Fistula of a pancreatic pseudocyst into the superior mesenteric and portal veins causing erythema nodosum and aseptic polyarthritis – case report and review of literature

1University of Belgrade, Faculty of Medicine, Clinical Center of Serbia, First Surgical Clinic, Belgrade, Serbia; 2University of Belgrade, Faculty of Medicine, Belgrade, Serbia; 3Clinical Center of Serbia, Clinic of Orthopaedic Surgery and Traumatology, Belgrade, Serbia; 4North Middlesex University Hospital NHS Trust, Division for Surgery and Cancer Services, London, United Kingdom

Received: August 15, 2020
Revised: May 12, 2021
Accepted: May 18, 2021
Online First: May 19, 2021
DOI: https://doi.org/10.2298/SARH200815043G

Abstract: A case of a 45-year-old man with a pancreatic pseudocyst that ruptured into the superior mesenteric and portal veins. This caused an unusual presentation of erythema nodosum and aseptic polyarthritis.

Keywords: Pancreatic pseudocyst, Fistula, Erythema nodosum, Aseptic polyarthritis

*Accepted papers are articles in press that have gone through due peer review process and have been accepted for publication by the Editorial Board of the Serbian Archives of Medicine. They have not yet been copy-edited and/or formatted in the publication house style, and the text may be changed before the final publication. Although accepted papers do not yet have all the accompanying bibliographic details available, they can already be cited using the year of online publication and the DOI, as follows: the author’s last name and initial of the first name, article title, journal title, online first publication month and year, and the DOI; e.g.: Petrović P, Jovanović J. The title of the article. Srp Arh Celok Lek. Online First, February 2017.

When the final article is assigned to volumes/issues of the journal, the Article in Press version will be removed and the final version will appear in the associated published volumes/issues of the journal. The date the article was made available online first will be carried over.

*Correspondence to:
Nikica M. Grubor
Clinical Center of Serbia, First Surgical Clinic, Institute for Digestive Diseases, Koste Todorovica 6, Belgrade 11000, Serbia
E-mail: gruborn13@gmail.com
Fistula of a pancreatic pseudocyst into the superior mesenteric and portal veins causing erythema nodosum and aseptic polyarthritis – case report and review of literature

SUMMARY
Introduction Extra-pancreatic complications of acute and chronic pancreatitis that do not relate to vital organs are rare. The most common include subcutaneous panatitis, arthritis, bone marrow fat necrosis and vasculitis. These associated conditions have been termed Pancreatic Disease Syndrome (PDS), which can occur not only with pancreatitis but also in other pancreatic diseases. PDS is believed to be caused by circulating pancreatic enzymes, which can occur when the pancreas is in direct communication with the circulation. Pancreatic pseudocyst erosion into the superior mesenteric and portal veins is extremely rare; and there have only been 22 previously reported cases in literature. The authors endeavoured to describe a manifestation of PDS with formation of a pseudocyst-portal fistula, its complications, and propose adequate surgical management.

Case outline We present a 37-year-old man with chronic alcoholic pancreatitis and a pancreatic pseudocyst within the head of the pancreas which communicated with the main pancreatic duct on one side and eroded into the superior mesenteric and portal veins on the other, causing erythema nodosum-like vasculitis, and polyarthritis. The patient was initially treated conservatively, but subsequently required multiple arthrotomies and finally underwent pylorus preserving duodenopancreatectomy and direct repair of the affected veins.

Conclusion The majority of cases required aggressive surgical intervention due to heightened risk of hemorrhage. In patients who develop disseminated fat necrosis, an earlier surgical intervention can be justified. The authors would recommend that where practical a pylorus-preserving pancreatectoduodenectomy should be performed.

Keywords: Pancreas; Pseudocyst-portal vein fistula; Pancreatic disease syndrome

SAŽETAK
Uvod Екстра-панкреатичне компликације акутног и хроничног панкреатита које се не односе на виталне оргane су веома ретке. Најчешћа компликација је субкутани паникулитис, артритис, масна некроза косне сржи и васкулитис. Ова асоцирана стања се једним именом називају синдром болести панкреаса (ПДС), и могу се јавити не само уз панкреатитис већ и у другим болестима панкреаса као што су тумори, трауама, и лигијаза панкреатичних канала. ПДС је вероватно узрокован циркули-шућим ензимима панкреаса (конкретно липазе) када је панкреас у директној комуникацији са крвотоком. Ерозија псеудоцисте панкреаса у горњу мезентеричну и портну вену је веома редак догађај; постоје само 22 претходно објављене случаје панкреатично-порталних венских фистула у лите-ратури. Аутори су настојали представити обојење које настаје код ПДС-а ретким формирањем псеудоцисто-порталних фистула, могуће комплика-ције, уз препоруку о адекватном хируршком трет-ману са детаљним прегледом светске литература.

Приказ болесника Представљамо необичан случај тридесетседмогодишњег човека са хроничним алко-холим панкреатитисом и панкреатитисом главе пан-креаса која једном у станима комуницира са главним панкреатичним водом, а другом је широком ерози јама у контакту са горњом мезентеричном и портном веном, изазивајући васкулитис налик нодозном еритему (Erythema nodosum) и панкреатитис. Иницијално, пацијент је лечен конзервативно али су накнадно урађене многоструке артритомије када је у крајњем акту урађена пилорус-резервирајућа дуоденопанкреатектомија и директна реконструк-ција оштећених вена.

Закључак Већина случајева захтевала је агресивно хируршко лечење, јер је опасност од крварења велика. Ранија хируршка интервенција може бити оправдана и ако се код болесника развија дисеминирана некроза масти која додатно погоршава исход. Аутори препоручују да се у пракси учини, пилорус-резервирајућа панкреатикодуоденектомија.

Кључне речи: Панкреас; Псеудоцистична-портална венска фистула; Синдром болести панкреаса (ПДС)
INTRODUCTION

Pancreatic pseudocysts often follow acute pancreatitis, and though they can resolve spontaneously, they can also be associated with potential complications. These include bleeding [1, 2], ruptures into the abdominal cavity [3], splenic vein obstruction [4], portal vein thrombosis [5, 6], and the formation of fistulae into the surrounding organs [6, 7, 8] and the inferior vena cava [9]. Erosion of a pancreatic pseudocyst into the portal vein to create a pancreas duct-portal vein fistula (PPF), however, is extremely rare with only 22 other previously reported cases [5, 6, 10–28].

CASE REPORT

A 37-year-old man, with a 15-year history of alcoholism presented with worsening epigastric pain requiring admission to a peripheral hospital. On examination he was found to have a tender upper abdomen and had a hematest-positive melaena stool. Apart from a moderate leucocytosis, other laboratory tests were within normal limits. An upper endoscopy revealed a hiatus hernia and Helicobacter pylori gastropathy. An ultrasound (US) scan defined a 5 × 4.5 cm hypoechogenic lesion within the uncinate process of the pancreas, which on computed tomography (CT) scan appeared to be inhomogeneous with a 2 cm central hypodense area. An US-guided fine needle aspiration (FNA) of the lesion produced a dark green-rusty dense fluid, with a high pancreatic enzyme content. Though anti-Helicobacter pylori treatment gave only mild relief of his symptoms, he refused operative drainage of the pancreatic pseudocyst, taking his own hospital discharge.

Two weeks later he was admitted to a second hospital with worsening abdominal pain, and four days later developed erythema nodosum-like cutaneous lesions on the front and sides of both his lower legs. Within two weeks he had developed a moderate fever, raised
serum and urine amylase, generalized arthralgia, restricted active and passive joint motion, and swelling of all the major joints.

He was transferred to our Institution because of a clinical deterioration, and on admission was found to be pale and lethargic, with generalized arthralgia, large joint effusions and abdominal pain. His fibrinogen was 10.4 g/L, WBC $25 \times 10^9$/L, and ESR 110/1 h. The cyst within the head of the pancreas had recollected on repeat CT, and now demonstrated a central contrast-enhancing area (Figure 1.). He passed further melaena stool after admission, but a repeat upper endoscopy once more showed no active bleeding site.

Over the next 24 hours he developed spontaneous discharge of a dense, viscous, light-brown pus-like material from his swollen left knee. Surgical arthrotomies of his other large joints were performed, after which his joint pains and swellings resolved. Neither direct examination nor cultures of the joint samples were positive for bacteria, and histology found only non-specific aseptic inflammation of the synovial membranes and joint capsules.

Despite a general improvement in his condition the patient’s epigastric pain continued and the decision was made to operate on the pancreatic pseudocyst. At laparotomy a cyst-like lesion was found within the head of the chronically inflamed pancreas, close to the mesenteric vein. No fat necrosis was found within the abdomen. Cyst aspiration was performed and blood-like aspirate obtained; containing 58,040 U/L of amylase on laboratory analysis. The cyst was formally opened with the aim of performing a cystojejunostomy, particularly as there was a chance that the blood that had been aspirated might have been from an accidentally punctured blood vessel. Following exploration, the bleeding became more brisk, requiring tamponade, and fearing an arterial aneurysm a pylorus preserving pancreatic head resection was performed.

After pancreatic transection, the head was slowly and carefully dissected from the very adherent superior mesenteric and portal veins. Unfortunately, the brisk bleeding
continued, and the bleeding source was established as a 2.5 × 0.5 cm communication between
the cyst cavity and the portal vein (Figure 2.). A temporary clamp was placed to control the
bleeding and the fistula was oversewn, making use of the thickened cyst wall.

Pathological analysis of the resected specimen confirmed a broad fistula between the
cyst (and the superior mesenteric) and portal veins; an additional fistula was also identified
between the cyst and the pancreatic duct (Figure 3.).

The patient’s postoperative recovery was uneventful, with an almost immediate
resolution in his abdominal symptoms. After a rehabilitation programme and intense
physiotherapy, the patient regained most of his musculoskeletal function, remaining
ambulatory and well at a recent six-year review.

A written consent was obtained from the patient for the publication of this paper.

DISCUSSION

The precise mechanism of pancreatic pseudocyst and portal vein fistula (PPF)
formation remains unknown [10]. Pancreatic enzymes activated by intestinal enterokinases
are thought to be responsible for the erosion into neighboring blood vessels [14]. Any venous
thrombosis in these vessels is then likely to be dissolved by these same enzymes, thereby
allowing their free flow into the blood circulation, causing PDS [18].

There have been twenty-two previously documented cases of fistulae between a
pancreatic pseudocyst and the portal vein (PPF) [5, 6, 10–28]; almost all of these being single
case reports. Together with this currently reported case these have been predominantly male
patients (82% or 19/23 patients) with a mean age of 50 years (range 29–82 years) at
presentation and most had a history of chronic alcohol abuse and chronic pancreatitis. The
majority presented with abdominal pain and of those tested all had a raised serum amylase
[22]. One patient had recurrent gastrointestinal bleeding and pain [18].
Fifteen (65%) had pseudocyst formation in the head of the pancreas (in close proximity to the portal vein), and four patients had pseudocysts involving the tail. Including this current case, 10 (43%) were suffering pancreatic disease syndrome (PDS) [14, 17, 22], erythema nodosum was evident in 8 (35%) [10–16, 22], polyarthritis in seven (39%) [11–17] and disseminated fat necrosis in 5 (28%) patients [17, 22].

Conventional invasive and noninvasive imaging can often (though not always consistently) identify a PPF [22]. Contrast enhanced CT scan can demonstrate thrombus within the portal vein in PPF patients, though does not typically demonstrate the fistula. MRI/MRCP can demonstrate increased fluid signal in the portal vein, assess the pancreatic ductal system and identify other extrinsic pathology. US can also demonstrate absent portal vein flow from thrombus formation, but not necessarily the fistula formation. Endoscopic retrograde cholangiopancreatography (ERCP) will demonstrate a fistula but only if the pseudocyst directly connects to the pancreatic duct. Percutaneous transhepatic portography (PTP) by definition directly visualizes the portal system and can also yield portal vein fluid for analysis [22]. Image-guided (CT or US) cystography and angiography can also be useful.

Of the (now 23) reported PFF cases, four (17%) were diagnosed through ERCP [5, 6, 23, 24], four (17%) through cystography [19, 20, 27], three (13%) through PTP [18, 21, 22], two (11%) through MRI/MRCP [25, 26], one through CT [28], and one (4%) through angiography [11].

In this particular reported case despite having had 2 upper endoscopies, an US and two CT scans, the diagnosis of a PPF was only actually made during surgery and then confirmed through pathological analyses. Of the remaining reported PPF cases, two were similarly diagnosed during surgery [12, 17], while five (22%) were only discovered at post mortem [10, 13–16]. Thus, despite multimodal diagnostics 8 (35%) patients had their diagnosis established either at surgery or at post mortem.
The majority of these patients can be managed expectantly, and PPF have been known to close spontaneously [23]. However, prompt surgical intervention is indicated where disseminated fat necrosis develops or when there is a significant clinical deterioration, as these are associated with significantly poorer outcomes, and even death [6, 15, 25].

Nine of the 23 PPF patients underwent surgery. A pylorus preserving pancreaticoduodenectomy was performed in two patients [12, 22], similar to the procedure which our patient also underwent; resulting in the immediate resolution of the PDS. Another patient underwent surgical ligation of the incoming vessels with no symptom improvement. A Whipple’s procedure was then performed at a second sitting which resulted in the disappearance of the “pancreatic disease syndrome” [11]. A fifth patient underwent local pancreatic resection and pancetaticojejunostomy; unfortunately, this patient had recurrence of subcutaneous fat necrosis, but this fortunately responded to steroids [17]. An unusual sixth patient with 3 cysts underwent splenectomy and a partial left pancreatectomy. Following this the dilated pancreatic duct and the pancreatic pseudocyst walls were opened longitudinally and a “Y” side-to-side pancreaticojejunostomy was performed. A catheter was then inserted through the splenic vein into the portal tree to drain it externally and to prevent portal hypertension during the postoperative period. The catheter stopped draining pancreatic juice after a few days and the drain was removed 15 days postoperatively [20]. This patient was doing well at the time of publication two years after surgery. A seventh patient had simple operative drainage of their ascites and after three months was discharged from hospital. They were noted to be well at the time of publication [19], however no time period for this was stated. One further patient underwent pancreaticojejunostomy [18], another a pancreaticoenterostomy [25].

Despite the successful closure of the PPF, some of these surgically managed patients continued to suffer serious disability from ongoing recurrent extrapancreatic disease.
Our patient clearly suffered from chronic alcoholic pancreatitis with an associated pseudocyst. However, we failed to recognize that the pre-operative dark brown aspirated fluid and the presence of contrast within the central area of the cyst on CT indicated a probable communication of the cyst with a neighboring blood vessel. In retrospect these findings obviously warranted angiographic imaging. The absence of contrast within the peripheral area of the cyst should also have been recognized as resulting from thrombosis. The laboratory findings of high concentrations of amylase from the intraoperative blood aspirated from the cyst would have also indicated a possible cyst-portal fistula. The upper gastrointestinal bleeding with a normal upper endoscopy can also be explained by the pathology finding of a communication between the pancreatic pseudocyst and the pancreatic duct; and this could have been identified earlier by endoscopic retrograde cholangiopancreatography (ERCP). The direct emptying of the pancreatic enzymes into the mesenteric and portal veins was probably the cause of the PDS, which completely resolved after surgery.

The authors would recommend that where practical a pylorus-preserving pancreaticoduodenectomy should be performed. This resulted in a rapid resolution in our patient’s PDS symptoms, which has also been the experience of other authors with similar cases [12, 22].

**Conflict of interest:** None declared.
REFERENCES

1. Greenstein A, DeMaio EF, Nabseth DC: Acute hemorrhage associated with pancreatic pseudocysts. Surgery 1971;69:56-62 [PMID:5312732]

2. Gadacz TR, Trunkey D, Kiefier RF Jr. Visceral vessel erosion associated with pancreatitis. Case reports and a review of the literature. Arch Surg 1978;113:1438-40 [PMID:310667]

3. Grover NK, Gulati SM, Taneya OP: Spontaneous intraperitoneal rupture of the pseudopancreatic cyst. Am J Gastroenterol 1973;59:67-72 [PMID:4686474]

4. Turrill FL, Mikkelsen WP: "Sinistral" (left-sided) extrahepatic portal hypertension. Arch Surg 1969; 99:365-8 [PMID:5363350]

5. Yamamoto S, Takeshige K, Aradawa T, Kuroda H, Kanda S, Takayama T, Katada N. Case report of a pancreatic pseudocyst ruptured into the splenic vein causing extrahepatic portal hypertension. Jpn J Surg 1982;12:387-90 [PMID:7143823]

6. McCormick PA, Chronos N, Burroughs AK, McIntyre N, McLaughlin JE: Pancreatic pseudocyst causing portal vein thrombosis and pancreatico-pleural fistula. Gut 1990;31:561-3 [PMID:2351306]

7. Bedingfield JA, Anderson MC: Pancreatoportal fistula. Pancreas 1986;1:283-90 [PMID:3575310]

8. Nordback I, Sand J: The value of endoscopic pancreatogram in peritoneal or pleural pancreatic fistula. Int Surg 1996; 81:184-6 [PMID:8912090]

9. Nizze H, Hempel A, Paech R. Pancreatic pseudocyst with vena cava erosion, necrotizing panniculitis and polyarthropathy. Pathologe 1986;7(6):348-52 [PMID:3809119]

10. Zeller M, Hetz HH. Rupture of a pancreatic cyst into the portal vein. Report of a case of subcutaneous nodular and generalized fat necrosis. JAMA 1966;195: 869-71 [PMID:12608186]

11. Trapp RG, Breuer RI, Crampton AR, Davis JH, Derman RE, Larson RH, Victor TA. Pancreatic duct arteriovenous fistula and the metastatic fat necrosis syndrome. Dig Dis Sci 1979;24:403-8 [PMID:4562262]

12. Potts JR 3rd. Pancreatic-portal vein fistula with disseminated fat necrosis treated by pancreaticoduodenectomy. South Med J 1991;84:632-5 [PMID:2035087]

13. Lee SH, Bodensteiner D, Eisman S, Dixon AY, McGregor DH. Chronic relapsing pancreatitis with pseudocyst erosion into the portal vein and disseminated fat necrosis. Am J Gastroenterol 1985;80:452-8 [PMID:2408464]

14. Sørensen EV. Subcutaneous fat necrosis in pancreatic disease. A review and two new case reports. J Clin Gastroenterol 1988;10:71-5 [PMID:3356888]

15. Skargard ED, Ellison E, Quenville N. Spontaneous rupture of a pancreatic pseudocyst into the portal vein. Can J Surg 1995;38:459-63 [PMID:7553473]

16. Packeisen J, Klingen D, Grezella F. Spontaneous rupture of a pancreatic pseudocyst into the portal vein. Z Gastroenterol 2001;39:961-4 [PMID:11778155]

17. Hammar AM, Sand J, Lumio J, Hirn M, Honkonen S, Tuominen L, Nordback I. Pancreatic pseudocyst portal vein fistula manifests as residivating oligoarthritis, subcutaneous, bursal and osseal necrosis: A case report and review of literature. Hepatogastroenterol 2002,49:273-8 [PMID:11941974]

18. Proacci C, Mansueto GC, Graziani R, Bicego E, Pederzoli P, Mainardi P, Bergamo Andreis IA, Valdo M, Azzolini D. Spontaneous rupture of a pancreatic pseudocyst into the portal vein. Cardiovasc Intervent Radiol 1995;18: 399-402 [PMID:8596128]

19. Takayama T, Kato K, Sano H, Katada N, Takeichi M. Spontaneous rupture of a pancreatic pseudocyst into the portal venous system. AJR Am J Roentgenol 1986;147:935-6 [PMID:3490165]

20. Pedrazzoli S, Petrini P, De Marchi L, Miotti D, Bonadimini B, Costantino V. An unusual complication of chronic pancreatitis: a recanalised portal tree communicating with a pancreatic pseudocyst. Am J Gastroenterol 1986;81:698-701 [PMID:3488677]

21. Noh R, Kim HJ. A pancreatic pseudocyst-portal vein fistula closed by endoscopic pancreatic stent insertion. Gastrointest Endosc. 2010 Nov;72(5):1103-5. doi: 10.1016/j.gie.2010.02.019. Epub 2010 Jun 11. PubMed PMID: 20541748.

22. Brown A, Malden E, Kugelmans M, Kortz E. Diagnosis of pancreatic duct-portal vein fistula; a case report and review of the literature. J Radiol Case Rep. 2014 Mar 1;8(3):31-8. doi: 10.3941/jrcr.v8i3.1552. eCollection 2014 Mar. Review. PubMed PMID: 24967026; PubMed Central PMCID: PMC4035366.

23. Willis SM, Brewer TG. Pancreatic duct-portal vein fistula. Gastroenterology. 1989 Oct 1;97(4):1025-7.

24. Van Steenbergen W, Ponette E. Pancreaticoportal fistula: A rare complication of chronic pancreatitis. Gastrointest Radiol. 1990 Dec 1;15(1):299-300.

25. Yoon SE, Lee Y-H, Yoon K-H, Choi CS, Kim H-C, Chae KM. Spontaneous pancreatic pseudocyst-portal vein fistula presenting with pancreatic ascites: strength of MR cholangiopancreatography. BJR. 2008 Jan 1;81(961):e13-6.

26. Riddell A, Jhaveri K, Haider M. Pseudocyst rupture into the portal vein diagnosed with MRI. BJR. 2005 Mar 1;78(927):265-8.
27. Rasmussen IC, Karlson B-M, Löfberg A-M. Biliary Pancreatic Portal Fistula as a Complication of Chronic Pancreatitis. Upsala Journal of Medical Sciences. 2006 Jan 1;111(3):329–38.

28. Dawson BC, Kasa D, Mazer MA. Pancreatic pseudocyst rupture into the portal vein. South Med J. 2009 Jul;102(7):728–32.
Figure 1. Computed tomography showing contrast within the central area of the cyst – C; SV – splenic vein; SMA – superior mesenteric artery
Figure 2. Diagram showing operative findings. C – pancreatic pseudocyst; PV – portal vein; SV – splenic vein; PD – pancreatic duct; CPF – cyst portal fistula; CPDF – cyst pancreatic duct fistula.
Figure 3. The intra-operative specimen. C – pancreatic pseudocyst; PD – pancreatic duct; CPDF – cyst pancreatic duct fistula; VP – Vater’s papilla; CBD – common bile duct