DEVELOPMENT OF SPONTANEOUS RENAL HEMORRHAGE ASSOCIATED WITH ACUTE PANCREATITIS IN A PATIENT ON HEMODIALYSIS FOR CHRONIC RENAL FAILURE: A CASE REPORT

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ABSTRACT

Objective*: We present one rare case of spontaneous renal hemorrhage(SRH) in a 32-year-old woman with systemic lupus erythematosus(SLE) undergoing maintenance HD, and she subsequently developed acute pancreatitis(AP). These complicated illnesses she suffered brings us into question whether there is a causal relationship between SHR and AP in HD patient.*

Methods*: A CT scan of the abdomen supported the evidence of renal hemorrhage.In view of the markedly raised pancreatic enzymes and CT findings, the acute pancreatitis was also diagnosed.*

Results*: Multi-factors lead to the development of the disease. The factors such as anticoagulation used during HD, uraemia-associated functional platelet abnormalities, immunosuppression (corticosteroid), intimal arterial fibrosis and hypertension often combine to cause SRH. Other possibilities can be considered for the mechanism of AP: SHPT, gastrointestinal hormones and immunological condition.*

Conclusion*: SRH and AP are both potentially life threatening condition in patients with end-stage renal disease(ESRD). A detailed understanding of pathophysiological processes and immunological aspects in patients is the basis for the development of therapeutic strategies that will provide significant reductions in morbidity and mortality.*

Keywords*: Spontaneous renal hemorrhage, Wünderlich syndrome, hemodialysis, acute pancreatitis.*

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Introduction

Spontaneous renal hemorrhage (SRH) is an uncommon but well-known urological emergency, which was initially described by Wünderlich in 1856 as a kind of spontaneous nontraumatic renal hemorrhage confined to the subcapsular and perinephric space with the calssic Lenk triad, including acute flank or abdominal pain, palpable flank mass, and hypovolemia. SRH is usually occurred in those uremic patients who developed acquired renal cystic disease (ARCD) after chronic hemodialysis (HD). The reported mortality in this series was 38%[(1)].

Bleeding in ARCD is different from that observed in polycystic kidneys where the hemorrhage is limited to one or several cysts and does not spread into subcapsular or perinephric space. Acute pancreatitis (AP) is another potentially life threatening acute inflammatory condition of the pancreasm among patients with end-stage renal disease(ESRD). Abnormal exocrine pancreatic function has been found in 10-64% of patients with ESRD. A large cohort study to date proves uremic patients who underwent HD had a higher risk of AP in comparison to the general population[(2)]. AP is usually mild with minimal organ dysfunction, but in about 20% of affected patients the disease becomes

severe and is associated with complications and a high risk of mortality[3].

As is well known that renal failure is an uncommon cause of AP, possibly owing to the use of drugs, uremia, and secondary hyperparathyroidism accompanied by hypercalcemia. While the ESRD patients undergoing dialysis have different epidemiologic risks than renal failure patients. So increasing reports have been published for new factors. The pathogenetic role in the development of AP in these patients has been proposed. The outcome were wondered when the patient developed the two risky diseases of SHR and AP. Early detection and proper treatment are needed to prevent the condition from deteriorating further and to minimize mortality. Here, one rare case was reported that SRH in a 32-year-old woman with systemic lupus erythematosus(SLE) undergoing maintenance HD, and she next developed AP. Though rare, it brings into question whether there is a causal relationship between SHR and AP in HD patient.

Case

A 32-year-old woman was admitted to hospital with right flankpain with nausea and vomiting and intermittent irritable bowel syndrome for six hours after the regular hemodialysis. She was on chronic HD for the past 10 years because of end-stage renal failure (ESRD). She had a medical history of systemic lupus erythematosus (SLE) for 16 years, and was receiving a maintenance regimen of low-dose prednisolone. Five years ago, she developed diabetes mellitus because of prednisolon and the blood sugar levels were controlled by the oral hypoglycemic drug. Previous ultrasound showed bilaterally small kidneys, each measuring about 7-8 cm.

On admission, she was pale, physical examination showed a heart rate of 90/min, respiratory rate of 22/min, body temperature of 37.1 and a blood pressure of 130/90 mmHg, which was much lower than her average pressure level. The physical examination revealed on diffuse abdominal distention and mild rebound pain without rigidity. The blood cells test showed that white blood cell count and platelets were unremarkable except for a fall of hemoglobin of 3 g/dL compared to baseline. Serum chemistry panels were normal including the level of lipase and amylase. But the strongly elevated phosphate level (11.129 mg/dL) and iPTH level (1041 pg/mL) were observed. Thrombin time and partial thromboplastin time also were normal at 11.9 and 25 seconds, respectively. Her lupus related blood tests were negative. A CT scan of the abdomen revealed ARCD, with small, poorly perfused kidneys with multiple cysts. CT also visualized large amounts of right perirenal, pararenal and retroperitoneal hematoma exerting severe compression on the renal parenchyma (Figure 1), but no apparent renal tumor was detected. Because of high bleeding tendency, the nephrectomy was refused by the patient. Because her hemodynamics were increasingly stable after fluid resuscitation without any blood transfusion although blood had been prepared, emergency angiography was also not performed. The patient was put on absolute bed rest and HD without heparin was performed about one month.

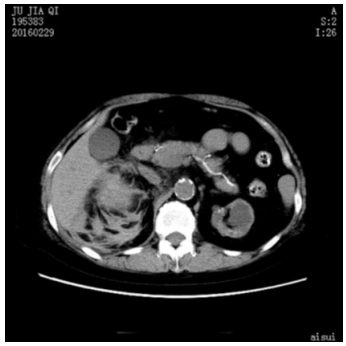

Fig. 1: CT showed a distorted right kidney contour with enlargement compared with the atrophic multi cystic left kidney. And a hypodense area surrounding the right renal parenchyma.

One week later, she complained of sudden severe abdominal pain along with nausea, vomiting and fever. Her observations showed a temperature of 38.1, pulse rate of 90 per minute and a blood pressure of 126/90 mmHg. There was mild epigastric tenderness and no mass was palpable per abdomen. Investigation revealed serum lipase of 627 U/L, amylase of 2000 U/L, hemoglobin of 78g/L, C-reactive protein of 196.2 mg/L, which were much different from the baseline detected at the admission. An emergent CT scan was done which revealed the enlarged hematoma compared with the initial scan (Figure 2).

Notably, a swelling pancreas was found but without any findings of per-pancreatic exudation and peripancreatic fat stranding or periancreatic fluid collection. There was no evidence of gall stones and dilation in the common biliary duct. However, the calcification of splenic artery and parenchyma could predispose to pancreatic anomalies.

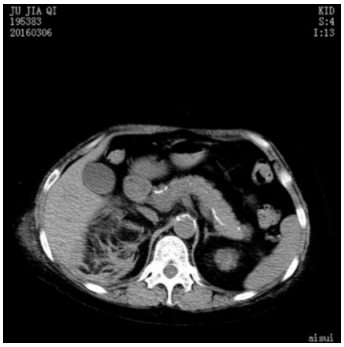

Fig. 2: Abdominal CT shows a slightly increased size of pancreas with the calcificated splenic artery and parenchyma, but without per-pancreatic exudation and peripancreatic fat stranding.

In view of the markedly raised pancreatic enzymes and CT findings, the acute pancreatitis was diagnosed. She was managed conservatively with regular monitoring and supportive treatment with pain control, fasting and intravenous fluids resuscitation. She was discharged after 4 weeks of admission with normal serum chemistry work-up results.

Because the possibility of underlying malignancy must always be kept in mind even though CT does not always show specific finding. So three months later, a follow-up CT scan was performed and showed complete resorption of the perirenal hemorrhage, a normal size pancreas and no apparent renal tumor was detected (Figure 3).

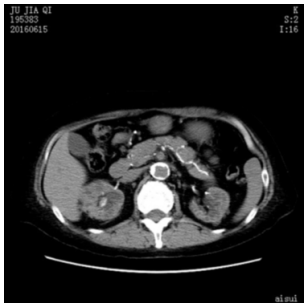

Fig. 3: At 3 months after the hemorrhage, the follow-up CT showed complete resorption of the perirenal hemorrhage and no apparent renal tumor was detected.

Discussion

In patients on chronic hemodialysis, acute abdominal pain is a common presentation which may herald a medical or surgical emergency. According to a recent retrospective study, in the HD population, the main causes of acute abdomen pain are spontaneous intra-abdominal hemorrhage (21.2% of patients) and non-occlusive mesentiric ischemia(18.1%) on descending order of frequency[4-5]. SRH and AP can also be the causes of acute abdominal pain and may carry a high risk of morbidity and mortality.

SRH is an uncommon and high risk event, particularly in those who developed acquired renal cystic disease (ARCD). ARCD occurs in up to 95% of prolonged dialysis patients[6].

SRH in ARCD includes small, poorly perfused kidneys with numerous fluid-filled cysts and a sizeable crescent- or biconvex-shaped subcapsular hematoma exerting compression on the adjacent renal parenchyma. A computed tomography (CT) scan is the most valuable tool for examination of suspected SRH. Results of a meta-analysis showed that the CT is 100% sensitive for the detection of retroperitoneal hematomas and has a higher sensitivity and spectificity than ultrasound for identification of an underlying renal mass[7].

The multifactorial pathogenesis of SRH involves renal carcinoma, angiomyolipoma, vascular diseases and arterial intimal fibrosis and so on. Vascular diseases were reported that SRH is a very common offer, such as lupus-associated vasculititis and micro-vasculitis particularly polyarteritis nodosa, microscopic polyangiitis and Wegeners' granulomatosis[7-8]. Renal carcinoma or solid mass were also not noted in the CT. Due to the long history of SLE, the markers of SLE activity were performed, including the level of complement and anti-dsDNA antibody, but the results were negative.

Moreover, the negative antineutrophil cytoplasmic antibody tests and neither polyarteritis nodosa nor pauci-immune vasculitis had been found. So the vasculitis seems to impossible. On the basis of clinical context, several other factors such as anticoagulation used during HD, uraemia-associated functional platelet abnormalities, immunosuppression (corticosteroid), intimal arterial fibrosis and hypertension often combine to cause spontaneous hematoma of the kidney[9].

In the past, radical nephrectomy was recommended in SRH due to the increased risk of renal cell carcinoma (RCC) in HD patients. However, Tonolini et al. found that this concern is probably overstated because most HD patients undergo periodic sonographic surveillance, and none of the patients had underlying RCC(10). So a conservative therapeutic approach (bed rest, transfusion support and withdrawal of anticoagulation) was given. Unfortunately, a week later, the patient suffered a more serious abdomen pain and the tests showed that she developed an acute pancreatic abnormality.

AP is usually defined as acute abdominal pain and with an increase in serum levels of pancreatic enzymes. The diagnosis is also supported by an abnormal imaging procedure (ultrasound(US) or contrast-enhanced computed tomography(CT)), which the later is the gold standard for morphological evaluation of the pancreas.

Serum amylase and lipase are frequently elevated in chronic renal failure either due to the decreased renal clearance of these enzymes or due to the pancreatic damage because of the renal failure and dialysis. Royse et al. demonstrated that serum amylase levels were more than threefold elevated in only 7% of patients with CKD and serum lipase levels of >300μg/L (>60 IU/L) are unusual in patients with renal failure and may be indicative of pancreatitis[11].

Thus, the diagnosis of AP in patients with CKD is generally made when there is a clinically suspicion and an elevation of serum amylase and lipase levels more than threefold above the upper limit of normal or if this level of elevation is absent, but there is an abnormal radiological investigation (US or CT)[12]. In this case, the swelling pancreas was present and the serum amylase was sharply increased exceeding threefold the upper limit of normal in a short period which totally different from the basic level when the patient was admitted. The evidences got from seizure of the abdominal pain, blood chemical test and the pancreatic enlargement of CT can prove the diagnosis.

Among the general population, the alcoholic injury, hyperlipidemia, hyperparathyroidism, celiac disease, cholelithiasis, pancreas divisum are the contributors to AP[13,14]. Other causes are reported in some literature to be risky factors of HD patients, such as the use of drugs, uremia, malnutrition, interventional or surgical procedures and secondary hyperparathyroidism (SHPT) accompanied by hypercalcemia[2,15].

However, in most episodes of pancreatitis observed among dialysis patients, few of the classical causes of pancreatitis were present. In this case, the patient had no alcohol, hyperlipidemia or surgical history. There was no evidence of gall stones and dilation in the common biliary duct in CT. It was reported that AP is a recognized complication of SLE, the patients receiving immunosuppressive treatment regimen and corticosteroids, which probable drug-induced pancreatitis.

Moreover, pancreatitis occurred in 32% of the lupus patients with ESRD, this frequency was much higher than that observed patients with SLE[16]. A multiplicity of factors may cause pancreatic injury, vasculitis, autoimmune mechanisms, and various drugs, notably corticosteroids and azathioprine, have been considered as likely causative agents. The patient had no special medications that might be prone to cause AP except for prednisolon. There was no evidence to vasculitis, which has been discussed above. Meanwhile, in the present patient, this autoimmune mechanism also is kept in mind, but appeared unlikely. Despite the long history of SLE, none of our patient was positive for autoantibodies and complements that would suggest any associate with SLE-related disease.

In this patient, other major possibilities can be considered for the mechanism of pathogenesis: SHPT, gastrointestinal hormones and immunological condition. Our patient gradually developed hypercalcemia and was diagnosed with SHPT during the disease. Non-contrast CT scan of the abdomen showing the multiple calcifications indicated the chronic impairment of pancreatitis, which maybe the result of hypercalcemia and hyperparathyroidism. The chronic impairment of pancreas provided the basic of pancreatitis.

In patients with renal insufficiency, concentration of gastrointestinal hormones such as cholecystokinin, serum gastric inhibitory peptide, and glucagon are significantly increased. This increase in hormone concentrations causes hyper secretion of pancreatic enzyme, predominantly trypsin[17]. With the pancreatic hemodynamic disorder and the excess ionic calcium, it promotes the more trypsin which causing over-section of pancreatic enzymes and possibly leading to impaired pancreatic function and pancreatic abnormalities.

The last, the changing immunological condition should be considered. The SRH induces the related cytokines released, which play a major role in the pathogenesis of AP as underlying systemic inflammatory response, tissue damage, and organ dysfunction. Early pathophysiological events occurring during AP include intrapancreatic activation of digestive enzymes (causing local tissue damage) and release of proinflammatory mediators (such as IL-6, IL-10 and TNF-a) by resident macrophages and acinar cells. Systemic release of proinflammatory mediators in AP causes a generalized inflammatory response[18-19]. It may partly explain that the patient suffered AP after SRH without any traditional contributors.

Conclusion

Here, an uncommon case to cause more attention about the SRH and AP in HD patient was reported. The risk of renal cell carcinoma (RCC) in SRH patients is overstated, so the conservative therapeutic approach is advised if the patient's condition is stable. The close monitoring and early supportive care improved the clinical outcome. Even though CT didn't show specific finding, the possibility of underlying malignancy are still kept in mind. So a follow-up CT scan is needed. And a detailed understanding of pathophysiological processes and immunological aspects in patients is the basis for the development of therapeutic strategies that will provide significant reductions in morbidity and mortality.

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