Case Rep Clin Pract Rev, 2002; 3(4): 234-238

Acute intermittent porphyria with acute pancreatitis and liver dysfunction

Murat Saruc[1], Nurten Turkel[1], Hakan Yuceyar[1], Semin Ayhan[2], Mehmet Akif Demir[2], Mine Can[3]

[1] Department of Gastroenterology, Celal Bayar University, School of Medicine, Manisa, Turkey
[2] Department of Pathology, Celal Bayar University, School of Medicine, Manisa, Turkey
[3] Department of Radiology, Celal Bayar University, School of Medicine, Manisa, Turkey

key words: acute pancreatitis • liver failure • porphyria • pleural effusion

SUMMARY

Background: *We reported a case with acute intermittent porphyria who demonstrated acute pancreatitis and liver dysfunction.*
Case Report: *A 44-year-old white male with type II diabetes mellitus presented with colicky right upper quadrant and epigastric pain, nausea and vomiting during last two days. Two weeks prior to these complaints, he had had an upper respiratory tract infection and used some drugs including terfenadine and co-trimoxazole. Physical examination revealed that he was mentally confused and he had jaundice. Abdominal examination revealed diffuse tenderness. Clinical, laboratory findings, liver histology, pancreas cytology and CT scan showed the presence of acute pancreatitis, mild liver failure and pleural effusion. His urine color was pink-purple and got darker in urine collection bag. Porphyrin studies revealed markedly elevated urine porphobilinogen, aminolevulinic acid, coproporphyrin, and uroporphyrin which suggested the diagnosis of acute intermittent porphyria. All these studies established the diagnosis of acute intermittent porphyria causing acute pancreatitis, mild hepatic failure, pleural effusion and neurological signs. The patient was kept at rest and treated with total parenteral nutrition without allowing oral food intake. Large amount of glucose was given by central venous route. A broad spectrum antibiotic was administered. Liver function, as well as clinical and laboratory findings of pancreatitis improved after two weeks of hospitalization. He has now been on follow-up for 6 months and he has not had any complaints.*
Conclusion: *When a clinician cannot find the etiology of acute pancreatitis and/or liver failure in patients, especially with neurological disorders, acute porphyria must be included in differential diagnosis.*

BACKGROUND

Porphyrias are inherited or acquired disorders of specific enzymes in the heme biosynthetic pathway [1]. These disorders are classified as either hepatic or erythropoietic depending on the primary site of overproduction and accumulation of porphyrin precursor or porphyrin, but some have overlapping features. The major manifestations of hepatic porphyrias are neurological, including abdominal pain, neuropathy, and mental disturbances, whereas erythropoietic porphyrias characteristically cause cutaneous photosensitivity [2,3].

Since porphyrias are uncommon and their symptoms are nonspecific, the diagnosis depends on a high index of suspicion. Confirmation by appropriate laboratory testing is essential [3]. Porphyrias may present with various signs and symptoms which are difficult to distinguish from many other clinical conditions. In this paper, the case with acute intermittent porphyria who demonstrated acute pancreatitis and liver dysfunction is presented and discussed.

Author's address: Dr. Murat Saruc, Merkez Efendi Mah. Altin Sok., Kirazlik-Ince Apt. No: 8/5 45020, Manisa, Turkey, email: msaruc@hotmail.com

CASE REPORT

A 44-year-old white male with type II diabetes mellitus presented with colicky right upper quadrant and epigastric pain, nausea and vomiting during last two days. The pain demonstrated increase in severity after meals. His family members recognized that his personality changed and a tendency to fall asleep occurred. He could be hardly woken up. During that period he experienced effort dyspnea. Two weeks prior to these complaints, he had had an upper respiratory tract infection and used some drugs including terfenadine and co-trimoxazole. He does not smoke or drink alcohol. He had never experienced any symptoms like those before this episode. There was no family member with similar symptoms.

Physical examination revealed normal arterial blood pressure and regular pulse of 88 per minute and normal body temperature. He was mentally confused and could hardly cooperate without any other neurological sign. Jaundice was present on his skin and sclera. Chest examination showed the loss of respiratory sounds in 1/3 lower parts of the both lungs. His abdominal examination revealed diffuse tenderness to palpation without rebound tenderness and with normal bowel sounds.

Serum fasting glucose level was 239 mg/dl. White blood cell count was 21.000/mm^3. Serum amylase and lipase were 1400 and 4200 IU, respectively, and remained elevated for the next four days. Total bilirubin was 7.5 mg/dl (direct bil: 4 mg/dl; indirect bil: 3.5 mg/dl). AST and ALT levels were 154 and 178 IU respectively. All initial laboratory investigations are presented in Table 1. Chest rentgenogram revealed bilateral pleural effusion. Ultrasound could not show any gallbladder or bile duct anomaly or stone. Abdominal CT scans were consistent with acute pancreatitis, showing enlarged pancreas, peripancreatic fluid collection, and hypodense necrotic areas in the head of the pancreas (Figure 1). These clinical, laboratory, and imaging findings suggested acute pancreatitis. However, in addition to acute pancreatitis there were liver failure, reduced mental alertness and pleural effusion. To clarify the etiology of acute pancreatitis, an ERCP procedure was attempted but it failed to cannulate the papilla due to papillary edema. MRCP revealed normal intra- and extrahepatic bile ducts (Figure 2). MRI showed the presence of acute pancreatitis with necrosis on the head of the pancreas. Ultrasound-guided needle aspiration was performed from this necrotic area. Cytological evaluation confirmed acute pancreatitis with the evidence of fatty

Table 1. Initial laboratory investigations.

Parameter	
White Blood Cell	21000/mm^3
Red Blood Cell	435x10^4/μl
Ht	33.2%
Hb	11.1g/dl
Platelet	410 K/μl
Glucose	239mg/dl
Amylase	1400 IU/l
Lipase	4200 IU/l
T. bilirubin	7.5 mg/dl
D. bilirubin	4 mg/dl
I. bilirubin	3.5 mg/dl
T. protein	7.3 g/dl
Alb	4.1 g/dl
AST	154 IU/l
ALT	178 IU/l
LDH	320 IU/l
ALP	223 IU/l
BUN	15 mg/dl
Cre	0.8 mg/dl
T. Cholesterol	187 mg/dl
Triglyceride	140 mg/dl
Na	135 mEq/l
K	3.9 mEq/l
Cl	100 mEq/l
Prothrombin time	15sec (INR:1.2)
Urine glucose	(++)
Urine protein	(–)

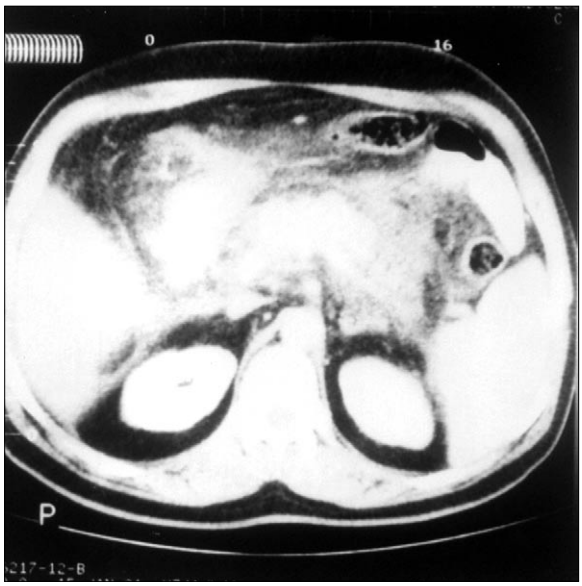

Figure 1. Abdominal CT image of the patient revealing acute pancreatitis by enlarged pancreas, peripancreatic fluid collection, and hypodense necrotic areas in the head of the pancreas.

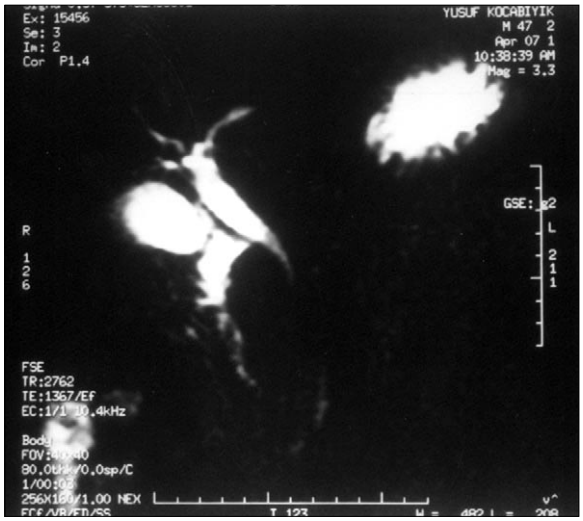

Figure 2. MRCP of the patient with normal gallbladder and common bile duct.

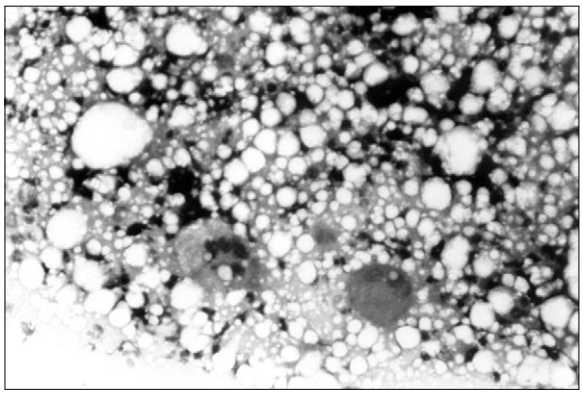

Figure 3. Cytopathologic findings of fatty necrosis with multinucleated histiocytes, polymorphonuclear leukocytes and vacuolated background. (Hematoxylin&Eosin ×2)

Table 2. Results of the porphyrin studies.

Parameter	Results	Normal
Urine PBG	2.59 mg/day	0–2 mg/day
Urine ALA	8.70 mg/day	0–7 mg/day
Urine COPRO	274 μg/day	0–160 μg/day
Urine URO	260 μg/day	0–60 μg/day

necrosis and microcalcifications (Figure 3). Culture of this aspirate and gram staining indicated sterile necrosis.

On the second hospital day, the patient complained of urinary retention which required catheterization. The color of obtained urine was pink-purple and got darker in urine collection bag. Because of the urine color, acute porphyria was suspected. Porphyrin studies revealed markedly elevated urine porphobilinogen, aminolevulinic acid, coproporphyrin, and uroporphyrin which suggested the diagnosis of acute intermittent porphyria (Table 2). The markers of viral and autoimmune hepatitis and studies for hemolysis could not clear the etiology of hepatic dysfunction. Liver biopsy was nonspecific with sinusoidal dilatation and mononuclear cell infiltration of portal space (Figure 4). Pleural fluid chemistry was transudate with normal amylase and low protein levels. EEG and neurological examination did not suggest any etiology for altered mental status.

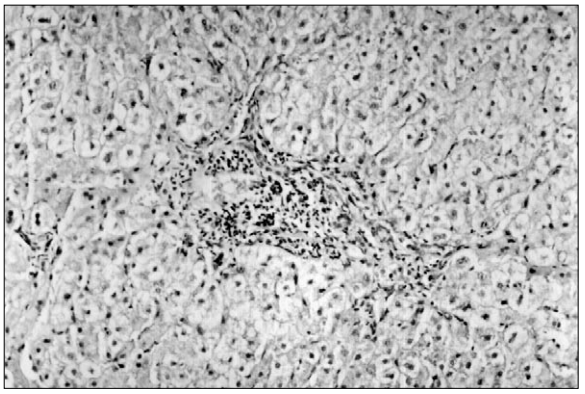

Figure 4. Non-diagnostic liver histology with mononuclear cell infiltration of portal space.

All these studies established the diagnosis of acute intermittent porphyria causing acute pancreatitis, mild hepatic failure, pleural effusion and neurological signs.

The patient was kept at rest and treated with total parenteral nutrition without allowing oral food intake. Large amount of glucose was given by central venous route. A broad spectrum antibiotic was administered. Liver function, clinical and laboratory findings of pancreatitis improved after two weeks of hospitalization. Pleural effusion was resolved. Mental status and urine color of the patient became normal on the 10th day of treatment. Repeated CT scan suggested normal pancreas anatomy without pancreatic phlegmon, pseudocyst or extrapancreatic fluid collection. He has now been on follow-up for 6 months and he has not had any complaints.

DISCUSSION

The acute attack is the characteristic aspect of the acute porphyria. It is often precipitated by ingestion of certain drugs or by infections, fasting or excessive alcohol consumption [1,2]. The attack usually starts

with severe pain in the abdomen, back or limbs. The patient is very restless, cries and often behaves in an apparently hysterical manner. Neuropathy affects the motor fibers more than the sensory fibers [1].

Our patient presented with acute pancreatitis, mild liver failure and neurological symptoms. Porphyria studies confirmed the diagnosis of acute intermittent porphyria. In the literature, there are a few case reports describing patients who presented with acute pancreatitis or liver failure due to acute intermittent porphyria [4–7]. Recently Komatsu et al. reported a similar case who had erythropoietic protoporphyria with severe liver dysfunction and acute pancreatitis [3]. Shiraki et al. reported a patient with acute intermittent porphyria who developed acute pancreatitis during an attack of acute intermittent porphyria [6]. In that patient, serum amylase, AST and bilirubin levels were increased after the cessation of abdominal pain, as seen also in Komatsu's patient. Shiraki et al. speculated that acute pancreatitis may have been caused by a spastic obstruction of the sphincter of Oddi, because autonomic neuropathy may be associated with acute intermittent porphyria and cause gastrointestinal spasms or dilatation [6]. If porphyric neurotoxicity was the cause of pancreatitis, the slow and gradual recovery from pancreatitis was consistent with the course of improvement in the elevated porphyrin levels. Porphyric neurotoxicity may be caused by excessive levels of the porphyrin precursors, heme deficiency in nerve tissue, and finally depletion of essential substrates or cofactors arising from the heme biosynthetic pathway defect.

Komatsu also suggests two possibilities for the cause of abdominal pain and jaundice in acute porphyrias. The first one is choledocholithiasis, which was not present in our patient. A more likely possibility is protoporphyrinogen-induced hepatic damage and spasm of the papilla [3]. Our ERCP attempt was unsuccessful, which might have been due to spasm of the papilla. Increased production of ALA and PBG, which are porphyrin precursors, may be harmful for liver tissue [3]. There are some reports in the literature suggesting that liver failure may develop during an attack of acute porphyria [3,5]. In our patient, viral hepatitis markers, autoimmune markers and other tests could not determine the etiology of liver failure. Liver histology was nonspecific and nondiagnostic, either.

MRCP showed normal intra- and extrahepatic bile ducts, but MRI revealed the presence of a heterogeneous mass in the head of the pancreas. US-guided fine needle biopsy and cytological examination of this material documented the diagnosis of acute pancreatitis with microcalcifications and fatty necrosis. All these findings revealed that there were no etiologies of liver failure and acute pancreatitis other than acute porphyria.

In the treatment of acute porphyria attacks, carbohydrate loading and/or heme therapy are recommended [1,2]. Carbohydrate loading has been shown to suppress the excretion of porphyrin precursors in humans with acute porphyria and in animal models of porphyria, and has been reported to lead to clinical improvement [1,2,3]. Carbohydrate administration should be initiated as soon as the diagnosis is established, either intravenously or orally. In our patient, we could not use the oral route because of acute pancreatitis, but large amount of intravenous glucose was infused by a central route until all symptoms subsided. Heme therapy replenishes the depleted intracellular heme pool that regulates the heme biosynthetic pathway and thus reduces the over production of porphyrin precursors [1,2,3]. Heme when given intravenously binds to hemopexin and albumin and is taken up mainly by the liver. Heme molecules can be given intravenously as hematin (heme hydroxide) or heme arginate. However, there are no heme preparations available in Turkey, and that is why we could not give it to our patient.

Our patient had diabetes mellitus and elevated blood glucose levels. Heme deficiency in the liver of acute intermittent porphyria patients stimulates an increase in ALA-synthases which triggers an escalating metabolic chain reaction, leading to an increase in porphyrin content. This reaction can be reduced by treating the patient with glucose. Andersson et al. studied the effects of diabetes mellitus in patients with acute intermittent porphyria [8]. None of the patients showed symptoms of acute intermittent porphyria after the onset of their diabetes. Three patients had had recurrent, severe attacks for many years but when their diabetes became manifest, their urinary ALA and PBG levels decreased and the acute intermittent porphyria symptoms resolved. We speculated that elevated plasma glucose levels of our patient caused by his diabetes might be beneficial for him. His previous disease might have played an important role in the rapid recovery from his recent illness.

CONCLUSION

Acute porphyria is a rare cause of acute pancreatitis and liver failure. For this reason, the diagnosis and treatment of porphyria-related pancreatitis and liver

failure may be delayed. When a clinician cannot find the etiology of acute pancreatitis and/or liver failure in patients, especially presenting with neurological disorders, acute porphyria must be included into differential diagnosis, at least urine color which would confirm the diagnosis with phosphorus pink should be checked.

REFERENCES

1. *Anderson KE: The porphyrias, (in:) ed. Wyngaarden JB, Smith LH, Bennett JC. Cecil Textbook of Medicine. 19th ed. W B Saunders Company, Philadelphia, 1992; 1126-32*
2. *Werman HAS: The porphyrias. Emerg Med Clin North Am, 1989; 7: 927-42*
3. *Komatsu K, Shimosegawa T, Uchi M et al: Erythropoietic porphyria with severe liver dysfunction and acute pancreatitis. J Gastroenterol, 2000; 35: 391-5*
4. *Shiraki K, Takase K, Tameda Y, Kosaka Y: Acute pancreatitis associated with acute intermittent porphyria. Nippon Rinsho, 1995; 53: 1479-83*
5. *Kobza K, Gyr K, Neuhaus K, Gudat F: Acute intermittent porphyria with relapsing acute pancreatitis and unconjugated hyperbilirubinemia without overt hemolysis. Gastroenterology, 1976; 71: 494-6*
6. *Shiraki K, Matsumoto H, Masuda T et al: A case of acute intermittent porphyria with acute pancreatitis. Gastroenterol Jpn, 1991; 26: 90-4*
7. *Glencross PM, Ledingham DD, Alexander JA: Acute porphyria presenting with hyperamylasemia. Dig Dis Sci, 1991; 36: 370-2*
8. *Andersson C, Bylesjo I, Lithner F: Effects of diabetes mellitus on patients with acute intermittent porphyria. J Intern Med, 1999; 245: 193-7*