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Case Report

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A Real Neglected Problem With a Grave Prognosis: Nephrogenic Ascites

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Abstract

Nephrogenic ascites is described as a clinical condition of refractory ascites in patients with end-stage renal disease (ESRD) on renal replacement therapy. This entity was first described in 1970. Many nephrologists do not believe in nephrogenic ascites. The underlying etiologies can be multifactorial including a combination of poor nutrition, inadequate dialysis and ultrafiltration, increased peritoneal membrane permeability, and overall uremia. The nephrogenic ascites is a rare syndrome and is often associated with a grave prognosis especially if it is not diagnosed early and treated. In the present study, we report a 27-year-old woman with past medical history of diabetes type 1 (diagnosed at age 11), ESRD secondary to diabetic nephropathy on hemodialysis (diagnosis in December 2017), bilateral diabetic retinopathy, ovarian cyst, hypertension, and anxiety who presented to the emergency department for evaluation of intractable abdominal pain, nausea and vomiting for 2-day duration. She was found to have large ascites. Diagnostic paracentesis was done and found to be exudative with serum ascites albumin gradient (SAAG) of 0.7. After detailed workup, hepatic, cardiac, infectious and malignant causes for ascites were ruled out. The diagnosis of ascites of nephrogenic origin was made. Given the patient's situation and her inability of self-care, she is not a good candidate for intra-abdominal dialysis. The patient has been treated conservatively with salt/fluid restriction and intensive hemodialysis with ultrafiltration.

Keywords: Nephrogenic ascites; End-satge renal disease; Hemodialysis; Ultrafiltration; Continuous ambulatory peritoneal dialysis

Introduction

Nephrogenic ascites is a syndrome of refractory ascites seen in patients with end-stage renal disease (ESRD) on renal replacement therapy usually maintenance hemodialysis [1, 2]. The underlying pathophysiology is still not fully understood and treatment options are limited. Herein, we are describing a patient who was taken to the emergency department with refractory ascites.

Case Report

A 27-year-old woman with a past medical history of diabetes type 1 associated with latent autoimmune diabetes of adulthood diagnosed from the age of 11 years, ESRD secondary to diabetic nephropathy on hemodialysis (diagnosed in December 2017), bilateral diabetic retinopathy, ovarian cyst, hypertension, and anxiety was brought to the emergency department for evaluation of intractable abdominal pain, nausea and vomiting. These health issues started 2 days prior to emergency visit at the hospital. The patient has a history of multiple admissions with similar presentations. She was found to have large ascites.

It was observed that the patient was a young woman, anxious at the moment but alert and oriented × 3. She was pale but had no jaundice or lymphadenopathy. Her blood pressure was 218/108 mm Hg. Her cardiac and respiratory exam was unremarkable.

Abdominal examination showed abdominal distension, mild tenderness, and positive shifting dullness. The normal bowel sounds, no dilated veins and no palpable masses were found in the examination of the abdomen. Extremities exam was remarkable for bilateral +1 leg edema.

Her laboratory investigations revealed blood urea nitrogen (BUN) of 42 mg/dL, serum creatinine (Cr) of 6.1 mg/dL, serum calcium of 8.8 mg/dL and serum phosphorus of 4.8 mg/dL, white blood cell (WBC) of 12.0, hemoglobin (Hb) of 9.6, and platelets of 428. The patient's international normalized ration (INR) on checking was within the normal range. Computed tomography (CT) scan of the abdomen/pelvis with intravenous and oral contrast was significant for moderate to be marked as abdominal ascites with hepatomegaly and a somewhat reticular pattern of enhancement suggesting possible cirrhosis. Hepatitis B and C serology had been negative in the previous admissions of the patient. Liver function test (LFT) of the patient was also conducted which was within normal limits. Therapeutic/diagnostic paracentesis was done and

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resulted as: fluid appearance of xanthochromia; fluid WBC of 892/µL; fluid red blood cell (RBC) of 5,120/µL; fluid polynuclear WBC of 0%; fluid mononuclear WBCs of 0%; fluid lymphocytes of 34%; fluid unclassified cell of 66%; fluid glucose of 134 mg/dL; fluid total protein of 5.7g/dL; fluid albumin of 2.0g/dL; fluid lactic dehydrogenase (LDH) of 226 IU/L; and fluid amylase of 25 IU/L. Serum albumin from December 12, 2018 was 2.7 g/dL. SAAG was calculated to be 0.7. Cytology showed chronic inflammatory and rare mesothelial cells, and no malignant cells were identified. Culture of ascitic fluid did not grow any organisms. With predominance of lymphocytic cells, ascetic fluid was sent for acid fast bacillus (AFB) and Gold QuantiFERON test was requested. All results were negative.

Hepatobiliary ultrasonographic (US) exam with Doppler did not show any finding suggesting portal vein thrombosis or Budd-Chiari syndrome.

In the previous admission, CT scan abdomen/pelvis showed a complex ovarian cyst and cancer antigen 125 (CA-125, U/mL) was slightly elevated. Repeat CT abdomen/pelvis and transvaginal ultrasound (TVUS) did not reveal any ovarian cyst. Echo did not show any elevation in right ventricular pressure with ejection fraction (EF) of 60%.

Based on the detailed workup, hepatic, cardiac, infectious and malignant causes for ascites were ruled out. The diagnosis of ascites of nephrogenic origin was made.

Because of her comorbidities and non-compliance with treatment, the patient was a poor candidate for intra-abdominal dialysis and renal transplant. The patient has been treated conservatively with salt/fluid restriction and intensive hemodialysis sessions with ultrafiltration. A gradual reduction in ascites was noted and abdominal girth had been reduced by about 40% with management. But because of her non-compliance with hemodialysis sessions, the patient keep presenting to the emergency room with the same complain.

Discussion

This case represents a medical condition known as dialysis-related ascites, a problem that has been seen in ESRD patients on hemodialysis. The prognosis, prevalence and outcomes are not well known as no large evidence-based data are available [3]. The pathogenesis of nephrogenic ascites is not well established and could be due to a combination of factors such as poor nutrition status, patient's non-compliance, and a late presentation that results in delayed initiation of appropriate renal replacement therapy [3].

The underlying pathophysiologic factors that contribute to nephrogenic ascites formation include: 1) Hepatic vein hydrostatic pressure secondary to liver disease could lead to accumulation of protein-rich fluid in the peritoneal cavity, and the absence of varices on endoscopy and SAAG of less than 1.1 g/dL reinforce the absence of clinically significant degree of postal hypertension [4]; 2) Changes in peritoneal membrane permeability caused by an inflammatory effect of uremic toxins, circulating immune complexes, and prior exposure to dialysis solutions, hemosiderosis, renin-angiotensin-aldosterone system (RAAS) activation [1, 5, 6]; 3) Obstruction of lymphatic channels caused by inflammatory infiltrate resulting in an alteration in the peritoneal fluid absorption and ascetic fluid accumulation [6-8]; and 4) Other predisposing factors could be hypoalbuminemia, hyperparathyroidism, congestive heart failure, constrictive pericarditis, pancreatitis, and cirrhosis with portal hypertension [9].

On biopsy, the peritoneum grossly appears normal but histological examination usually shows chronic inflammatory and mesothelial cells with a variable degree of fibrosis [10, 11].

The diagnosis of nephrogenic ascites is made by exclusion and requires complete workup to rule out hepatic, cardiac, infective and malignant causes of ascites. In about 15% of cases, detailed evaluation might reveal secondary causes for ascites formation.

Recommended evaluation for nephrogenic ascites starts with the history of the patient and their physical examination. The history of the patient shows massive ascites with minimal peripheral edema in a dialysis patient. It is also noted that the patients usually have cachexia, dialysis-related hypotension, and anorexia. The recommended general blood chemistries include BUN, Cr, LFTs, hepatitis panel, thyroid- stimulating hormone and iron studies.

The ultrasound of abdomen with portal venous Doppler, echocardiogram with right and left atrial pressure estimation is done when it is relevant. According to the condition of the patient, it is also suggested that abdominal CT scan, laparoscopy with peritoneal biopsy should also be done to rule out liver disease with portal hypertension, peritoneal infection/malignancy, pancreatic causes and cardiac causes such as cardiomyopathy.

The paracentesis and ascetic fluid analysis is of great importance to get a fair idea about the condition of the patient. The paracentesis and ascetic fluid analysis shows that the ascites has straw color which is linked with cirrhosis. Exudate (high protein), SAAG < 1.1, WBC count 25 - 150 cells/mm^3 with low neutrophil count and lymphocyte predominance were also observed in the paracentesis and ascetic fluid analysis. The negative cultures/AFB cultures, negative cytology were also observed. The SAAG < 1.1 indicates non-portal hypertension which is suggested to be the peritoneal cause of ascites [12].

If not treated, nephrogenic ascites is associated with grave prognosis. The average survival ranges from 7 to 10.7 months, with 44% chances of dying within 15 months of diagnosis. The clinical course in a patient with refractory nephrogenic ascites is marked by worsening cachexia and progression to death [1, 2, 13]. In contrast, the majority of responders and long-term survivors had resolution of ascites with treatment. The survival rate in those patients is found to be closer to the survival rate of ESRD without ascites [14, 15].

Management of nephrogenic ascites is complicated and includes a variety of medical and surgical modalities. Salt and fluid restriction, intensive hemodialysis with ultrafiltration and intravenous albumin infusions with a high protein diet are given in the initial stages to control the ascites, but this is limited by severe hypotension [9, 10]. Continuous ambulatory peritoneal dialysis (CAPD) is also effective in the treatment of

ascites [1, 6, 10]. This modality of treatment improves nutrition and reduces ascites by removal of protein-rich fluid which limits the fluid shift to the peritoneal space by oncotic pressure [16], but this modality is often associated with protein loss secondary to repeated removal of large volume of protein-rich fluid. Peritoneovenous shunt is another option that was found to be effective in controlling nephrogenic ascites formation, but this option is not free of complications that include shunt malfunction and infections [3].

Other modalities that are associated with less predictable outcome include intra-abdominal steroid injections and binephrectomy [3].

Renal transplant is the only definitive treatment for nephrogenic ascites with complete resolution of the ascites within 2 - 6 weeks [17]. The recurrence of ascites may occur at any time of graft failure or at any time up to 3 years due to various reasons [18, 19].

Conclusions

Nephrogenic ascites is a rare condition of grave prognosis. The etiology is unknown but is thought to be multifactorial. As the patient is suffering from it and the condition is not improving therefore, the initial treatment options include salt and fluid restriction, daily intensive hemodialysis with ultrafiltration along with intravenous albumin infusion and high protein diet. CAPD and peritoneovenous shunt are alternative options which are not free of complications. Renal transplant is the only definitive treatment option associated with complete resolution of the ascites but recurrence of ascites is possible within a specified time due to various reasons.

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None to declare.

Conflict of Interest

The authors report no conflict of interest.

Informed Consent

Not applicable.

Author Contributions

RAZ is the first author, collected data, guided the literature search, and wrote the manuscript. HAA, GF, JM and EM helped collecting data and writing the article. FE reviewed and supervised the study.

Data Availability

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

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