Journal of Gastrointestinal Surgery (2021) 25:3137–3148
https://doi.org/10.1007/s11605-021-05071-5

ORIGINAL ARTICLE

Pancreatic-Portal Vein Fistula: a Rare Diagnosis with Wide-Ranging Complications—13-Year Experience of a Pancreas Center of Excellence

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Received: 6 April 2021 / Accepted: 4 June 2021 / Published online: 12 July 2021

Abstract

Purpose To determine factors affecting mortality, and long-term patency of portal vein, in patients with pancreatic-portal vein fistula (PPVF).

Methods Consecutive cases of PPVF at the University of Pittsburgh Medical Center from 2008 to 2020 were retrospectively identified. Clinical history, imaging studies, management strategies, complications, and long-term outcomes were analyzed.

Results Fourteen patients, representing the largest PPVF cohort reported to date (mean age 58.6 years, 64.3% women, median follow-up 10 months [1–98 months]) were identified. Underlying chronic pancreatitis was seen in 9 (64.3%) patients, while 5 (35.7%) developed PPVF with first attack of acute pancreatitis. PPVF involved proximal main portal vein (MPV) in 10 (78.6%) patients. Of the 5 patients (35.7%) who died, all had occlusive (n=4) or near-occlusive (n=1) PPVF-associated filling defect (FD) in the MPV. Conversely, 7 of 9 survivors (87.5%) had subocclusive FD and patent MPV. In patients with sepsis (n=5), 1 underwent surgical necrosectomy and survived, while 3 of 4 (75%) patients without debridement died.

Conclusion Occlusive/near-occlusive PPVF-associated MPV FD, and sepsis, are associated with high mortality rates, while subocclusive MPV FD is associated with survival and long-term MPV patency. PPVF is a potentially life-threatening, and possibly under-diagnosed, entity that warrants early clinical suspicion for timely diagnosis, to facilitate optimal management.

Keywords Pancreatic-portal vein fistula · Recurrent acute pancreatitis · Chronic pancreatitis · Hemosuccus pancreaticus

Introduction

Pancreatic-portal vein fistula (PPVF) is a communication between the portal venous system and the pancreatic ductal system. First described in 1966,[1] it is a rare diagnosis, often encountered in the setting of acute or chronic pancreatitis (CP), with local complications. Fewer than fifty cases have been reported in the English literature.[2–5] PPVF is associated with high morbidity and mortality, with a wide range of outcomes ranging from full recovery to rapid deterioration and death.[3]

The natural history of PPVF starts with pancreatic enzyme leakage, resulting in severe inflammation, digestion, weakening, and rupture of peripancreatic blood vessels. Autodigestion of (peri)pancreatic structures can result in arterial complications, including pseudoaneurysm formation, and bleeding.[6,7] However, this process can also involve the main portal vein (MPV). The presenting symptoms and signs of PPVF include bleeding, sepsis, and portal vein filling defect (FD) resembling portal vein thrombosis (PVT). Patients can also present with

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systemic lipolysis, subcutaneous fat necrosis, or pancreatic panniculitis.[1,8] Due to its varied presentation, the diagnosis of PPVF heavily depends on imaging studies and clinical suspicion.

There exists no standardized diagnostic method for PPVF. Furthermore, treatment is individualized and varies widely by institutions and practitioners. This series of 14 patients represents the largest cohort of patients with PPVF reported from a single institution to date. We sought to determine the factors affecting mortality, and long-term patency of portal vein in our cohort, and describe the spectrum of complications. With a review of the literature, we aim to outline major trends in this rare diagnosis's natural history and outcomes. Highlighted are four specific cases that represent the range of diagnostic techniques, treatment strategies, and outcomes.

Methods

We retrospectively identified, and reviewed, all consecutive cases of PPVF from 2008 to 2020 at the University of Pittsburgh Medical Center (UPMC). This cohort was supplemented by cases from a radiology database prospectively maintained by a pancreaticobiliary radiologist (AD). Ethical approval was obtained from the Institutional Review Board. PPVF was diagnosed when a non-enhancing FD in the portal venous system was contiguous with, and similar in attenuation (on CT scan) or signal intensity (on MRI) to, an adjacent pancreatic fluid collection. A filling defect of water attenuation, or signal intensity, was also considered diagnostic of PPVF when contiguous with an adjacent pancreatic fluid collection. Diagnosis of chronic pancreatitis was confirmed on imaging using the American Pancreatic Association Practice Guidelines.[9] PVT (evidenced by non-enhancing higher than water attenuation filling defect in the portal vein, or non-visualization of a previously visible portal vein on contrast-enhanced cross-sectional examination) was diagnosed on imaging. Sepsis associated with PPVF was defined by signs of systemic infection (including but not limited to positive blood cultures) worsening despite appropriate clinical treatment and at least 2 of the following: respiratory rate $\geq$ 22/min, altered mentation, or systolic blood pressure $\leq$ 100 mmHg in the absence of other identified sources of bacteremia. Four cases were selected through the authors' consensus to illustrate the full range of diagnostic modalities, interventions, and outcomes.

Results

Case Series

A total of 14 patients had PPVF between 2008 and 2020. They aged between 41 and 73 years old, with 5 (35.7%) being male. Nine (64.3%) patients had evidence of calcific CP at presentation, while the other 5 patients (35.7%) developed PPVF from their index episode of acute pancreatitis (AP) . A history of heavy alcohol use was seen in 8 patients (57.1%). In one patient with a history of idiopathic pancreatitis, the insulting injury that led to PPVF was distal pancreatectomy and postoperative pancreatic fistula. Three additional patients had idiopathic pancreatitis and 2 had gallstone pancreatitis. The time to diagnosis of PPVF from symptom onset related to the most recent episode of pancreatitis or the inciting event ranged from 8 to 40 days. Multiple diagnostic imaging modalities were required to make the diagnosis in more than half of our patients: contrast-enhanced computed tomography (CECT) and magnetic resonance cholangiopancreatography (MRCP) were the two most common modalities used. In 11 patients (78.6%), the site of the vascular fistula was in the MPV, at or close to the spleno-portal confluence, typically at 12 to 2 o'clock position. In 2 patients (14.3%), the fistula was along the distal superior mesenteric vein (SMV), communicating with the walled-off necrosis (WON) in the pancreatic uncinate process. PPVF involved left portal vein (LPV) in one (7.1%) patient. "Thrombus" or filling defect (FD) in the MPV was noted in 13 patients (92.9%); 6 patients (42.9%) received therapeutic anticoagulation.

Eleven (78.6%) patients survived the acute phase (first month). One patient who survived had an endovascular stent placement, as described ahead. Among the 10 patients who did not undergo an endovascular stent placement, and survived the acute phase, 3 patients with occlusive or near-occlusive FD in the MPV developed chronic MPV occlusion. The remaining 7 patients with subocclusive FD in the MPV (n=6), or FD limited to the left portal vein (n=1), had patent MPV at the last follow-up. However, 4 of the 7 patients with long-term MPV patency developed chronic occlusion of other vessels, including LPV, distal SMV, and distal splenic vein (SV), when these veins had occlusive or near-occlusive intraluminal filling defects.

In total, 5 patients in our cohort died, 3 from short-term (within a month) complications to which PPVF may have contributed; 1 died 9 months after presentation from recurrent acute on chronic pancreatitis; and the last died 25 months after presentation from end-stage liver disease complicated by portal hypertension to which PPVF, and PVT, may have contributed. All the patients who died had either occlusive (n=4) or near-occlusive (n=1) filling defect in the MPV. Seven out of 9 (77.8%) patients alive at last follow-up had subocclusive filling defect in the MPV at presentation, which was later resolved. In the remaining 2 patients, one had a near-occlusive filling defect in the MPV that progressed to chronic MPV occlusion, but this patient was alive at the last follow-up 7 months from presentation, while the second had an occlusive MPV filling defect and had an occluded MPV at the 3-month follow-up. Occlusive, or near-occlusive FD may be associated with higher mortality.

In our cohort, 5 (37.5%) patients developed sepsis from PPVF. One patient recovered after operative debridement. Three out of the rest 4 (75%) patients died. Thus, sepsis without source control may also be associated with higher mortality. The clinical characteristics of all 14 patients are seen in Table 1. Patient cases 1 through 4 are examined in detail.

Case 1: Incidental Finding of PPVF That Is Resolved with Surgery, Without Long-Term Sequelae

A 65-year-old man presented to a satellite hospital with his first episode of AP, with epigastric abdominal pain, and lipase >15,000 U/L. On day 5, he developed a fever to 104 °F, tachycardia, and agitation and was transferred to the intensive care unit and given antibiotics. CT scan on day 7 revealed a new fluid collection in the pancreatic head. He was transferred on day 9 to the UPMC for further management. CECT on day 10 revealed a low-density FD within the proximal MPV, contiguous with and similar in density to the adjacent peripancreatic acute necrotic collection (ANC), consistent with PPVF (Figure 1a, b). There were also air bubbles in the ANC, supporting the diagnosis of infected necrosis. Meropenem was continued, and he remained stable until day 13 when he again became febrile and tachycardic. On day 14, he underwent an open necrosectomy, where evidence of ductal disruption in the pancreatic neck was seen. Retroperitoneal surgical drains and a gastrojejunal tube were placed for drainage and nutrition, respectively. CECT on day 21 prior to discharge home (Figure 1c) showed a persistent subocclusive filling defect in the proximal MPV, still contiguous with the adjacent debridement field, suggesting persistent PPVF. On day 117, he presented after his surgical drain fell out: ERCP with PD stent placement was performed for therapy of pancreatic duct leak, and the external drain was replaced. CECT 7 months postoperatively (3 months after the drain was removed definitively) showed a patent PV but a narrowed porto-splenic junction (Figure 1d), suggesting resolution of the PPVF. He remained free from abdominal symptoms at his most recent follow-up 33 months after his initial presentation.

Case 2: PPVF Diagnosis Contributing to Long-term Sequelae of Portal Hypertension

A 51-year-old woman with recurrent acute on chronic pancreatitis secondary to alcohol presented with new abdominal pain after a similar episode 8 months prior. CECT showed peripancreatic stranding and enlarging walled-off necrotic collections (WON) that were continuous with a new occlusive FD of similar low attenuation in the MPV, and its branches, as well as distal SMV (Figure 2b and c, compared to Fig. 2a). These findings were consistent with a PPVF, though it was not recognized at that time. She also had thrombosis of the splenic artery, occlusion of the SV, infarction of the entire spleen, and ischemic changes involving the distal ileum, which are resolved with conservative management. She was treated with therapeutic anticoagulation. CECT 6 months later demonstrated chronic MPV occlusion with cavernous transformation (Figure 2d). However, no evidence was seen of a persistent PPVF. She subsequently tested positive for anticardiolipin and beta-2 glycoprotein antibodies: therapeutic anticoagulation was discontinued due to recurrent alcohol use 3 months later. She developed cirrhosis complicated by portal hypertension, and experienced acute decompensation with hepatic encephalopathy and hepato-renal syndrome, and expired 2 years after her PPVF presentation.

Case 3: PPVF Complicated by Acute Hemorrhage

A 41-year-old man with alcohol-related recurrent AP presented to a satellite hospital with severe abdominal pain. An unenhanced CT revealed intra- and peripancreatic fluid collections, and expansile low attenuation focus within MPV, which was interpreted as an acute thrombosis. He was started on therapeutic intravenous heparin infusion and transferred to our center. Subsequent CECT revealed a new low-density lobulated expansile occlusive FD in the MPV, raising concerns for a PPVF (Figure 3b, compared to Fig. 3a). On day 3, he developed fever and hypotension, and blood cultures grew *Streptococcus anginosus*, and *Citrobacter freundii*, for which antibiotics were initiated. Interval CECT on day 9 showed enlarging WON, with hyperdense internal components, suggestive of acute bleeding. Therefore, intravenous heparin was discontinued. MRCP on day 14 revealed an expanded MPV containing internal T1- and T2-weighted signal hyperintensity (Figure 3c, d). The similarity of signal characteristics and continuity of the MPV with adjacent peripancreatic WON suggested a persistent PPVF. On day 15, he developed hematemesis: esophagogastroduodenoscopy revealed hemosuccus pancreaticus. Selective angiograms of the celiac trunk and SMA demonstrated no arterial bleeding. However, transhepatic portal venogram exhibited disruption of the MPV at spleno-portal confluence, with active extravasation into the adjacent WON collections (Figure 3e). A covered endovascular stent was deployed, extending from the distal SMV to the MPV bifurcation. Post-deployment portal venogram showed excellent flow through the stent and resolution of the extravasation (Figure 3f). He was discharged with a nasojejunal tube for pancreatic rest and nutrition. After discharge, he continued to have abdominal pain despite abstinence from alcohol. Six months after discharge, he returned to using alcohol: he developed recurrent acute pancreatitis complicated by necrosis at the head of the pancreas and fluid collection adjacent to the stented PV. He presented to the emergency department for abdominal pain and dyspnea, suffered cardiopulmonary arrest, and expired despite attempted resuscitation.

Table 1 Clinical characteristics of fourteen patients with a diagnosis of PPVF in the University of Pittsburgh Medical left from 2008 to 2020

#	Age/ gender	H/O EtOH abuse	Pancreatitis history	Serum amylase/lipase at diagnosis	Imaging and pathology[b] findings[c]	Site of fistula	Extent of pancreatic collection in portal system	Complications	Therapeutic anticoagulation	Invasive procedure	PV morphology and signs of portal HTN at the last follow-up	Follow-up	Outcome at the last follow-up
1	65/M	Yes	PPVF diagnosed at the index attack of AP	>3000/>15,000	CECT*†	PV at confluence	Subocclusively into PV and near-occlusive component at the distal splenic vein	Sepsis	-	Open necrosectomy	Multiple perigastric and gastrohepatic varices, chronic and distal splenic vein occlusion	33 months	No GI symptoms
2	51/F	Yes	CP[a]	330/2612	CECT*†	PV at confluence	Occlusively to involve entire portal vein and branches as well as distal SMV	-	Yes	-	Cavernous transformation of PV, cirrhotic morphology of the liver, extensive collateral vessels. No splenomegaly	25 months	Death due to end-stage liver disease
3	41/M	Yes	CP[a]	29/918	CECT*†, EUS§, MRCP†, portal venogram†	PV at confluence and distal PV	Occlusively involve main PV, distal Splenic vein, as well as distal SMV	Bleeding (PPVF), sepsis	Yes	SMV and PV stent	Patent PV and SMV stent, occluded splenic vein	9 months	Death
4	68/F	-	PPVF diagnosed at the index attack of AP	313/335	CECT*†, US§, MRCP†, portal venogram†, intravascular ultrasound†, pathology†	PV at confluence	Near occlusively to mid PV	Sepsis	Yes	SMV and SV stent across portal confluence	-	1 month	Death
5	64/M	Yes	CP[a]	3387/9651	CECT§, pathology†	PV at confluence	Subocclusively to mid PV	Liponecrosis	-	Open necrosectomy	Patent	98 months	No GI symptoms
6	71/F	-	CP[a]	144/82	CECT*†, MRCP†	PV at confluence	Subocclusive in proximal PV and nearly occlusive distal	Sepsis	-	Open necrosectomy	Occluded distal SMV and distal SV, upper abdominal collaterals	33 months	Chronic pancreatitis, biliary stricture, bowel

Table 1 (continued)

#	Age/ gender	H/O EtOH abuse	Pancreatitis history	Serum amylase/lipase at diagnosis	Imaging and pathology[b] findings[c]	Site of fistula	Extent of pancreatic collection in portal system	Complications	Therapeutic anticoagulation	Invasive procedure	PV morphology and signs of portal HTN at the last follow-up	Follow-up	Outcome at the last follow-up
							SMV/confluence						obstruction
7	75/F	-	PPVF diagnosed at the index attack of AP	25/14	CECT*†	PV at confluence	Subocclusive in proximal PV	None	Yes	-	Narrowing of portal vein confluence	35 months	No GI symptoms
8	51/F	Yes	CP[a]	102/246	MRCP*†	Distal LPV	Subocclusive	-	-	-	Stenosis of PV, splenomegaly	17 months	Chronic pancreatitis
9	47/F	-	CP[a], PNET, POPF	NR/NR	CECT*†	PV at confluence	Subocclusive along PV, occlusively into distal SMV	-	Yes	-	Occluded SMV multiple mesenteric omental collaterals	11 months	Chronic pancreatitis
10	53/M	Yes	PPVF diagnosed at the index attack of AP	NR/615	CECT*†, MRCP†	PV at confluence	Occlusively throughout PV and its branches	Bleeding (GDA)	-	-	-	1 month	Death (GDA bleed)
11	73/F	-	CP[a]	18/414	CECT*†, MRCP†	Distal SMV	Subocclusively along distal SMV and entire portal vein and occlusively into left portal vein	Sepsis	Yes	-	-	1 month	Death
12	57/F	-	CP[a]	NR/3546	CECT*†, MRCP†	PV at confluence	Subocclusively length of PV and occlusively into LPV	Pancreatico-pleural fistula	-	-	Chronic occlusion of the left PV	2 months	Chronic pancreatitis
13	52/F	Yes	CP[a]	830/2193	CECT*†,	Distal SMV	Occlusively along distal SMV and near occlusively along proximal PV	-	-	-	Occlusion of SV and PV with cavernous transformation of PV	2 months	Chronic pancreatitis
14	52/M	Yes		NR/118				None	-				

Table 1 (continued)

#	Age/ gender	H/O EtOH abuse	Pancreatitis history	Serum amylase/lipase at diagnosis	Imaging and pathology[b] findings[c]	Site of fistula	Extent of pancreatic collection in portal system	Complications	Therapeutic anticoagulation	Invasive procedure	PV morphology and signs of portal HTN at the last follow-up	Follow-up	Outcome at the last follow-up
			PPVF diagnosed at the index attack of AP		MRCP*†, CECT	PV at confluence	Occlusively to involve entire portal vein			Robotic cystogastrostomy	Occluded main, left and right PV, SV	3 months	Chronic pancreatitis

AP acute pancreatitis, *CP* chronic pancreatitis, *PNET* pancreatic neuroendocrine tumor, *POPF* postoperative pancreatic fistula, *CECT* contrast-enhanced CT, *EUS* endoscopic ultrasound, *MRCP* magnetic resonance cholangiopancreatography, *PVT* portal vein thrombosis, *SMV* superior mesenteric vein, *SV* splenic vein, *PV* portal vein, *GDA* gastroduodenal artery, *M* male, *F* female

a, diagnosis established using the American Pancreatic Association Practice Guidelines in Chronic Pancreatitis[9]; *b*, if available; *c*, * raised initial suspicion, † confirmed diagnosis, § negative findings

Case 4: PPVF Complicated by Persistent Systemic Infection

A 68-year-old female without a history of pancreatic disease presented to a satellite hospital with abdominal pain, and non-bloody emesis, preceded by 1 month of early satiety, fatigue, and 1 week of blood-tinged diarrhea. CECT revealed a pancreatic tail "mass," evidence of colitis, and PVT. She was transferred to the UPMC for further management. Therapeutic anticoagulation with IV heparin was initiated. The patient developed tachycardia and respiratory failure without clear etiology. CECT on day 7 revealed enlarging heterogeneous ANCs in and adjacent to the pancreatic body and tail, suggesting AP with pancreatic ductal disruption. Also noted was a low attenuation subocclusive MPV FD, contiguous with an adjacent ANC, concerning for a PPVF (Figure 4a). Therefore, heparin was discontinued. MRCP on day 8 demonstrated a heterogeneous T2 hyperintense occlusive filling defect in the MPV (Figure 4b). On day 12, portal venogram did not show any evidence of a fistulous connection, but biopsy of the intraluminal filling defect revealed whitish specimen interpreted as necrotic material by pathology. However, on day 18, increasing leukocytosis led to repeat portal venogram and endovascular ultrasound which revealed a wall defect at the spleno-portal confluence continuous with the adjacent ANC (Figure 4c, d). Two covered stents were deployed from the SV and SMV into the MPV, respectively (Figure 4e, f). The patient developed persistent polymicrobial bacteremia (*Streptococcus caprae*, *Streptococcus epidermidis*, *Proteus mirabilis*, and *Enterococcus faecalis*). CECT on day 31 showed patent SMV stent but occluded SV stent. She succumbed later from worsening ascites, and evidence of pneumoperitoneum, complicated by feculent ascites, due to suspected colonic perforation.

Discussion

PPVF is a potentially life-threatening complication, related to acute and chronic pancreatitis. We suspect that PPVF may be underdiagnosed, due to recent increasing incidence (11 out of 14 cases in our cohort diagnosed after 2017), without an identifiable shift in risk factors favoring PPVF formation.[2–5] Imaging of PPVF usually demonstrates fluid collection, within the lumen of a partially or completely occluded MPV, identified as a filling defect of similar attenuation or signal intensity as and in continuity or contiguity with a (peri)pancreatic collection, rather than a conventional thrombus.[4,10] On CECT, water attenuation filling defect within the MPV in the appropriate clinical context is highly suggestive of PPVF but is often misdiagnosed as PVT.[2] MRI, especially fluid-sensitive sequences such as single-shot fast spin echo (SSFSE), and MRCP, can more confidently diagnose PPVF by demonstrating hyperintense fluid signal within the portal venous system

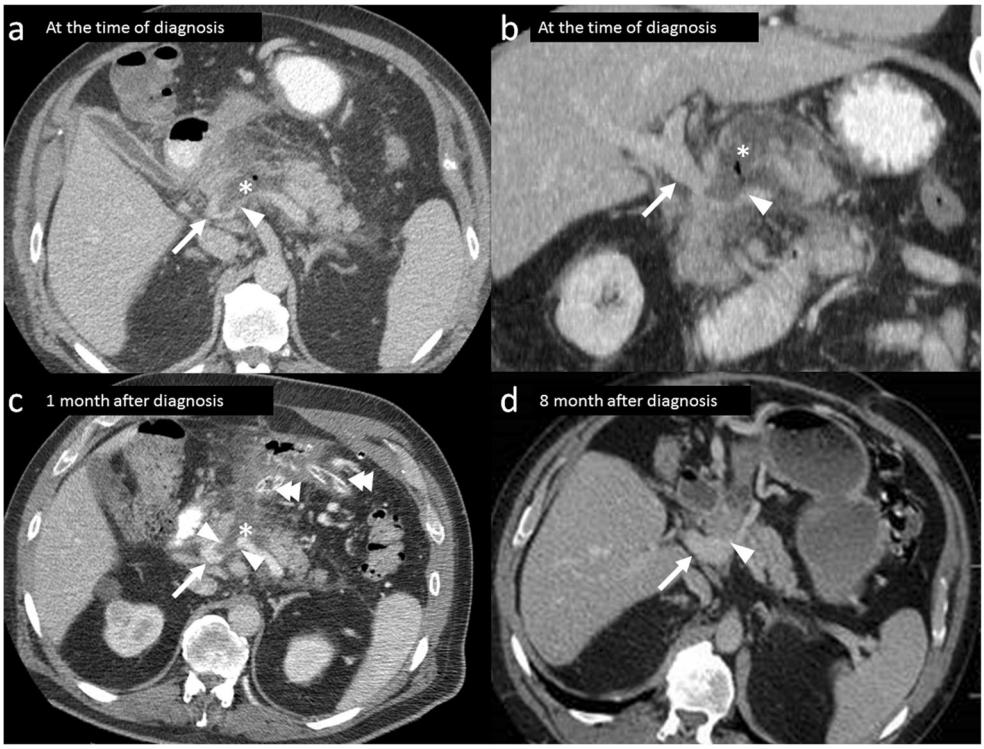

Fig. 1 CT images of case 1. Axial and coronal CECT images (**a** and **b**) at initial presentation show infected pancreatic necrosis containing gas (asterisk) directly extending (arrowheads) into the portal vein (arrow) consistent with PPVF. Axial image from CECT obtained after surgical debridement (**c**) shows that the necrotic collection was widely drained by surgically placed drains (double arrowhead), but the PPVF (arrowheads) was left untreated. Axial image from follow-up CECT obtained 7 months later shows patent portal vein (**d**; arrowhead)

on T2-weighted images[2,10] (Figure 5). Additional clues to the diagnosis of PPVF include expansile MPV, and attenuation/signal intensity of intraluminal contents of the MPV, similar to a contiguous peripancreatic collection. Transabdominal ultrasound and endoscopic ultrasound are operator-dependent modalities that are rarely confirmatory.[4]

The sample size of this cohort remains too small to draw conclusions about the specific clinical characteristics that have

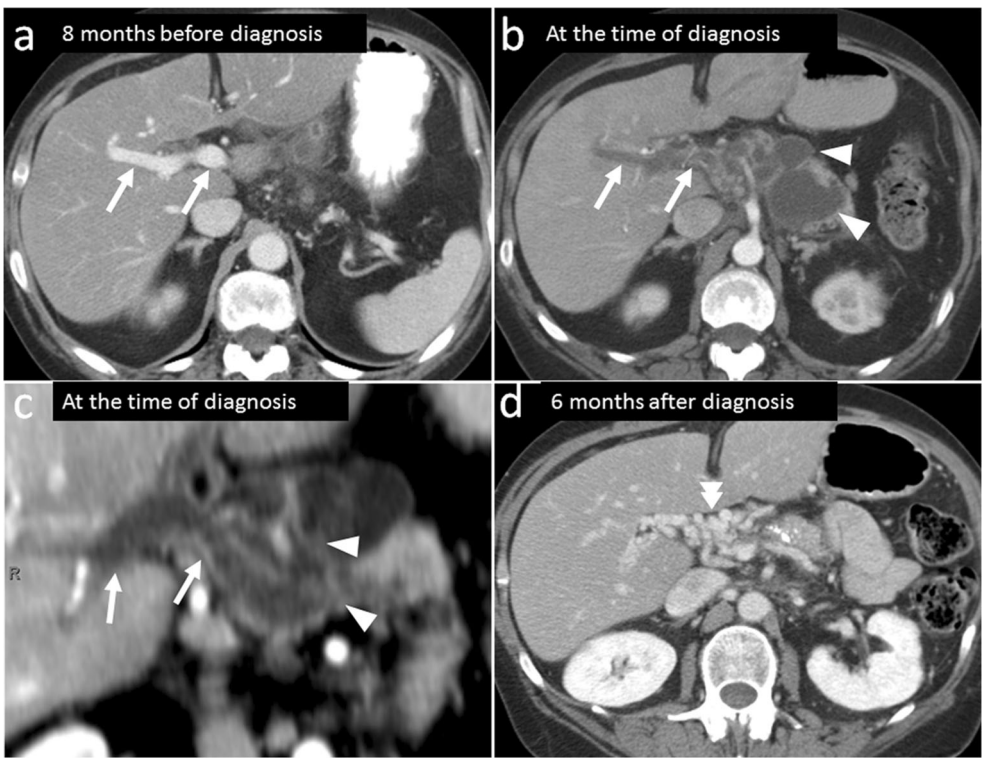

Fig. 2 CT images of case 2. Panels shows the natural progression of PPVF in this patient. Axial CECT image from a year before presentation (**a**) shows patent portal vein and its branches (arrows). Walled-off necrotic collections were evident in and around the pancreas (not shown in the image). Axial image (**b**) and corresponding coronal reconstruction (**c**) from CECT obtained during presentation show occlusion of the portal vein and its branches (arrows) with intraluminal low-attenuation filling defect similar to and contiguous with adjacent intra- and peripancreatic walled-off necrotic collections (arrowhead) consistent with PPVF. An axial image from a 6-month follow-up CECT scan (**d**) shows chronic occlusion of the portal vein with extensive cavernous transformation (double arrowhead)

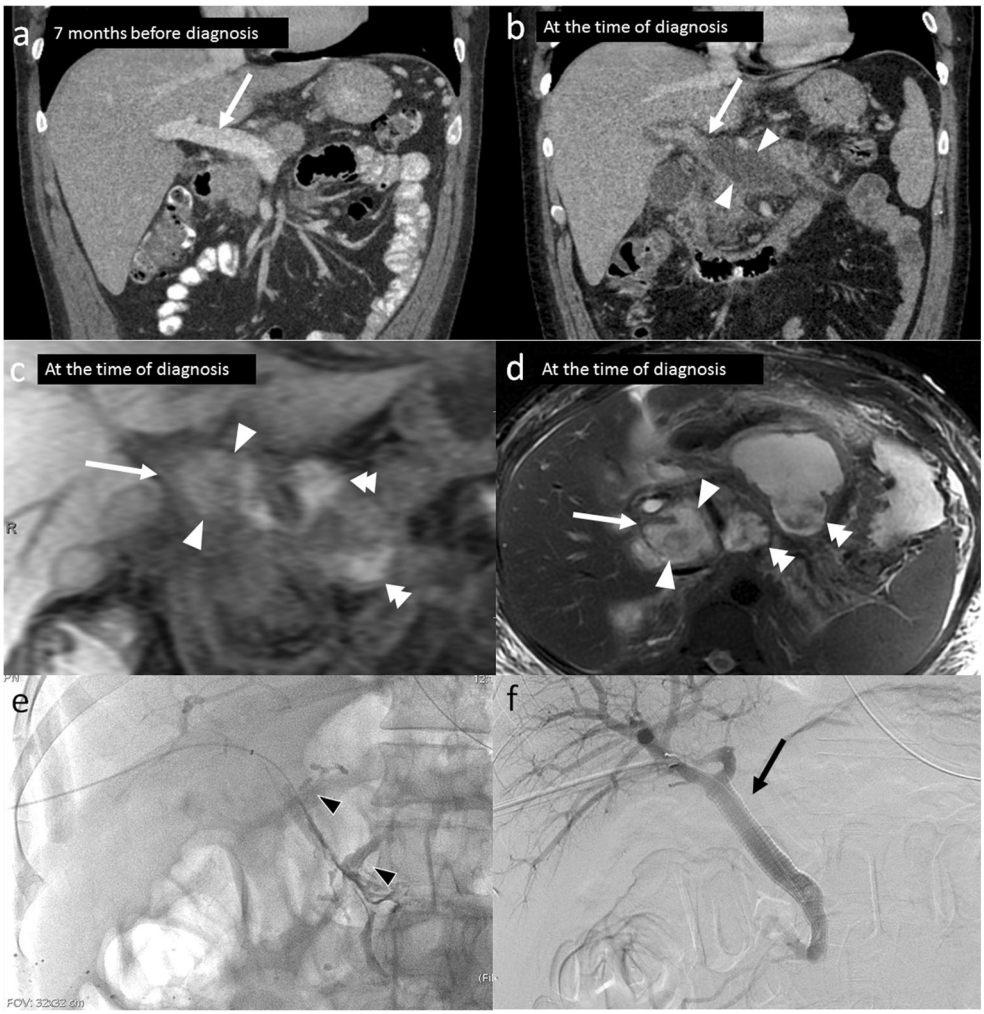

Fig. 3 CT, MRI, and portal venography images for case 3. Prior to the presentation leading to the diagnosis of PPVF, axial CECT image (**a**) shows patent portal vein (arrow). Coronal CECT image (**b**) and coronal pre-contrast T1-weighted (**c**) and axial Fat-sat T2-weighted (**d**) images at the time of presentation show an expansile filling defect (arrow heads) in the portal vein (arrow) that is low in density with heterogeneous T2 and T1 hyperintense areas within, similar to adjacent walled-off necrotic collections (double arrowheads) containing hemorrhagic components. An image from transhepatic portal venography (**e**) shows contrast extravasation from the portal vein. Fluoroscopic image obtained after deployment of a covered stent from distal SMV portal bifurcation (**f**) shows resolution of the contrast extravasation and patency of portal vein and its branches

precipitated PPVF in these individuals. A prior study from our center evaluating the natural history of necrotizing pancreatitis in a cohort of 167 patients (70% male, 71% transferred from outside facilities) treated between 2001 and 2008 and followed up for a median of 34 months did not include data on PPVF; however, it offers a useful comparison population of patients with acute necrotizing pancreatitis.[11] Of greatest interest is the mortality comparison: we note that the 2016 study showed a mortality rate of 24% (18 during hospital stay, 9 within 1 year, 13 after 1 year) consistent with previous literature.[11] Our case series shows a mortality rate of 35.7% (5/14) at a median of 10 months (range 1–98 months) of follow-up. The higher mortality rate in this subset is not surprising as prior literature regarding PPVF has largely highlighted the dramatic presentations and sometimes catastrophic outcomes of this entity.[3,4] The variety of experiences of the patients in our series is worth also noting, however, with recognition that some patients recover with relatively few symptoms when managed carefully in a multidisciplinary fashion.

Invasive imaging can confirm PPVF by demonstrating clear communications between anatomic structures involved. Extension of contrast from the pancreatic duct into the portal venous system, directly or through a peripancreatic collection at ERCP, is one example. However, when an obstructed pancreatic duct opacifies incompletely, or when a peripancreatic collection communicates with the portal venous system, but not with the pancreatic duct, this technique may be limited in its confirmatory capacity.[10] Portal venography can also be used to demonstrate a communication by opacification of an adjacent peripancreatic collection that communicates directly with the portal venous system.[12] A fistulogram performed through a percutaneous drainage catheter can additionally be used to illustrate communication between peripancreatic collections and nearby vascular structures.[10]

The treatment of PPVF remains highly individualized and can depend on associated complications. Management for acute on chronic pancreatitis forms the foundation of the treatment plan,[13–15] while preventing and/or early detection of further vascular and infectious complications are critical. Benefits of invasive or surgical therapies warrants an understanding that significant morbidity and mortality may persist despite technical success. Based on the collective clinical

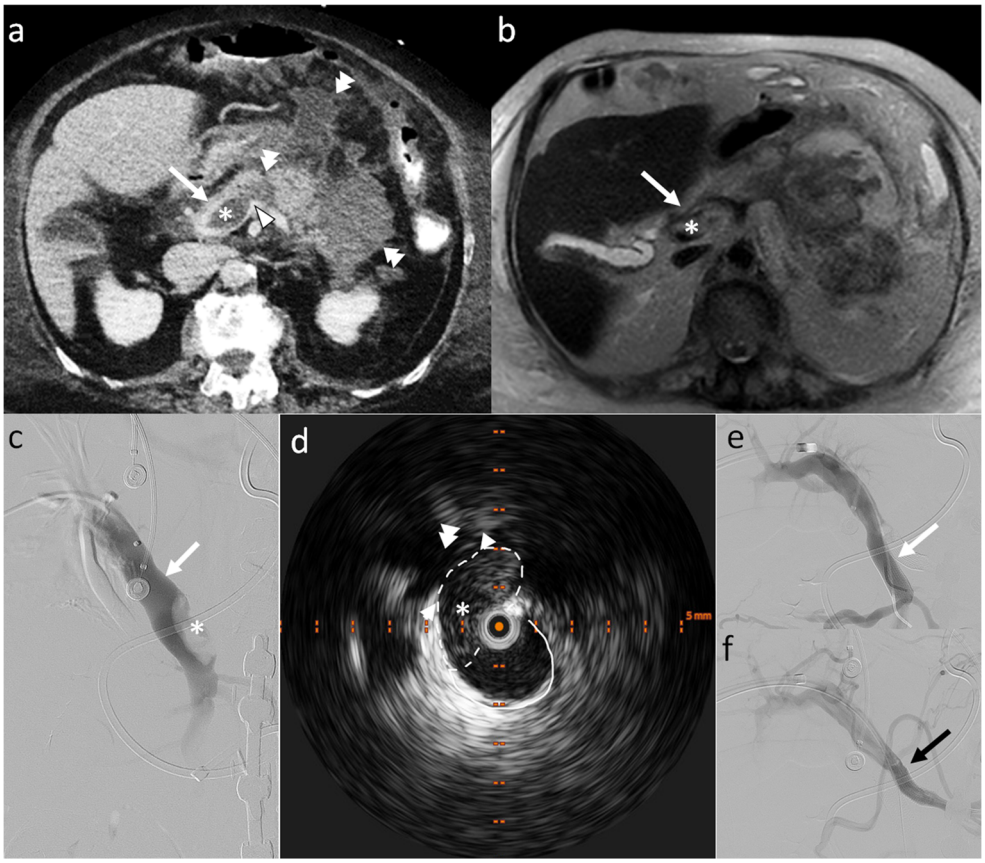

Fig. 4 CT, MRI, and IVUS (intravascular ultrasound) of portal vein and portal venography images for case 4. Axial contrast-enhanced CT image (**a**), corresponding axial T2-weighted MR image (**b**), portal venogram (**c**), and IVUS of portal vein (**d**) show low-attenuation and high T2-signal filling defect (asterisk) within the proximal portal vein (arrow) contiguous with (arrow head) an adjacent acute necrotic collection (double arrowhead). The continuous white line delineates the portal vein, and the dashed white line delineates the intravascular necrotic material. Note the portal vein wall defect at the site of PPVF (arrow heads on **d**). Portal venogram images (**e** and **f**) obtained after placement of covered stents in splenic vein (short arrow) and SMV (long arrow) extending across the filling defect in portal vein demonstrate patency of the respective stents and vessels

experience from our institution, we propose the following diagnosis and treatment algorithm for PPVF (Figure 6).

Rates of PVT in PPVF have been reported between 75 and 92% in prior series.[2,3,5] In our cohort, PVT or SMV thrombosis was the most common initial misdiagnosis of PPVF in all patients who were initially managed at outside institutions and in some from our institution. Without complete information on the image characteristics of MPV occlusion, the true prevalence of PVT remains unknown. Although PVT can develop during the course of PPVF, it is worthy to note that the initial FD is not a thrombus but contents in the (peri)pancreatic collections. Although often initiated, the role of systemic anticoagulation in the setting of PPVF and PVT remains unclear and must be decided on an individual basis as the risk assessment of thromboembolic versus hemorrhagic complications has not yet been established.

Subocclusive filling defects within the portal venous system are more likely to resolve, while occlusive or near-occlusive filling defects from PPVF are likely to cause chronic occlusions. The later was also associated with high mortality in our series as it was present in all deaths: 3 patients who died within 1 month after presentation and 2 who died at 9 and 25 months after presentation. Seven out of the 9 patients alive at the last follow-up had subocclusive filling defect (n=6) or no filling defect involving MPV.

PPVF-related gastrointestinal hemorrhage has been reported to occur in 17%[3] to 24%[5] of patients. In our cohort, GI bleeding occurred in 1 patient (7%), who eventually died from recurrent acute on chronic pancreatitis 9 months later (case 3). Hypothetically the contents of pancreatic or peripancreatic collection may act as a plug in the fistulous connection, and the fluid collection environment constitutes a higher-pressure system than the portal venous system.[16] This may explain why hemorrhagic events in PPVF are seen less frequently than sepsis or MPV occlusion. Among patients who had GI bleeding, reported mortality is between 12.5[5] and 25%.[3] Herein, we presented two examples of novel use of transhepatic portal venous stenting in PPVF for acute hemorrhage (case 3) or high risk of hemorrhage (case 4). In these two patients, vascular stent placement represented an alternative that allowed for survival in the acute setting. In case 3, the patient survived an additional 9 months with the stent in place and patent in the end. The risk of recurrent or persistent systemic infection after placement of a vascular prosthesis, in the setting of either current bacteremia or a communicating infected collection, must be weighed against the risk of exsanguination. MPV stenting may serve as an option in the treatment for PPVF complicated by acute hemorrhage, while its long-term patency remains unknown, and its outcome to be further studied.

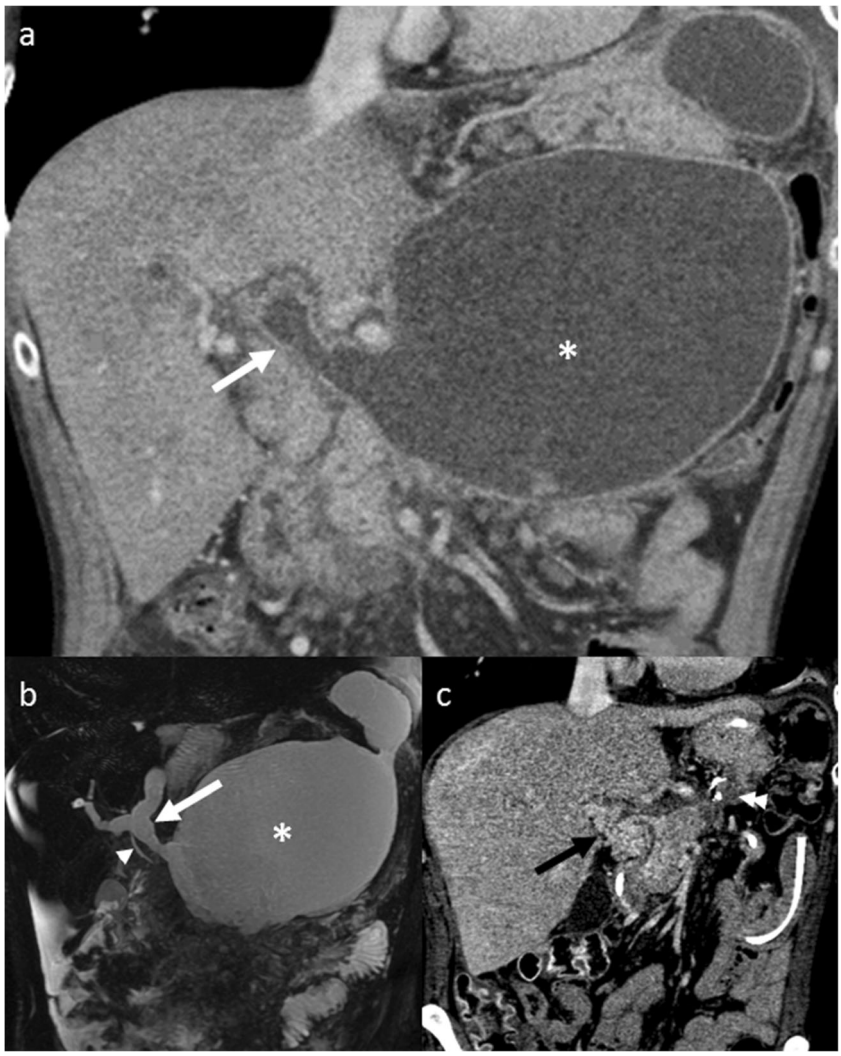

Fig. 5 Coronal contrast-enhanced CT image (**a**) and subsequent coronal MRCP image (**b**) of a 52-year-old man with acute necrotizing pancreatitis demonstrate a large acute necrotic collection (*) in the pancreatic body/tail directly communicating with main portal vein (white arrows) which is low in attenuation on CT and hyperintense on MRCP images. Note the nondilated common bile duct (arrowhead) adjacent to the main portal vein on the MRCP image (**b**). Coronal CT image (**c**) obtained 2 months after the onset of acute pancreatitis demonstrates cavernous transformation (black arrow) of main portal vein as well as postsurgical changes from robotic pancreatic debridement and cystgastrostomy (double arrowheads) with near resolution of the necrotic collection

Sepsis related to PPVF developed in 5 patients (35.7%) in our cohort, higher than that in published series, 21%[5] and 22%.[4] In our cohort, sepsis frequently occurred when (peri)pancreatic collections with radiological features of infection communicated with the MPV (Figure 1a, b). Sepsis from PPVF requires prompt intervention. Comparing our cohort with published cases, patients with PPVF-related sepsis had very high mortality rate: in our patients who had sepsis due to PPVF (n=5), one patient recovered after operative debridement, while without source control, 3 out of the rest 4 (75%) patients died. Similarly, previously published data showed that two patients with sepsis survived after percutaneous drainage,[17] or endoscopic ultrasound-guided drainage (EUS-D) of the necrotic collection,[3] while 1[18] out of 3[19,20] patients (33%) died when without source control.

The role of surgical necrosectomy remains poorly characterized. PPVF-related sepsis often occurred amid an acute flare of CP or AP, with fistulizing infected (peri)pancreatic collections at an anatomical location inconvenient for endoscopic or percutaneous methods. Therefore, open necrosectomy should be considered early. Portal vein repair would be extremely challenging due to extensive inflammation and should not be the primary goal. In cases with favorable anatomy, and low hemorrhagic risk, pancreatic duct stenting to achieve anatomical isolation between the portal venous system and the pancreatic ductal system has been reported with success.[21,22] EUS-D is another method to achieve source control in PPVF patients with infected (peri)pancreatic collections.[3,22,23] However, UGIB after EUS-D in PPVF has been reported, and its risk should be carefully evaluated.[3,4,23]

Lipolysis with PPVF was seen in 1 patient in our cohort, and it has been associated with a mortality rate of approximately 60%.[3,4] The pathophysiology of this phenomenon remains poorly understood but is thought to be due to the release of pancreatic lipase into the bloodstream. It then manifests as subcutaneous lobular panniculitis, arthritis, or intraosseous fat necrosis.[1,3,8]

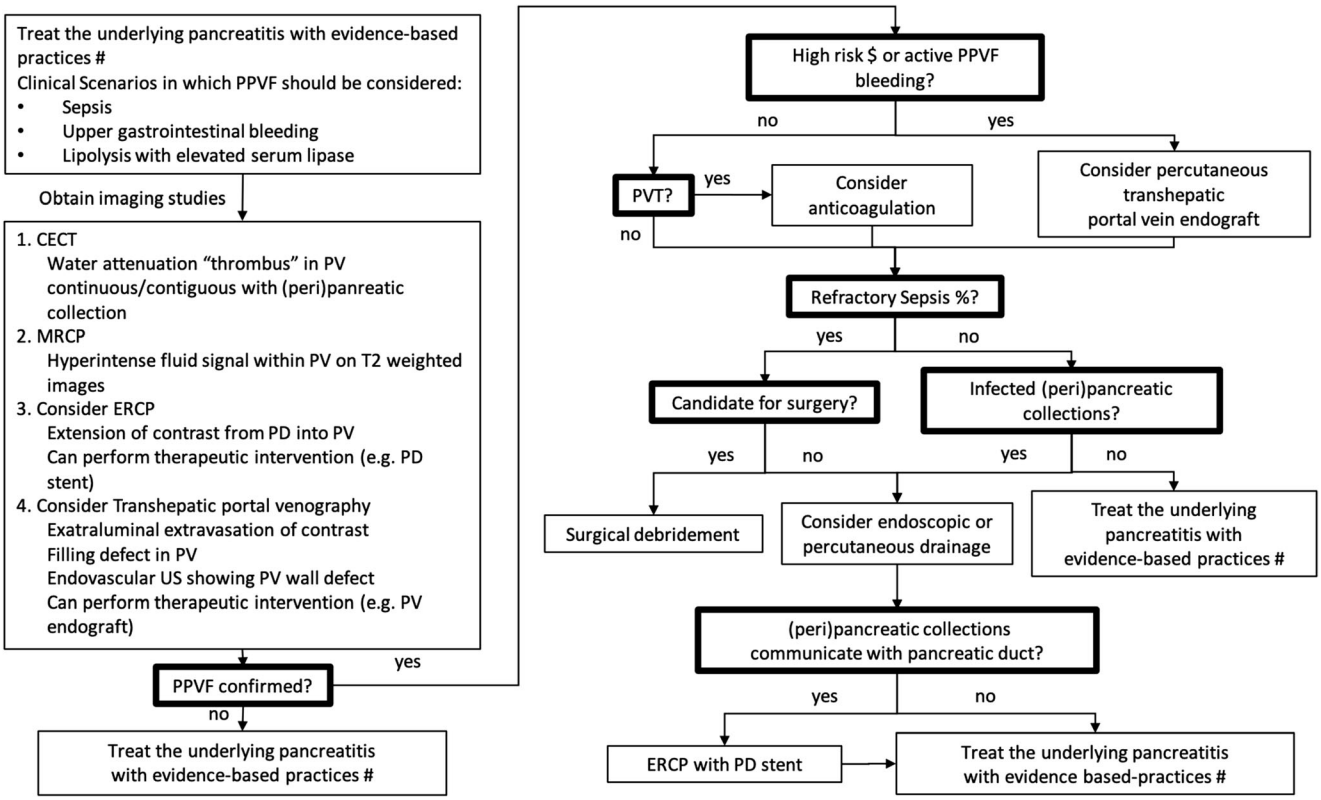

Fig. 6 Proposed algorithm for diagnosis and treatment of PPVF. PPVF, pancreatic-portal vein fistula; PVT, portal vein thrombosis; PV, portal vein; PD, pancreatic duct; EUS, endoscopic ultrasound; CD, cyst drainage

Conclusion

PPVF is a rarely reported but potentially an underdiagnosed condition, most commonly associated with recurrent acute on chronic pancreatitis, complicated by (peri)pancreatic necrosis. Early suspicion of PPVF is critical. PPVF-associated sepsis without debridement and occlusive or near-occlusive MPV FD correlate with high mortality rates, while subocclusive MPV FD is associated with survival and long-term MPV patency. While management remains highly individualized, we report the novel use of transhepatic portal venography and endovascular stenting as a management strategy for acute hemorrhage secondary to PPVF. Increasing recognition of this rare but serious diagnosis and subsequent timely treatment may lead to improved outcomes in future studies.

Declarations

Conflict of Interest The authors declare no competing interests.

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