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ORIGINAL ARTICLE

Splanchnic vein thrombosis in severe acute pancreatitis: a 2-year, single-institution experience

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Abstract

Objectives: This study aimed to determine current practice in the management and outcome of splanchnic vein thrombosis complicating acute pancreatitis (AP).

Methods: An audit of prospectively collected data for all patients presenting with AP was conducted. Patients with splanchnic vein thrombosis were grouped according to vessel involvement and whether or not systemic anticoagulation was administered.

Results: Of 127 consecutive patients admitted with AP, 20 had splanchnic venous thrombosis; in all cases the thrombosis was associated with a severe attack of AP. Involvement of the splenic vein (SV), portal vein (PV) and superior mesenteric vein (SMV) was observed in 14, 10 and three patients, respectively. Involvement of more than one vessel was observed in six patients (SV and PV in four patients; SMV and SV in one patient; all three veins in one patient). Thromboses were colocalized with collections in 19 patients. Only four patients received systemic anticoagulation. Resolution of thrombosis was observed in six patients over a median of 77 days. No significant differences were observed in recanalization rates following anticoagulation ($P = 0.076$). No complications associated with systemic anticoagulation occurred. One patient developed liver failure associated with progressive PV thrombosis and one patient died.

Conclusions: Splanchnic vein thrombosis is a relatively common observation in severe AP and is associated with pancreatic necrosis and peripancreatic collections. Recanalization is observed in almost a third of patients, irrespective of whether or not they receive systemic anticoagulation.

Keywords

acute pancreatitis, complications < acute pancreatitis

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Introduction

Splanchnic vein thrombosis is a rare complication of acute pancreatitis (AP).[1,2] It often involves the portal vein (PV), splenic vein (SV) and superior mesenteric vein (SMV), either in combination or separately. Splanchnic vein thromboses *per se* are associated with prothrombotic or hypercoagulable disorders, but in the context of AP a more direct inflammatory process has been implicated.[3] Splanchnic vein thrombosis is often an incidental finding on radiological imaging performed to assess the severity of an attack of AP; however, its clinical manifestations may include signs and symptoms that overlap with those of the pancreatitis.[3,4] Although the natural history of splanchnic vein thrombosis in AP is unclear, severe haemorrhage, bowel ischaemia, portal hypertension and liver failure have been reported.[1] Based on the results of a large, prospective, multicentre study, the European Network for Vascular Disorders of the Liver (EN-Vie) recommended the utilization of early anticoagulation in patients with acute PV thrombosis in non-cirrhotic, non-malignant patients.[5] Furthermore, SV thrombosis associated with ascites was found to have a poor prognosis, suggesting that such patients should receive anticoagulation and/or thrombolysis.[5]

Patients with severe AP are perceived to be at increased risk for haemorrhage as a result of pseudoaneurysms, the need for

pancreatic debridement and the frequent utilization of radiological drainage to treat infective collections. Given the heterogeneous study population in the recently published European study,[5] and the inherent perceived risk for early anticoagulation in patients with severe AP, the aim of the present study was to review a single-institution experience of the management and outcome of patients with splanchnic vein thrombosis specifically associated with AP.

Materials and methods

A retrospective analysis of prospectively collected clinical data for patients diagnosed with splanchnic vein thrombosis associated with an attack of AP was conducted. The study centre was a tertiary referral centre at the Royal Free Hospital, London. Data were collected for the period from January 2008 to December 2009 inclusive. The study was approved by the local research ethics committee.

An attack of AP was defined according to clinical (acute abdominal pain requiring hospitalization) and biochemical (serum amylase or lipase levels exceeding three times the upper limit of normal) criteria or radiologically by contrast-enhanced computed tomography (CT). The severity of AP was classified in accordance with the Atlanta Criteria.[6]

Venous complications were diagnosed on imaging studies which included dynamic dual-phase, contrast-enhanced CT, magnetic resonance imaging (MRI) and/or colour Doppler ultrasonography (US).

Patients with chronic pancreatitis, known malignancy, cirrhosis or established portal hypertension were specifically excluded as a result of established prothrombotic states and the likelihood of pre-existing splanchnic vein thrombosis.

Data pertaining to the aetiology of AP, severity, location of thrombosis, complications associated with thrombosis (portal hypertension, ascites, liver failure, gastric varices, gastrointestinal haemorrhage, small bowel ischaemia), treatment and intervention were recorded. All patients were screened for proteins C and S deficiency, Leiden Factor V and antithrombin III.

In patients who were anticoagulated, a therapeutic dose of low molecular weight heparin was administered when established sepsis had been treated (1 mg/kg). Patients were subsequently fully anticoagulated with the vitamin K antagonist, warfarin, upon discharge [international normalized ratio (INR) 1.8–2.0].

Mortality was defined as in-hospital mortality or mortality within 30 days of discharge. All patients were routinely followed up in specialist outpatient clinics.

Results

A total of 127 patients with AP were admitted to the Royal Free Hospital, London between 1 January 2008 and 31 December 2009. Severe attacks of AP were recorded in 32 patients (25.2%), all of whom had dynamic contrast-enhanced CT imaging at the time of their index admission. Splanchnic vein thrombosis was detected in 24 (18.9%) patients, of whom four were excluded because they had a background of chronic pancreatitis with pre-existing SV thrombosis. The remaining 20 (15.7%) patients (Table 1) were all tertiary referrals. The aetiology of AP was gallstones in nine patients, and alcohol-related in 11. The median age at presentation was 53.5 years (range: 36–81 years), and the sample included nine men. Radiological findings and outcomes are shown in Table 1. The median hospital stay was 32.5 days (range: 6–228 days). Median follow-up was 18 months (range: 15.5–36 months).

All 20 patients had a severe attack of AP. Pancreatic and/or peripancreatic collections were present in 19 patients at the time of transfer, although secondary infective complications developed in eight patients. Six patients were managed with radiologically guided drainage catheters alone, and two patients underwent pancreatic necrosectomy performed using a minimally invasive percutaneous technique. One patient underwent a total colectomy as a result of colonic ischaemia and closed pancreatic irrigation without debridement. There was one death.

Pattern of splanchnic vein thrombosis

The splanchnic vessel to thrombose most commonly was the SV in 14 patients, followed by the PV in 10 patients and the SMV in three patients (Table 1).

Thrombosis occurred in the SV in isolation in eight patients and in the PV in isolation in five patients. Isolated SMV thrombosis was observed in only one patient. The remaining patients demonstrated a combination of SV and PV thromboses (four patients), SMV and SV thromboses (one patient), or SV, PV and SMV thromboses (one patient).

There was a clear association between the sites of necrosis/peripancreatic collection and the vessels thrombosed in 16 patients (Table 2).

Overall, only four patients were anticoagulated; all of these had PV thrombosis (three as inpatients during index admission). Of these, in only one patient did the indication for anticoagulation differ significantly from indications in those who were not anticoagulated. In this patient the progression of the thrombosis into the intrahepatic branches of the PV was associated with impaired liver function (ascites). No clear indications were observed to distinguish the other three patients who were anticoagulated from patients who did not receive anticoagulation (Table 1). Hepatic decompensation occurred in only one patient, in whom a combination of SMV, PV and SV thromboses was seen. A patient with gallstone severe necrotizing AP was readmitted 14 days after discharge with ascites and mild jaundice. Contrast-enhanced CT demonstrated thrombus propagation in both the left and right PVs. The patient was immediately anticoagulated and responded well to potassium-sparing diuretics (spironolactone).

Follow-up and outcome

Laboratory investigations for coagulation disorders were negative in all patients. Resolution of thrombosis was observed in six

Table 1 Patient demographic data, pattern of necrosis, splanchnic vessels thrombosed and recanalization rates

Patient	% necrosis	Infected necrosis	Vessel thrombosed	Colocalized collection	Anticoagulated	Recanalized
1	70% DP	Yes	PV	Yes	No	Yes
2	100% TP	Yes	SV	Yes	No	Yes
3	70% PP	No	PV	Yes	Yes	No
4	50% DP	No	PV, SV	Yes	Yes	Yes
5	50% PP	No	PV, SV	Yes	No	Yes
6	50% DP	Yes	SV	Yes	No	No
7	100% TP	No	PV	Yes	No	No
8	100% PP	Yes	SV	Yes	No	No
9	50% PP	No	PV	Yes	No	No
10	No necrosis	No	SV	Yes	No	No
11	70% DP	Yes	SV	Yes	No	No
12	No necrosis	No	PV	Yes	Yes	Yes
13	No necrosis	No	SV	No	No	No
14	30% PP	No	PV, SV	Yes	Yes	No
15	70% PP	Yes	SMV	Yes	No	Yes
16	70% PP	No	PV, SV, SMV	No	No	No
17	No necrosis	No	SV	No	No	No
18	70% DP	Yes	SV	Yes	No	No
19	100% TP	No	PV, SV	Yes	No	No
20	70% DP	Yes	SV, SMV	No	No	No

DP, distal pancreas; PP, proximal pancreas; TP, total pancreas; PV, portal vein; SV, splenic vein; SMV, superior mesenteric vein.

Table 2 Pattern of splanchnic vein thrombosis and recanalization rates

Vessel thrombosed		*n*	Colocalized collections, *n*	Anticoagulated, *n*	Recanalized, *n*	
					Without anticoagulation	With anticoagulation
PV (all)		10	9	4	2	2
	PV only	5	5	2	1	1
	PV + SV	4	4	2	1	1
	PV + SV + SMV	1	0	0		
SV (all)		14	10	2	2	1
	SV only	8	6	0	1	0
	SV + SMV	1	1	0	0	0
SMV (all)		3	2	0	1	0
	SMV only	1	0	0	1	0

PV, portal vein; SV, splenic vein; SMV, superior mesenteric vein.

of 20 patients over a median period of 77 days (range: 10–180 days). Recanalization was observed on imaging in two patients who did and in four patients who did not receive anticoagulation (Table 2).

Of the 14 patients in whom recanalization was not observed, three developed cavernomas demonstrated on contrast CT at follow-up. The remaining 10 patients developed collaterals around the SV territory. Recanalization was observed in only one patient with SV thrombosis.

Portal vein thrombosis was observed in 10 patients, four of whom received anticoagulation. Recanalization was observed in two of the patients who did and two of the six patients who did not receive anticoagulation therapy (Fisher's exact test, $P = 0.076$) (Table 2).

None of the patients had haemorrhagic complications related to the development of portal hypertension. The single mortality in this series occurred in a patient with gallstone pancreatitis with complete pancreatic necrosis. An initial scan on day 5 following admission demonstrated PV and SV thromboses. The patient recovered from an initial transient respiratory and renal failure, but subsequently developed left colonic ischaemia manifesting as a perforation on day 28. A contrast CT scan confirmed the diag-

nosis and demonstrated near complete resolution of the PV thrombus and persistence of SV occlusion. A total colectomy was performed. However, the patient died from ensuing sepsis-related multi-organ failure on day 34.

Discussion

Splanchnic vein thrombosis complicating an attack of severe AP is uncommon and has a reported incidence of 1–2%.[1] The vessel that is by far the most commonly involved is the SV (in 70% of patients); this involvement may be related to its very close proximity to the inflamed pancreas and is supported by a clear association between peripancreatic inflammation and direct venous compression by collections in 80% of patients in this series. This result is supported by descriptions in the literature of vascular complications as late phenomena in the course of necrotizing AP.[4] This also suggests that the most appropriate way of treating and possibly preventing splanchnic vein thrombosis in AP is probably by intervening to drain infected peripancreatic collections in a timely manner.

From a pathophysiological point of view, splanchnic venous thrombosis may be linked to inherited coagulation disorders, such as deficits of protein C or protein S,[7] or acquired coagulopathies such as antithrombin III deficiency. Intra-abdominal inflammation associated with AP itself may cause transient procoagulation disorders.[8]

In this series, four patients had a severe form of PV thrombosis with intrahepatic extension into both main branches of the PV. These were the only patients to be anticoagulated. Six other patients with PV thrombosis did not receive anticoagulation, which suggests the lack of a standardized treatment in the setting of AP. This probably reflects the reluctance of surgeons to give therapeutic doses of heparin in the context of severe pancreatitis with potentially infected peripancreatic collections or pancreatic necrosis that may require urgent drainage, and the potential for haemorrhagic complications. It should be remembered that almost all of these patients had significant pancreatic and peripancreatic collections that merited percutaneous drainage, and two patients underwent pancreatic necrosectomy.

According to a recent Europe-wide, multicentre, prospective study, treatment with anticoagulation is efficacious but has a lower rate of resolution than intravascular infusion of thrombolytics.[5] Early diagnosis and treatment with anticoagulant therapy, heparin and vitamin K antagonists allowed recanalization in about one third of patients, especially in recently formed thromboses.[5] The type of anticoagulation (heparin or vitamin K antagonists) administered does not appear to influence recanalization, as demonstrated in the study published by Plessier *et al.*[5] Ascites and PV thrombosis with concomitant SV obstruction were identified as factors predictive of worse evolution.[5]

Within the current study a higher rate of recanalization was observed amongst patients who received anticoagulation. Interestingly, however, the rate of recanalization observed in patients with splanchnic vein thrombosis who did not receive anticoagulation was similar to that in the anticoagulation arm of the EN-Vie study.[5] The disparity may be explained by the heterogeneity of disorders included in the European study, in which a local risk factor was identified in 21% of patients, and one or more prothrombotic abnormalities were identified in 52% of patients. By contrast, none of the patients in this series were found to have procoagulation disorders, albeit that the population cohort was comparatively smaller.

Splanchnic vein thrombosis did not resolve in 14 patients, representing a rate of non-resolution with anticoagulant treatment similar to that found in the literature.[5,7–11] The majority of the 14 patients with splanchnic venous thrombosis that did not recanalize had SV thrombosis (Table 1) and, not surprisingly, 11 developed collaterals mainly around this area and three developed porto–portal collaterals manifesting as cavernomas. None of these patients developed portal hypertension, probably because the flow was shunted through the collaterals and cavernomas. Patients with cavernoma are at risk for potentially fatal intra-abdominal haemorrhage, recurrent thrombosis and extrahepatic biliary obstruction. Of greater interest, however, was the similar rate of recanalization among patients with PV thrombosis, irrespective of treatment with anticoagulants.

Mortality associated with acute SMV thrombosis in the general population is high, at 20–50%,[12,13] depending on the grade of obstruction, the collateral vascularization, comorbidities, and delay in diagnosis and treatment. However, in the current series SMV thrombosis did not appear in itself to be an indication for anticoagulation therapy, and no associated complications were observed. However, based on our experience and given the limitations of the current study, we would advocate anticoagulation if there is evidence of progression of PV thrombosis, ascites and/or SMV thrombosis (in view of the increased risk for mortality).

Conclusions

Splanchnic vein thrombosis is a relatively common observation in patients with severe AP; in the vast majority of patients it is associated with pancreatic necrosis and peripancreatic collections. Colocalization of peripancreatic collections and splanchnic vein thrombosis suggests that compression and perivascular inflammation are important mechanisms. Recanalization is observed in almost a third of patients, irrespectively of whether or not they receive systemic anticoagulation, and this may reflect the resolution of the AP itself and/or the drainage of adjacent collections. The role of systemic anticoagulation in splanchnic vein thrombosis associated with AP needs to be formally tested in a well-designed, prospective, randomized controlled trial.

Conflicts of interest

None declared.

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