing

All computed tomography (CT) scan reports were reviewed for presence of necrosis, PFC, PSMVT, or narrowing. CT scans for patients with positive findings were reviewed by 2 expert radiologists with specific interest in abdominal imaging. The radiologists were blinded to the clinical history and course of the patients. Whenever available, imaging studies from the referring hospitals were also reviewed.

CT evaluation was performed on multidetector helical CT scanners with 4–64 detector rows (General Electric Medical Systems, Waukesha, WI). Contiguous 5-mm–thick or 2.5-mm–thick axial sections were displayed from the diaphragm to the symphysis pubica. Patients undergoing a contrast-enhanced CT (CECT) received non-ionic intravenous contrast material (ioversol [Optiray 350; Mallinckrodt Imaging, Dublin, Ireland] or Isovue-370 [iopamidol injection 76%; Bracco Diagnostics Inc, Princeton, NJ]) that was administered at 3 or 5 mL/s at a volume of 125–150 mL. All patients were imaged in the portal venous dominant phase, and the majority, but not all, had multiphasic scans with additional imaging in the unenhanced and hepatic arterial dominant phase. Arterial and portal venous phases of intravenous contrast were timed by using bolus tracking software (SmartPrep software; GE Medical Systems).

The main portal vein (PV) and its branches, the superior mesenteric vein (SMV) and the SV were evaluated for patency, thrombosis, and narrowing. Vessels were defined as patent if the entire lumen was filled with contrast on enhanced images and there was no luminal narrowing. Thrombus was defined as a filling defect within the lumen of the vessel seen on contrast-enhanced images. Thrombi were classified as occlusive and non-occlusive, depending on the absence or presence of patent contrast-opacified lumen adjacent to the existing thrombus. Non-occlusive thrombi were further divided into those occupying more or less than 50% of the lumen on axial images. Narrowing of a vein was defined as $>$50% decrease in caliber of the lumen. In the presence of both thrombus and narrowing, only the