

NIA has changed, and now the standard fever, rash and eosinophilia triad is uncommon. In a review of over 150 cases, one of these symptoms was identified in 50% of patients, but all three in fewer than 5%.⁸

Histology is not necessary for the diagnosis of AIN if there is well-founded suspicion and potential causative agents can be removed.

The role of steroids in the treatment of drug-induced AIN has long been a subject of debate. At present, despite the absence of prospective randomized studies, it is accepted that steroid treatment is indicated and should begin immediately after diagnosis in order to reduce the risk of chronic kidney failure.⁹

It is sometimes difficult to identify the trigger drug in AIN, and re-exposure to the probable causative agent is not ethically justified. In our case, re-exposure enabled us to quickly establish the aetiological diagnosis.

In patients with a high suspicion of AIN, guidelines recommend suspending all PPIs. The most effective alternative treatment of acid reflux in these patients would be an H2 blocker, although evidence has shown these to be far less successful than PPIs in controlling symptoms, complications and relapse. Ideally, if patients can be screened for predictors of successful surgical outcome, total or partial fundoplication would be equally or even more effective than PPIs.

The most common indications for anti-gastroesophageal reflux surgery include: (a) need for maintenance medical treatment, mainly in young patients, (b) resistance to PPIs, and (c) uncontrollable complications. Fundoplication is also indicated in patients contraindicated for PPI therapy due to severe adverse effects.

In conclusion, PPIs are widely used in clinical practice, and have a good risk/benefit profile. However, given their potential for toxicity, they should be carefully prescribed and the duration of treatment should be controlled.

References

1. Forgacs I, Loganayagan A. Overprescribing proton pump inhibitors. *BMJ*. 2008;336:2–3.

2. Abraham NS. Proton pump inhibitors: potential adverse effects. *Curr Opin Gastroenterol*. 2012;28:615–20.
3. Min YW, Lim KS, Min BH, Gwak GY, Paik YH, Choi MS, et al. Proton pump inhibitor use significantly increases the risk of spontaneous bacterial peritonitis in 1965 patients with cirrhosis and ascites: a propensity score matched cohort study. *Aliment Pharmacol Ther*. 2014;40:695–704.
4. Jarchow-Macdonald AA, Mangoni AA. Prescribing patterns of proton pump inhibitors in older hospitalized patients in a Scottish health board. *Geriatr Gerontol Int*. 2013;13:1002–9.
5. Brewster UC, Perazella MA. Proton pump inhibitors and the kidney: critical review. *Clin Nephrol*. 2007;68:65–72.
6. Espejo B, Herrero JC, Torres A, Martínez A, Gutiérrez E, Morales E, et al. Nephritis intersticial inmuoalérgica vs. ateroembolismo de colesterol. *Características diferenciales*. *Nefrología*. 2003;23:125–30.
7. Praga M, Sevillano A, Auñón P, González E. Changes in the aetiology, clinical presentation and management of acute interstitial nephritis, an increasingly common cause of acute kidney injury. *Nephrol Dial Transplant*. 2015;30:1472–9.
8. Rossert J. Drug-induced acute interstitial nephritis. *Kidney Int*. 2001;60:804–17.
9. González E, Gutiérrez E, Galeano C, Chevia C, de Sequera P, Bernis C, et al. Early steroid treatment improves renal function recovery in patients with drug-induced acute interstitial nephritis. *Kidney Int*. 2008;73:940–6.

David Ruiz-Clavijo García^{a,*}, Alba Zúñiga Ripa^a, Belen González de la Higuera Carnicer^a, Eduardo Valdivielso Cortazar^b, Federico Bolado Concejo^a, Jesús Urman Fernández^a, Juan Jose Vila Costas^a

^a *Servicio de Aparato Digestivo, Unidad biliopancreática, Complejo Hospitalario de Navarra, Pamplona, Navarra, Spain*

^b *Complejo Hospitalario Universitario de A Coruña, A Coruña, Spain*

* Corresponding author.

E-mail address: davidruizcla@gmail.com

(D. Ruiz-Clavijo García).

2444-3824/

© 2016 Elsevier España, S.L.U., AEEH and AEG. All rights reserved.

Portal thrombosis and liver necrosis: Exceptional complication of acute pancreatitis[☆]



Trombosis portal y necrosis hepática: complicación excepcional de la pancreatitis aguda

Pancreatitis is a common disease with varied aetiology, and can give rise to various complications. We present a

previously unreported complication: portal vein thrombosis (PVT) associated with necrosis of liver segments II/III.

A 76 year-old man seen in the emergency room for abdominal pain lasting 48h accompanied by nausea, choluria and acholia. Personal history: hypertension and HLA-B27 ankylosing spondylitis, denies alcohol abuse. Examination: T: 36.4°C; BP: 135/85 mmHg; HR: 129 bpm; conjunctival icterus and diaphoresis; abdominal pain in epigastrium and both hypochondria with positive Murphy sign. Preliminary laboratory results: white blood cells: 18,000/ μ L (92% neutrophils); haemoglobin 16.6 g/dL; serum amylase 3549 U/L; ALT: 259 U/L; AST: 326 U/L; alkaline phosphatase: 182 U/L; total bilirubin: 9.8 mg/dL (direct: 7.2 mg/dL); C-reactive protein: 53.6 mg/dL and plasma lactate: 2.3 mg/dL.

Abdominal ultrasound showed gallbladder sludge and gallbladder wall thickening of 4 mm. Computed tomography (CT) scan showed signs of left portal vein thrombosis

[☆] Please cite this article as: Gonzales Aguilar JD, Ramia Angel JM, de la Plaza Llamas R, Kuhnhardt Barrantes AW, Ramiro Perez C, Valenzuela Torres JC, et al. Trombosis portal y necrosis hepática: complicación excepcional de la pancreatitis aguda. *Gastroenterol Hepatol*. 2017;40:88–90.

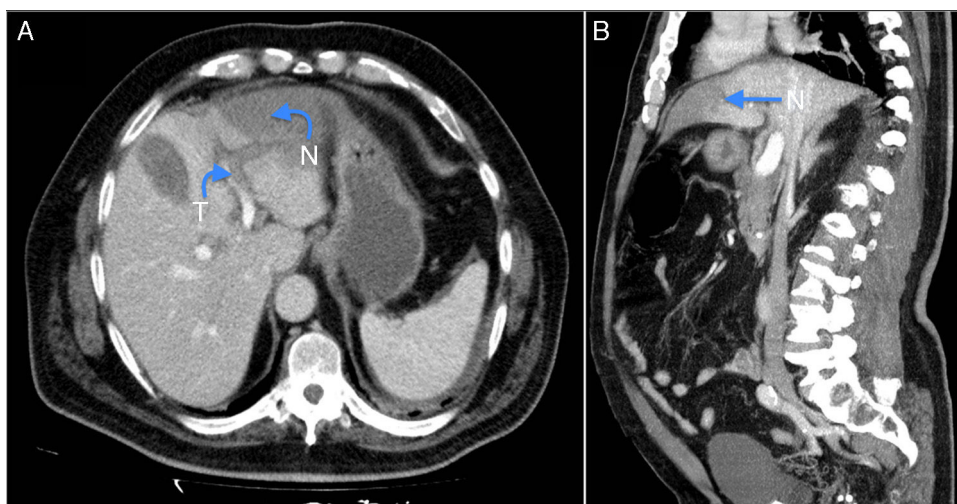


Figure 1 Abdominal CT scan. (A) Axial cut. N: hepatic necrosis; T: left portal vein thrombus. (B) Coronal cut: N: hepatic necrosis.

with lateral hepatic infarction (Fig. 1); small amount of perihepatic and perivesicular ascites; dilated common bile duct (13 mm) and pancreatic oedema (Fig. 2).

Treatment was started with sodium heparin and empirical antibiotic treatment (Imipenem®). At 48 h the patient presented fever, hypotension, leukocytosis and increased CRP. A new CT scan showed increased amounts of intraabdominal free fluid associated with clinical worsening and haemodynamic instability, despite intensive treatment. Emergency surgical treatment was decided, showing, 2.5 L choleperitoneum, necrosis of liver segments II/III; canicular perforation on the surface of the liver with release of bile. Left lateral hepatectomy was performed with cholecystectomy and exploration of the bile duct, which showed gallbladder sludge. Choledochotomy was closed after placement of a Kehr T-tube. Peritoneal fluid culture was sterile. Histology revealed extensive hepatic necrosis. After surgery, improvement was observed in symptoms, and pathological analytical parameters were normalized.

During his hospital stay the patient presented pneumonia and kidney and heart failure. He was discharged 95 days after surgery. Systemic causes of the thrombosis were ruled out. One year after discharge, the patient died suddenly at home while still receiving acenocoumarol therapy. No autopsy was performed.

Partial or complete PVT is a relatively common complication in patients with liver cirrhosis, although it can also occur in the absence of underlying liver disease.¹ Non-cirrhotic PVT can be caused by local (surgery, pancreatitis, pancreatic tumour)² or systemic factors (coagulation disorders, myeloproliferative disorders and prothrombotic conditions, such as Factor V Leiden mutation and protein C deficiency).^{1,2} Prevalence of PVT in acute pancreatitis is estimated at 8%.³

The aetiology of PVT in acute pancreatitis is multifactorial: cross-talk between coagulation and inflammatory pathways, elevation of proinflammatory cytokines (TNF, IL-1 and IL-6), which in turn regulate the increase in thrombin formation and reduce antithrombotic mechanisms,⁴ and pancreatic neutrophil and macrophage infiltration into the portal vein.

PVT can be acute or chronic, and depends on recanalisation to permit collateral circulation. Acute PVT is

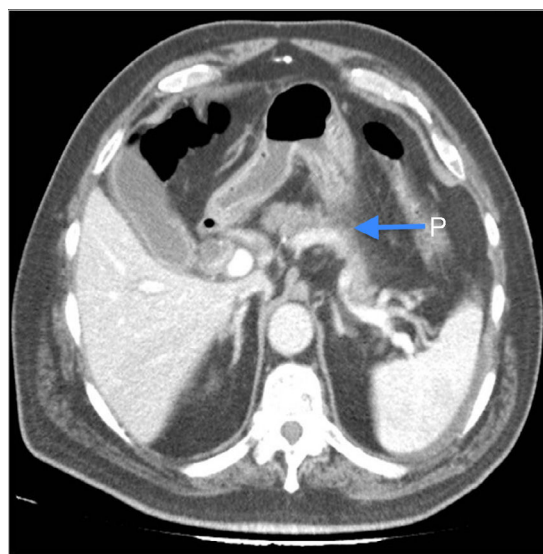


Figure 2 Abdominal CT scan. P: pancreatic oedema.

characterized by intestinal congestion that can progress to ischaemia, causing pain or bloating, diarrhoea, bleeding, nausea, vomiting, anorexia, fever, lactic acidosis, splenomegaly and sepsis. Chronic PVT can be almost asymptomatic due to re-canalisation, but the presence of oesophageal varices can cause gastrointestinal bleeding in 20–40% of cases.¹ The highest diagnostic yield in PVT is obtained with Doppler ultrasound (81% sensitivity and 93% specificity) and CT or MRI angiogram, which show the extent and characteristics of PVT (sensitivity 96% and specificity close to 100%).¹ The best method for diagnosing hepatic infarction is gadopentate disodium contrast-enhanced MRI, which shows the extent of the infarction, hepatic haemodynamics and hepatocellular function, differentiating between areas of hepatic infarction and reduced perfusion.^{4,5}

Few studies have described the complications associated with acute pancreatitis.⁶ We searched the PubMed database updated to 25-10-2015, with no language or date limitations, using the following string: (Pancreatitis) AND (Portal

Thrombosis) AND (Hepatic Necrosis), and retrieved only 11 articles. After reading the studies, we found one case of hepatic infarction associated with portal vein thrombosis in a patient with chronic pancreatitis who died from liver failure.⁴ Another article described a case of hepatic necrosis and portal vein thrombosis in a patient with chronic pancreatitis after placement of a pancreatic stent,⁷ while another study discussed a case of hepatic necrosis and portal vein thrombosis in a patient with liver cirrhosis following variceal ligation and endoscopic injection sclerotherapy.⁸ A less restrictive search using the string (Pancreatitis) AND (Portal Thrombosis) returned 260 studies in venous thrombosis (splenic, portal and mesenteric) associated with acute pancreatitis, include a meta-analysis of 947 studies, published in 2015, none of which associate portal thrombosis with hepatic necrosis.³

There are no randomized trials on the treatment of acute PVT, but anticoagulation therapy is the most widely accepted strategy. Re-canalization rate is 70% if anticoagulation is initiated in the first week of diagnosis, and 25% if started later.¹ Anticoagulation should be maintained for at least 2–4 weeks, and later replaced with oral anticoagulants, which should be maintained for a year. Other therapeutic strategies, such as local or systemic administration of thrombolytic agents should only be used in the event of total or partial therapeutic failure.⁹ However, we could find no recommendations in the literature regarding patients like ours, in whom the cause (pancreatitis) has resolved, and who have undergone hepatic and portal vein resection, removing the thrombus. We are unsure whether anticoagulation is necessary in these cases, and if so, how long it should be maintained. In hepatic infarction, treatment and prognosis depends on the extent of injury; partial infarction should be treated conservatively, while lobar or more complicated infarction require hepatectomy of the affected area.¹⁰

Conflicts of interest

The authors declare that there are no conflicts of interest.

References

1. Ponziani FR, Zocco MA, Campanale C, Rinninella E, Tortora A, di Maurizio L, et al. Portal vein thrombosis: Insight into physiopathology, diagnosis, and treatment. *World J Gastroenterol.* 2010;16:143–55.
2. Vinciane R, Larbi B, Marie-Pierre V, Dominique V, Bertrand C, Olivia H, et al. Extrahepatic portal venous system thrombosis in

recurrent acute and chronic alcoholic pancreatitis is caused by local inflammation and not thrombophilia. *Am J Gastroenterol.* 2012;107:1579–85.

3. Xu W, Qi X, Chen J, Su C, Guo X. Prevalence of splanchnic vein thrombosis in pancreatitis: a systematic review and meta-analysis of observational studies. *Gastroenterology Res Pract.* 2015;2015:245460.
4. Beger H, Buchler M, Kozarek R, Lerch M, Neoptolemps J, Warshaw A, et al. The pancreas: an integrated textbook of basic science, medicine, and surgery. 2nd ed. MA, USA: Blackwell Publishing, Inc.; 2008. p. 218–9.
5. Masahiro M, Akira Y, Yasuhiro K, Souichiro S, Shinya F, Shigenori Y, et al. Hepatic infarction complicated with acute pancreatitis precisely diagnosed with gadoxetate disodium-enhanced magnetic resonance imaging. *Intern Med.* 2014;53:2215–21.
6. Quintas P, Cubiella J, Trillo M, Fernández-Carrera JM, Frójan P, Fernández J. Absceso hepático y fístula biliar como complicaciones locales de una pancreatitis aguda: abordaje y tratamiento. *Gastroenterol Hepatol.* 2009;32:401–5.
7. Vimalraj V, Jeswanth S, Kannan DG, Krishnan CS, Surendran R. Acute portal vein thrombosis and massive necrosis of the liver. An unusual complication after stenting for chronic pancreatitis. *JOP.* 2006;7:660–4.
8. Yamashita K, Tsukuda H, Mizukami Y, Ito J, Ikuta S, Kondo Y, et al. Infarto hepático con trombosis portal. *J Gastroenterol.* 1997;32:684–8.
9. Ogren M, Bergqvist D, Björck M, Acosta S, Eriksson H, Sternby NH. Portal vein thrombosis: prevalence, patient characteristics and the risk of his life: a population study based on 23,796 consecutive autopsies. *World J Gastroenterol.* 2006;12:2115–9.
10. Giovine S, Pinto A, Crispiano S, Lassandro F, Romano L. Retrospective study of 23 cases of hepatic infarction: CT findings and pathological correlations. *Radiol Med.* 2006;111:11–21 [Article in English, Italian].

Jhonny David Gonzales Aguilar, Jose Manuel Ramia Angel*, Roberto de la Plaza Llamas, Andree Wolfgang Kuhnhardt Barrantes, Carmen Ramiro Perez, Jose del Carmen Valenzuela Torres, Cristina Garcia-Amador, Aylhin Joana Lopez-Marcano

Unidad de Cirugía Hepatobiliopancreática, Servicio de Cirugía General y Aparato Digestivo, Hospital Universitario de Guadalajara, Guadalajara, Spain

* Corresponding author.

E-mail address: jose_ramia@hotmail.com

(J.M. Ramia Angel).

2444-3824/

© 2016 Elsevier España, S.L.U., AEEH and AEG. All rights reserved.