greater than 1.1 g/dL is indicative of portal hypertension with a 97% accuracy, we performed 2 tests, which resulted in values <1.1% and ruled out both liver disease and heart failure. Even so, we continued screening for a liver disease, ruling out viral, alcoholic, and other possible causes of an autoimmune liver disease. We also ruled out infections and peritoneal carcinomatosis.

Given the findings from numerous tests, the diagnosis appears to be compatible with nephrogenic ascites. Given the patient's situation and inability for self-care, peritoneal dialysis is not an option. Kidney transplant is not an option either due to the associated comorbidities and the patient's important bilateral iliac atherosclerosis. As recommended by the gastrointestinal department, evacuation paracentesis continues to be administered upon demand. We intensified the dialysis treatment and added intra-dialysis parenteral nutrition, with progressive improvements in the patient's nutritional parameters and a complete disappearance of the ascites. Currently the patient is asymptomatic.

### Conflicts of interest

The authors affirm that they have no conflicts of interest related to the content of this article.


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## Postpartum hemolytic uremic syndrome with multiple organ involvement in a severe case


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**To the Editor,**

Postpartum hemolytic uremic syndrome (PHUS), first described in 1968, is defined as a thrombotic microangiopathy (TMA) typically following a normal delivery after a symptom-free interval (mean 26.6±35 days).[1] It usually occurs in primigravida with the mean age of 27.0±6 years and preeclampsia is historically associated with the disease.[1,2] The involvement of extrarenal vascular beds in PHUS has been less reported. Here we report for the first time a severe case of PHUS complicated by pancreatic necrosis, bilateral visual loss due to central retinal artery occlusion (CRAO) and disseminated intravascular coagulation (DIC).

A 20-year-old primigravid was admitted for edema and headache when she was 34 weeks pregnant. On presentation her blood pressure (BP) was 180/115mmHg and moderate edema on face was noted. Initial investigations showed 3+ proteinuria and normal serum creatinine (Scr) concentration. The diagnosis of preeclampsia was established and a cesarean section was performed in the 35th week of gestation.

Nine days later, the patient complained of oliguria, nausea with BP of 175/105 mmHg. Laboratory tests revealed hemolytic anemia, with hemoglobin of 81g/L, serum haptoglobin <0.2 g/L, and schistocytes shown in peripheral blood smear. Platelets (Plt) were markedly reduced at $41x10^9$/L and an acute rise of Scr to 463.2 µmol/L showed acute renal failure. The immunologic studies revealed negative anti nuclear antibody and Coomb's tests. Under suspicion of PHUS, antihypertensives, aspirin and furosemide were commenced on the 1st day of presentation and renal biopsy was performed on day 2.

The patient complained of left-upper abdominal pain after renal biopsy and developed a sudden bilateral painless visual loss. The subcutaneous bleeding over her upper arms was noted and she rapidly developed anuria, dyspnea, confusion, hypotension with BP of 70/50 mmHg. The ultrasound scan excluded the existence of perinephric / subcapsular hematoma caused by renal biopsy. The fundus exam revealed bilateral CRAO. Laboratory tests on day 3 showed elevated serum amylase, lipase and Scr up to 625 µmol/L, Plt down to $12.2x10^9$/L. The level of fibrinogen decreased to 3.82 µmol/L with delaying activated partial thromboplastin time and positive D-dimer. Computed tomography scan confirmed pancreatic necrosis. Renal pathology showed thickened glomerular capillary walls with subendothelial edematous expansion that forming double contouring and renal arteriolar intimal expansion with fibrin exudation on the arteriolar wall (Figure 1). Based on these findings, the diagnosis of PHUS complicated by pancreatic necrosis, CRAO and DIC was established.

She was treated with pulse methylprednisolone 500 mg/d and intravenous immunoglobulin (IVIG) 20 g/d for 3 days. Meanwhile, plasma exchange (PE) with fresh frozen plasma (FFP) infusion and CRRT were initiated. Anticoagulant therapy for DIC and CRAO were also carried out. On day 15, she was improved significantly and the uri-

nary output increased whereas the bilateral vision improved only slightly and hyperglycemia became noted. On review after 6 months of onset, she remained bilateral visual loss, elevated blood glucose and Scr when hemodialysis and subcutaneous injection of insulin were suspended. These showed the irreversible visual impairment, secondary diabetes mellitus dependent on insulin and the progression to CRF.

HUS and thrombotic thrombocytopenic purpura (TTP), collectively referred to as TMAs, occur with increased frequency during pregnancy or the postpartum period. These two disorders are considered by many to be manifestations of the same disease process; however, others consider HUS and TTP to be distinct entities.[3] Since TTP and HUS share many overlapping features, distinguishing the two disorders may be difficult.[4] As in the case we showed, the patient developed TMA with disturbance of consciousness that seemed to suggest TTP; however, the prominent renal insufficiency and the lack of diffused thrombi in renal tissue might support PHUS rather than TTP. Another differential diagnosis should be included in this case is hemolysis, elevated liver enzymes, and low platelets syndrome (HELLP syndrome). HELLP, usually associated with preeclampsia is more common in multiparous women and approximately 70% of HELLP occur prior to term, with the remainder usually occurring within 48 hours after delivery.[5] Patients with HELLP frequently present with severe right upper quadrant pain. Based on these characteristics of HELLP, we prefer to diagnose our case as PHUS.

Although the pathogenesis of PHUS is unknown, the previous cases reported[2,6,7] and the case presented here demonstrated preeclampsia could possibly trigger PHUS by causing platelet aggregation, deposition of microthrombi and occlusions in the microvasculature of the kidney, resulting in acute renal failure. The deficiency of ADAMTS-13, a metalloprotease that cleaves ultra-large von Willebrand factor (VWF) multimers observed in PHUS[8] which suggest PHUS may be also associated with ADAMTS-13 deficiency. Recent studies revealed alternative complement 3 convertase dysregulation were detected in most PHUS patients suggesting PHUS was probably associated with complement gene mutation.[9]

Multiple organ involvement such as pancreas and ocular structures were reported in non-pregnancy-related HSP,[10,11] whereas PHUS involving extrarenal vascular beds has been less reported so far except central nervous system and liver damage.[12,13] Does this mean PHUS have a better prognosis than non-pregnancy HUS? The case we described here developed multiple organ damage such as pancreatic necrosis, CRAO, DIC and progressed to secondary diabetes mellitus, bilateral visual loss and CRF eventually. The severe complications of pancreatic necrosis and CRAO might be the manifestations of TMA in PHUS, but might be more likely induced by DIC in this patient. Anyway, this case suggests PHUS could also involve multiple organ dysfunctions and result in bad outcomes even if the appropriate treatments have been given wihout delay.

The renal pathology in HUS is characterized by glomerular capillary subendothelial expansion, arteriolar fibrinoid necrosis, arterial edematous intimal expansion and vascular thrombosis. The preceding etiologic conditions of HUS and the histological findings appeared not to be related to each other.[14] Our case showed typical subendothelial edematous expansion and renal arteriolar intimal expansion with fibrin exudation which supported renal microangiopathy, but without diffused thrombi and fibrinoid necrosis in renal tissue which seemed to be inconsistent with the following development of multiple organ complications and the progression to CRF. This was considered to be due to the early performance of renal biopsy after the attack and the early pathological findings in PHUS presented here may be difficult to predict the disease development and poor prognosis.

In conclusion, pancreatic necrosis, CRAO and DIC were observed in PHUS. Although renal replacement therapy and PE with FFP infusion have improved the survival of PHUS significantly, multiple organ complications such as pancreatic necrosis, CRAO and DIC may cause severe sequelae and lead to a poor prognosis of PHUS.

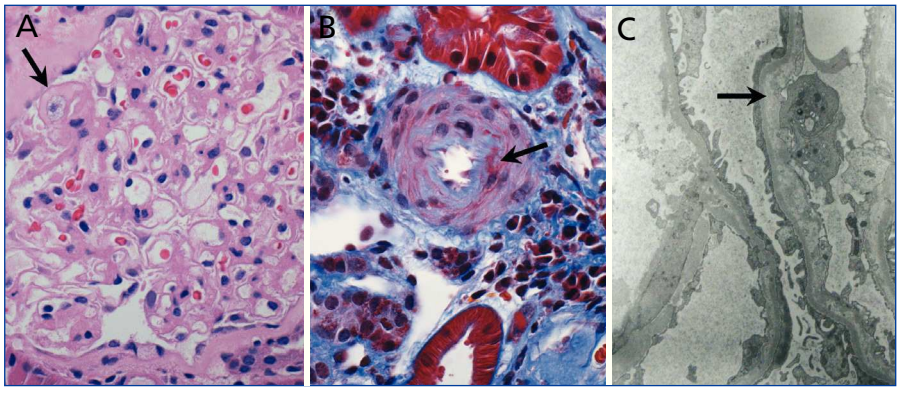


**Figure 1.** Renal biopsy findings in postpartum hemolytic uremic syndrome. (A) Light microscopy showing thickened glomerular capillary walls forming double contouring (H & E stain, x400). (B) Light microscopy showing renal arteriolar intimal expansion with fibrin exudation on the arteriolar wall (Masson stain, x400). (C) Electron micrograph showing thickened glomerular capillaries and subendothelial edematous expansion (x4000).

### Conflict of interest

The authors declare that there is no conflict of interest associated with this manuscript.

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# Primary sclerosing cholangitis and interstitial nephropathy: an emerging association?

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**To the Editor,**

Primary sclerosing cholangitis (PSC) is a chronic cholestatic liver disease characterised by inflammation and fibrosis in the intrahepatic and extrahepatic bile ducts, which primarily affects middle-age males.[1,2] It can occur as an isolated entity or in association with inflammatory bowel disease. The aetiopathogenesis of PSC has not been established, although growing evidence points towards genetic and immunological causes.[1]

Associated interstitial nephropathy in patients with chronic cholestatic liver disease was first described in the medical literature during the 1990s in paediatric patients, and it was suggested that this association might represent a new syndrome.[3,4]

Recently, the existence of a new disease, called "IgG4-related sclerosing disease" has been proposed.[5,6]

Here, we describe the case of a female patient diagnosed with PSC with severe interstitial nephropathy.

## CASE REPORT

A 77 year-old female was referred to the nephrology department due to plasma creatinine values of 2.4mg/dl. The patient's history included several surgical procedures: meniscus in 1985, thymoma with benign histology in 1999, nasal sinus polyps more than 20 years ago and again in 2008, varicose veins in 2006, cystocele in 2008, and hip fracture in July 2010. She was diagnosed with primary sclerosing cholangitis in 2003, and was under treatment with ursodeoxycholic acid. On several occasions, the patient had been placed retrograde biliary catheters and undergone sphincterotomy and dilation of the areas of stenosis. Inflammatory bowel disease had also been diagnosed around the same time. In later follow-up sessions, she underwent several colonoscopies, which occasionally produced normal results, and at other times revealed small ileocaecal and colonic ulcers. The patient also suffered an episode of pericarditis of unknown cause in January 2010, and had bilateral gonarthrosis. The patient was intolerant to oral iron supplements, and had no toxic habits.

At the first visit, the patient was taking zolpidem 10mg/day, ursodeoxycholic acid 1250mg/day, pantoprazole 40mg/day, mirtazapine 15mg/day, and occasional paracetamol and dextropropoxyphene.

The patient complained of intense fatigue, dyspnoea after moderate exercise, reduced appetite, occasional nausea associated with coughing, periodical constipation lasting 48 hours and alternating with diarrhoea that produced 3 or 4 evacuations per day, but with no pathological signs, nocturia twice per day for several months, diurnal urination every 3-4 hours, and no history of reno-ureteral lithiasis or haematuria.

As regards family background, the patient's parents both died at an elderly age, and three brothers had died as a result of tumours.

The physical examination revealed the following values for standard parameters: height: 159cm; weight: 53kg; blood pressure: 137/72mm Hg; heart rate: 95bpm. We did not observe jugular vein engorgement, carotid pulses were rhythmic and symmetrical, cardiopulmonary auscultation normal, and we observed hepatomegaly of approximately 4 finger-widths in