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Original Article

ORIGINAL ARTICLE

Haemolytic uraemic syndrome associated with pancreatitis: report of four cases and review of the literature

Justo Sandino-Pérez [1], Eduardo Gutiérrez[1], Fernando Caravaca-Fontán [2], Enrique Morales [1], Lucia Aubert-Girbal[1], Ramón Delgado-Lillo[3] and Manuel Praga[1,2]

[1]Department of Nephrology, Hospital Universitario, Madrid, Spain, [2]Department of Nephrology, Instituto de Investigación Hospital Universitario, Madrid, Spain and [3]Department of Nephrology, Hospital Ruber Juan Bravo, Madrid, Spain

Correspondence to: Justo Sandino-Pérez; E-mail: justosandino14@gmail.com

ABSTRACT

Background. The incidence of acute kidney injury (AKI) in patients with acute pancreatitis ranges from 15% to 40% and is associated with poor prognosis. Haemolytic uraemic syndrome (HUS) in the setting of acute pancreatitis is an uncommon association with fewer than 30 cases reported in the literature.

Methods. A retrospective review of the clinical records at our institution between January 1981 and December 2019 was carried out to identify patients with acute pancreatitis and HUS. Additionally, a literature review was conducted on this topic. The aims of the study were to describe the clinical course and outcomes of patients affected by this condition.

Results. Four cases of HUS following an acute pancreatitis were identified. The mean (±SD) age of the study group was 30 ± 6 years, all of which were males. Excessive alcohol consumption was the main cause of acute pancreatitis in all four patients. HUS with progressive AKI developed in a median interval of 2 days from the onset of pancreatitis (range 1–3 days). All patients required kidney replacement therapy during the course of follow-up. A kidney biopsy was performed in two patients, showing typical thrombotic microangiopathic features. One case was treated with eculizumab, whereas the rest were treated with supportive care and/or plasma exchange. A normalization of haematological parameters and complete recovery of kidney function were observed in all patients at last follow-up, although this improvement was significantly faster in the patient treated with eculizumab.

Conclusions. HUS may infrequently develop in patients with acute pancreatitis. An early identification of this complication is mandatory, and complement blockade with eculizumab may be associated with a faster kidney function recovery.

Keywords: acute kidney injury, complement, eculizumab, haemolytic uraemic syndrome, pancreatitis

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INTRODUCTION

According to the most accepted current classification, the term haemolytic uraemic syndrome (HUS) encompasses the following entities: typical HUS caused by Shiga toxin-producing *Escherichia coli*, primary atypical HUS (aHUS) caused by a dysregulation of the alternative pathway of complement and secondary HUS [1]. Among the latter, different aetiologies have been recognized, all of which share the common denominator of a direct damage on the vascular endothelium: drugs, autoimmune diseases, infections, cancer, haematopoietic stem cell transplantation and different types of glomerulonephritis are well-known causes of secondary HUS [1–6]. Injury of the vascular endothelium results in the typical histopathological lesions of thrombotic microangiopathy (TMA) and triggers the characteristic clinical presentation of HUS: microangiopathic haemolytic anaemia (MAHA), thrombocytopenia and organ failure, mostly affecting the kidneys [3].

Haemolytic uraemic syndrome (HUS) in the setting of an acute pancreatitis is an uncommon association whose underlying pathogenic mechanism has not yet been elucidated [2, 7].

Acute pancreatitis represents an inflammatory disorder of the pancreas, which may be due to a wide variety of aetiologies [8]. Gallstones, alcohol and endoscopic retrograde cholangiopancreatography are among the most common causes of acute pancreatitis [8]. The autodigestion of the pancreas and surrounding tissues by the pancreatic enzymes is the central pathogenic event in acute pancreatitis [9]. The systemic release of activated enzymes may cause endothelial damage, with subsequent activation of proinflammatory cascades that may ultimately result in multiple-organ failure [9, 10].

Pancreatitis has been described as a rare extra-renal manifestation in aHUS [2, 7]. However, pancreatitis itself may be a cause of secondary HUS [6]. Thus, a clinical conundrum can arise at the initial evaluation of a patient with HUS in the setting of an acute pancreatitis.

Several case reports of HUS following acute pancreatitis have hitherto been published [11–15]; however, the information about its management and the main outcomes of this pathological condition are scarce.

The aims of this study were to describe the clinical course, management and outcomes of four patients affected by this condition and to conduct a literature review on this topic.

MATERIALS AND METHODS

Patients

A retrospective review of the clinical records at Hospital Universitario 12 de Octubre between January 1981 and December 2019 was done to identify patients with acute pancreatitis and HUS. From a total number of 83 patients with a previous history of HUS, four cases had HUS associated with pancreatitis (diagnosed in 1981, 1997, 2000 and 2019, respectively).

Demographic, clinical and biochemical parameters of prognostic interest were compiled from the medical records. All biochemical parameters were analysed using routine laboratory methods. Patients were followed up until hospital discharge or death (whichever occurred first).

One patient (Case #4) had complement genetic and molecular analysis performed, following the same methodology extensively described elsewhere [16]. The following genes were analysed: *CFH*, *CFHR1–5*, *C3*, *CFI*, *MCP*, *CFB*, *THBD*, *DGKE* and *ADAMTS13*.

This study was conducted in accordance with the amended declaration of Helsinki. Given the retrospective and observational nature of the study, a waiver of informed consent from individual patients was granted.

Definitions

Acute pancreatitis was defined as two or more of the following criteria [8]: typical abdominal pain; serum amylase and/or lipase levels three times the upper limit of normal; and a contrast-enhanced computed tomography scan of the abdomen or magnetic resonance imaging findings consistent with acute pancreatitis.

The severity of acute pancreatitis was classified according to the 2012 Atlanta classification [17]. All patients had an abdominal ultrasound performed at the time of clinical diagnosis to rule out gallstone-associated pancreatitis.

HUS was defined by the presence of MAHA, thrombocytopenia (platelet count $<150 \times 10^9$/L), negative Coombs test, normal activity of ADAMTS-13, negative Shiga toxin and kidney function impairment with a serum creatinine concentration greater than the upper limit of the normal range [18].

Resolution of TMA was defined by a normalization of platelet count ($>150 \times 10^9$/L) and haemoglobin, disappearance of all the markers of MAHA and improvement of kidney function, with a $\geq$25% reduction of serum creatinine from the onset of treatment [4].

Recovery of kidney function was defined as the return to baseline serum creatinine levels.

Brief methods and literature review

This was a retrospective, observational, single-centre study. Descriptive statistics are presented as mean and standard deviation or median and interquartile ranges (IQR) for continuous variables, and absolute values and percentages for categorical variables. GraphPad Prism version 7.00 (GraphPad Software, La Jolla, CA, USA) was used for analyses and figures.

Ovid software was used to search the Medline database of published reports to identify additional patients who had HUS following pancreatitis. The terms searched were: 'hemolytic uremic syndrome' or 'thrombotic thrombocytopenic purpura-hemolytic uremic syndrome' or 'HUS' or 'thrombotic microangiopathy' or 'microangiopathic hemolytic anemia' or 'thrombocytopenia' and 'renal failure' or 'kidney failure' and 'pancreatitis'. All reviewed articles were searched to identify patients who had HUS diagnosed following the onset of pancreatitis.

RESULTS

CLINICAL CASES

Case #1: a 32-year-old male with a previous history of moderate alcohol intake presented with a right abdominal pain of few hours of evolution, jaundice and hyperamylasaemia of 2600 IU/L (reference values 40–140 IU/L) consistent with a severe acute pancreatitis. Over the next 3 days of admission, the patient developed a progressive kidney failure with decreased urine output despite intravenous hydration. Blood tests revealed a serum creatinine of 5.8 mg/dL (reference 0.6–1.2 mg/dL), together with anaemia of 7.7 g/dL (reference 13.5–17.5 g/dL), thrombocytopenia of 24×10^9/L (150–450 $\times 10^9$/L), serum lactate dehydrogenase (LDH) of 1471 IU/L (140–280 IU/L) and a peripheral blood smear

showing 4–5 schistocytes per high power field (/hpf). Haptoglobin was 23 mg/dL (reference 30–200 mg/dL), serum C3 levels were 160 mg/dL (reference 83–171 mg/dL) and C4 levels were 25 mg/dL (14–38 mg/dL). Blood pressure values remained around 150/80 mmHg.

A kidney biopsy was performed on the seventh day of admission due to a lack of improvement in kidney function and haematological parameters, despite supportive care. The glomeruli showed increased mesangial matrix, fibrin thrombi within the capillary lumina, together with moderate arteriolar hyalinosis, being these findings consistent with TMA lesions. With the suspicion of a secondary HUS in the setting of pancreatitis, kidney replacement therapy in the form of haemodialysis was initiated, in addition to supportive therapy with intravenous fluids and blood transfusions. During the course of follow-up and after 27 days of admission, kidney function began to improve spontaneously, reaching a serum creatinine of 0.9 mg/dL at discharge, with a complete recovery of haematological parameters.

Case #2: a 23-year-old male was admitted due to an abdominal pain after heavy alcohol consumption, with blood tests showing increased serum amylase of 780 IU/L, consistent with a severe acute pancreatitis. The patient was transferred to the intensive care unit (ICU) 24 h after hospital admission, due to an oliguric acute kidney injury (AKI) with a serum creatinine of 6.9 mg/dL, anaemia of 7.6 g/dL without signs of bleeding and a significant low platelet count (45×10^9/L). LDH was 2677 IU/L and peripheral blood smear revealed 6–8 schistocytes/hpf. Haptoglobin was 20 mg/dL, fibrinogen levels were 508 mg/dL and complement levels were normal. Blood pressure values remained around 170/90 mmHg. Serum laboratory tests for autoimmune diseases resulted in negative. A kidney biopsy was considered a hazardous procedure and was not performed at the physicians' discretion. With the suspicion of a secondary HUS, haemodialysis was initiated, as well as supportive care with intravenous fluids and plasma exchange (PEX). Seven sessions of PEX separated by 48 h were performed, 22 L of plasma volume were treated and reposition was made with fresh frozen plasma. On follow-up and after 25 days of hospital admission, the patient recovered baseline kidney function with serum creatinine of 1.2 mg/dL, and normalization of haematological parameters.

Case #3: a 30-year-old male with a history of moderate alcohol consumption 24 h before hospital admission presented with epigastric abdominal pain, hyperamylasaemia of 1697 IU/L and decreased urine output with a serum creatinine of 8.3 mg/dL, consistent with a severe acute pancreatitis with severe AKI. During the next 48–72 h, the patient developed dark-coloured urine, anaemia of 7.6 g/dL, thrombocytopenia of 63 $\times 10^9$/L, with an increase in serum LDH of 1325 IU/L and a peripheral blood smear showing 7–9 schistocytes/hpf. Fibrinogen levels were 279 mg/dL (reference range 150–400 mg/dL), haptoglobin 39.4 mg/dL, C3 levels 90 mg/dL and C4 levels 19.1 mg/dL. Coagulation tests were normal.

A kidney biopsy was performed, showing 50% of the glomeruli with proliferation of endothelial cells without relevant vascular lesions, and signs of acute tubular necrosis. With the suspicion of a secondary HUS, treatment with haemodialysis and PEX were initiated: four sessions separated by 48 h were performed, 12 L of plasma volume was treated and reposition was made with fresh frozen plasma. Additionally, empirical treatment with corticosteroids (three doses of 500 mg of 6-methylprendisolone) and intravenous immunoglobulins (five doses of 35 g each, separated by 48 h) were also prescribed due to the lack of early response to PEX and persistence of need of kidney replacement therapy. Kidney function slowly recovered over the course of 32 days of admission, reaching a serum creatinine of 0.85 mg/dL, together with a complete normalization of haematological parameters.

Case #4: a 37-year-old male with a recent history of moderate alcohol (gin and tonic) consumption presented to the Emergency Room with abdominal pain, hyperamylasaemia of 469 IU/L and increase of serum lipase of 2479 IU/L in the setting of a severe acute pancreatitis. The patient was hospitalized, and over the next 48 h after admission, he presented a decrease in urinary output, with blood tests revealing an AKI with a serum creatinine of 7.1 mg/dL that required ICU admission. Concomitantly, he developed anaemia (haemoglobin: 7.3 g/dL), low platelet count (28×10^9/L), increase in serum LDH of 2211 IU/L and peripheral blood smear revealed 3–5 schistocytes/hpf. ADAMTS-13 activity was 97% and haptoglobin 9 mg/dL (reference 30–200 mg/dL). Fibrinogen levels were 296 mg/dL. C3 and C4 levels were 104 and 14 mg/dL, respectively. Figure 1 summarizes the evolution of the main biochemical parameters during hospital admission. Blood pressure values were around 150/80 mmHg. All serological and autoimmune tests were negative, and the stool culture was normal. A kidney biopsy was not performed due to the low platelet count and, with the suspicion of a secondary HUS, treatment with eculizumab was initiated (900 mg weekly for a month and two doses of 1200 mg once every 2 weeks), prior meningococcal vaccination and prophylaxis with a beta-lactam antibiotic. The severity of kidney function impairment required the initiation of haemodialysis and received a single dialysis session. However, after the administration of eculizumab, the main haematological parameters normalized over the next 48 h, and the kidney function began to improve, reaching a serum creatinine of 0.9 mg/dL 12 days after admission. The patient received a total of six doses of eculizumab during the course of follow-up and, since the genetic and molecular analysis of complement neither revealed pathogenic mutations nor risk polymorphisms, this treatment was discontinued. No adverse events occurred with this therapy. Table 2 shows the evolution of analytic parameters of our cases.

LITERATURE REVIEW

Thirty-two cases of HUS associated with pancreatitis have been reported in the literature since 1978 [6,11–15,19–36]. Table 1 summarizes the main clinical characteristics and outcomes of these patients. The median age of the patients affected by this condition was 39 years (IQR 28–48), and 64% were males. Alcohol was the most frequent cause of acute pancreatitis, and accounted for 43% of the cases. The majority of cases had AKI, but only 31% required dialysis during the course of follow-up (although in 10 cases no specific information was provided about dialysis therapy). In most of the cases, HUS occurred shortly after the start of the pancreatitis, especially when the pancreatitis appeared to be clinically subsiding. It is important to note that the majority of cases were reported before 2005, most of them lacking histological study, but in the one case in which kidney biopsy was performed, typical features of TMA such as fragmented red blood cells in the capillary lumen, simplification and shrinkage of glomerular tufts, and intimal fibrosis of the interlobular artery were found, surprisingly no fibrin thrombi within the capillary lumina were present [30]. Of the total patients, 69% received PEX as the specific therapy for HUS.

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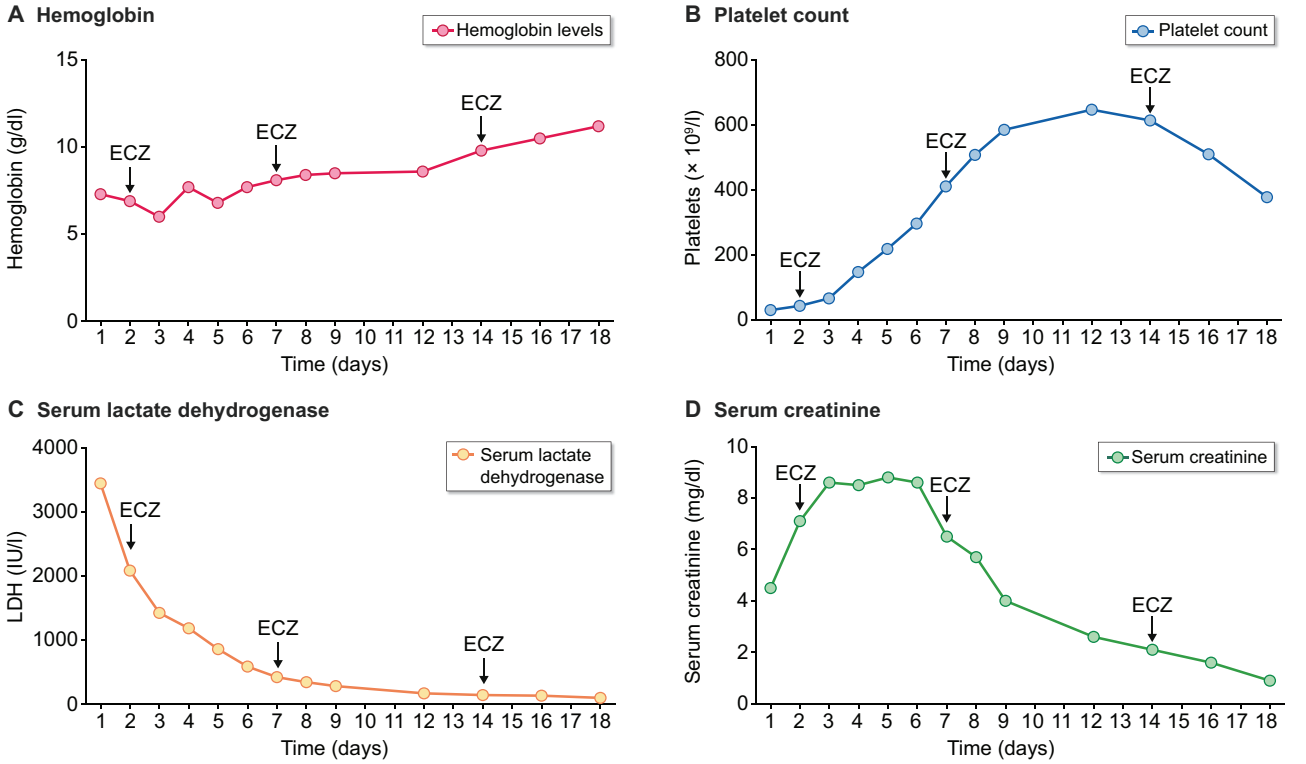

FIGURE 1: Evolution of biochemical parameters of Case #4 during hospital admission: **(A)** haemoglobin values (g/dL); **(B)** platelet count (×10^9/L); **(C)** LDH (IU/L); **(D)** serum creatinine (mg/dL). ECZ, eculizumab.

The overall outcomes were positive with the resolution of TMA and a complete recovery of kidney function over a median period of 29 days (IQR 16–30) from admission.

DISCUSSION

Herein, we reported four cases of secondary HUS following an acute pancreatitis and conducted a literature review on this topic. There are several major findings in this study. First, our results show that the association between HUS and pancreatitis is rare (5% of HUS at our institution). Secondly, HUS in the setting of acute pancreatitis is associated with the development of a severe AKI needing dialysis in all of our reported cases, and in almost one-third of those reported in the literature. Thirdly, the overall outcomes of this entity are good, both from a haematologic and nephrological perspective, but it is associated with prolonged length of hospital stay. Fourthly, our results suggest that treatment with eculizumab may be associated with a faster recovery of kidney function in this clinical scenario.

Microvascular endothelial cell damage is the hallmark lesion of all HUS associated TMAs [3]. However, while complement dysregulation is the main driver of the disease in aHUS, several aetiologies may induce endothelial damage and eventually result in the development of a secondary HUS [3, 37].

A recent study described a series of 110 cases of secondary HUS [6]. Drugs were the main trigger, accounting for almost one-third of the cases, followed by autoimmune diseases and infections. Complement gene variants were found in only 5% of the cases, and 40% of patients required dialysis at diagnosis. Interestingly, the authors also reported four cases of secondary HUS in the context of an acute pancreatitis [6]: two of those patients reached Stage 3–4 chronic kidney disease, and one patient end-stage kidney disease. Thus, HUS following an acute pancreatitis can also be associated with dismal outcomes.

The potential role of complement blockade in secondary HUS is still a matter of controversy [5, 37, 38]. Classically, treatment of the underlying condition was the mainstay of therapy in cases of secondary HUS, and adjunctive therapies such as PEX were only considered when the initial clinical course was not favourable. However, the availability of specific complement blockers such as eculizumab provided the opportunity to test its efficacy in this context. Our group was the first to describe the favourable effects of short courses of eculizumab in a series of 29 cases with secondary HUS caused by a myriad of aetiologies, but mainly drug-induced [4]. A rapid TMA resolution was observed in almost two-thirds of patients, together with kidney function improvement. However, these results could not be proven in the above-mentioned study in which 38 patients with severe secondary HUS were treated with eculizumab [6]. Thus, prospective, controlled trials are needed to properly evaluate the clinical efficacy of this treatment in secondary HUS.

In our study, only one patient was treated with eculizumab, while the remaining cases received supportive therapy and/or PEX. This was, in part, due to the fact that patients were diagnosed in different time periods. Notably, the recovery of kidney function was significantly faster in the patient treated with eculizumab, as compared with the rest of cases, and no adverse events were encountered. This result suggests the potential benefit of eculizumab for this entity in severe cases, or in those with persistent kidney function impairment despite supportive

Table 1. Clinical characteristics and outcomes of patients with HUS and pancreatitis reported in the literature[a]

Year (Ref)	Age-sex	Aetiology	SCr	PC	Hb	KRT	Kidney biopsy	Treatment	Haematological remission	Kidney outcome	Length of hospital stay (days)	Death
1978 [31]	18-M	Idiopathic	2.3	2	10.6	No	No	Splenectomy	Yes	CR	16	No
1989 [32]	55-F	Idiopathic	1.7	24	8.0	No	No	PEX	Yes	CR	10	No
1991 [33]	36-M	Alcohol	–	45	9.2	–	–	–	–	–	–	–
1992 [34]	55-M	GB	7.9	20	10.0	Yes	No	PEX	Yes	CR	–	No
1992 [34]	48-M	Alcohol	2.1	40	8.0	No	No	CS	No	–	–	Yes
1995 [35]	18-M	Alcohol	15.0	30	6.0	Yes	No	PEX	Yes	CR	23	No
1997 [36]	25-M	Alcohol	5.3	53	5.0	–	–	–	–	–	–	–
1998 [19]	28-F	Idiopathic	1.3	9	9.2	–	–	–	–	–	–	–
1998 [20]	65-M	GB	2.2	32	10.3	No	No	PEX	Yes	CR	–	No
1998 [21]	37-M	Alcohol	4.8	22	11.7	No	No	PEX	Yes	CR	–	No
2000 [22]	70-M	Idiopathic	2.4	22	7.7	–	–	–	–	–	–	–
2002 [23]	38-M	Alcohol	–	28	–	Yes	No	PEX	Yes	CR	–	No
2002 [24]	35-M	ERCP	2.2	15	5.3	No	No	CS and PEX	Yes	CR	30	No
2002 [25]	58-M	Alcohol	3.2	14	8.3	Yes	No	PEX	Yes	CR	30	No
2003 [13]	38-F	Alcohol	7.7	24	9.0	Yes	No	PEX	Yes	CR	30	No
2004 [26]	35-M	Alcohol	1.45	30	4.6	No	No	PEX	Yes	CR	–	No
2004 [26]	33-M	Alcohol	7.0	90	5.8	Yes	–	PEX	–	–	–	–
2005 [27]	55-F	ERCP	–	50	12.1	–	–	PEX and RTX	Yes	–	40	No
2005 [28]	19-M	GB	6.7	32	8.8	Yes	No	PEX	Yes	CR	60	No
2005 [29]	43-M	Alcohol	2.0	53	10.1	No	No	–	Yes	CR	–	No
2005 [29]	37-F	Sarcoidosis	4.1	74	9.6	No	No	PEX	Yes	CR	–	No
2006 [29]	35-F	GB	2.1	35	8.0	No	No	PEX	Yes	CR	–	No
2010 [30]	74-M	Idiopathic	6.4	20	6.4	Yes	Yes	PEX	Yes	PR	–	No
2011 [11]	23-M	ERCP	1.7	24	8.7	No	No	PEX	Yes	CR	11	No
2011 [12]	40-F	Idiopathic	5.7	11	5.9	No	No	PEX	Yes	CR	–	No
2014 [13]	38-F	Alcohol	1.45	32	8.8	Yes	No	PEX	Yes	CR	30	No
2016 [14]	21-F	ERCP	1.6	7	6.2	No	No	PEX and ECZ	Yes	CR	15	No
2017 [15]	61-F	Alcohol	1.8	25	9.3	No	No	PEX	Yes	PR	17	No

[a]Dashes represent data non-available; in this table, four additional cases reported in manuscript by Le Clech *et al.* [6] are not included.
CR, complete recovery; CS, corticosteroids; ECZ, eculizumab; ERCP, endoscopic retrograde cholangiopancreatography; F, female; GB, gallbladder stones; Hb, haemoglobin (g/dL); KRT, kidney replacement therapy; M, male; PC, platelet count ($\times 10^9$/L); PEX, plasma exchange; PR, partial recovery; RTX, rituximab; SCr, serum creatinine (mg/dL).

care, although further experience is needed before drawing firm conclusions. Due to a complete recovery of kidney function and the absence of complement genetic abnormalities in our case, eculizumab was discontinued after six doses with no relapses.

The association between pancreatitis and HUS has been reported both in paediatric and adult populations [11–15, 19–36]. According to the literature review conducted in this study, the most frequent clinical profile of patients with the association of HUS and acute pancreatitis was middle-aged males with a recent history of alcohol intake.

From a clinical standpoint, the association between HUS and acute pancreatitis may represent a challenge for clinicians. A differential diagnosis should be made between an aHUS with pancreatic involvement and secondary HUS following an acute pancreatitis. The presence of underlying genetic complement abnormalities may point towards an aHUS, although these results are usually not available until weeks or months after diagnosis. Conversely, a recent history of heavy alcohol consumption with the subsequent development of pancreatitis may point towards a secondary HUS. However, this association may be especially challenging when the type of alcohol consumed includes tonic water. Previous studies have reported that the small amount of quinine sulphate present in tonic drinks may trigger the development of a TMA through quinine-dependent platelet-reactive antibodies, and patients may be misdiagnosed as having HUS or thrombotic thrombocytopenic purpura [39]. In our study, anti-quinine antibodies could not be determined in Case #4, but the temporary association between heavy alcohol consumption and the severe acute pancreatitis make more plausible the hypothesis of a secondary HUS following pancreatitis.

The underlying pathogenic mechanism of HUS in the setting of an acute pancreatitis remains elusive [6]. It has been suggested that acute pancreatitis may lead to an endothelial damage through the release of tumour necrosis factor-alpha, interleukin-1, interleukin-6 and interleukin-8 [19, 35]. In addition, the release of proteases into the circulation could modify the circulating von Willebrand factor and favour the aggregation of platelets [29, 40].

This study is subject to limitations. The retrospective nature of the study and the small number of cases precluded to analyse the main factors associated with the development of HUS following pancreatitis. Complement genetic studies were not performed in all cases due to the different time periods of diagnosis. Despite these limitations, this study further contributes to the recognition of this association, its management and outcomes.

In conclusion, HUS may infrequently develop in patients with acute pancreatitis. An early identification of this complication is mandatory, and complement blockade with eculizumab

Table 2. Evolution of analytic parameters of our cases[a]

	Aetiology	Presentation	I-SCr	Max SCr	F-SCr	HD	Histology	Treatment	Time-to-resolution (days)	I-Hb	F-Hb	I-PC	F-PC	I-LDH	F-LDH	MAHA	C3	C4	Complete TMA response
1	Alcohol	Oliguric AKI + AP	5.8	10.4	0.9	Yes	ME, FBT, HC, AH	FT	27	7.7	8.2	24	233	1471	284	Yes	160	25	Yes
2	Alcohol	Oliguric AKI + AP	8.3	10	1.2	No	–	FT	30	7.6	12	63	398	1325	240	Yes	90	19	Yes
3	Alcohol	Oliguric AKI + AP	6.9	14.4	0.85	Yes	EE, ME, ATN	CS+PEX	13	7.6	14.7	45	346	2677	155	Yes	–	14	Yes
4	Alcohol	Oliguric AKI + AP	5.6	7.1	0.98	No	–	ECZ (six doses)	15	7.3	14.1	28	368	2211	284	Yes	158	32	Yes

[a]Dash lines represent data non-available.
ATN, acute tubular necrosis; I-SCr, initial serum creatinine (mg/dL); F-SCr, final serum creatinine (mg/dL); HD, need for haemodialysis; I-Hb, initial haemoglobin (g/L); F-Hb, final haemoglobin (g/L); I-PC, initial platelet count ($\times 10^9$/L); F-PC, final platelet count ($\times 10^9$/L); I-LDH, initial lactate dehydrogenase (IU/L); F-LDH, final lactate dehydrogenase (IU/L); AP, abdominal pain; FT, fluid therapy; CS, corticosteroids; PEX, plasma exchange; ECZ, eculizumab; MAHA, microangiopathyc hemolytic anemia; ME, mesangial expansion; FBT, fibrin thrombi; HC, haematic casts; AH, arteriolar hyalinosis; EE, endocapillar expansion; C3 (mg/dL, ref: 83–171 mg/dL); C4 (mg/dL, ref: 14–38 mg/dL); TMA, Thrombotic microangiopathy.

may be associated with a faster kidney function recovery. However, further prospective studies are warranted to better elucidate the main underlying mechanisms of this association and the best therapeutic approach.

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CONFLICT OF INTEREST STATEMENT

None declared.

DATA AVAILABILITY STATEMENT

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