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Ascites of unknown origin in infant: a rare case report

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ABSTRACT

Introduction. Ascites of unknown origin in infants are rare and diagnostically challenging. However, it can be associated with a poor prognosis if it is not treated promptly.

Case presentation. A 3-month-old boy infant was admitted to the Dr. Soetomo General Academic Hospital, Surabaya because of a 2-week history of progressive abdominal distension with massive ascites following fever onset. Laboratory parameter measurement revealed increased liver function test, hypoalbuminemia, and prolonged coagulation factor. Hepatitis markers were negative. TORCH serological examination showed non-reactive. Urinalysis, renal function test, and echocardiography were normal. The ascitic fluid analysis showed SAAG >1.1 g/dL. An abdominal ultrasound examination revealed ascites. MRCP showed hepatomegaly and ascites. A liver biopsy showed foci of polymorphonuclear and mononuclear inflammatory cell distribution among hepatocytes with no hepatic fibrosis. He was treated with antibiotics, steroids, diuretics, and albumin transfusion. There were no ascites and laboratory parameters were improved after treatment.

Conclusion. Progressive and rapid hepatic inflammatory mechanisms may play a role in the development of ascites. Steroids may be considered in cases of unexplained ascites thought to be related to liver injury to prevent further liver fibrosis.

Keywords: ascites, abdominal distension, hepatic fibrosis

INTRODUCTION

Ascites are defined as serous fluid accumulating in the peritoneal cavity. The most common causes of ascites in children are liver, kidney, and heart disease [1]. Identification of the underlying disease is important in the management of pediatric ascites. The history and physical examination are primary. Other modalities are used to support these findings. Laboratory parameter measurements such as liver function tests, renal function tests, and echocardiography should be performed to investigate the etiology of ascites. Other modalities such as abdominal ultrasound, Magnetic Resonance Cholangiopancreatography (MRCP), liver biopsy, and diagnostic paracentesis may be needed in children with newly diagnosed ascites [2].

There are many causes of ascites that can occur in the neonate and the pediatric patient. However, the most common causes of ascites are chronic liver disease and cirrhosis. Treatment of ascites depends on underlying etiology and includes sodium restriction, diuresis, paracentesis, albumin intravenous, antibiotics, surgical shunts, and transplantation [2]. This case report describes an infant who complained of abdominal distension due to ascites, which developed rapidly and was followed by abnormal liver function tests. However, with the administration of antibiotics, steroids, diuretics, and albumin transfusion, the ascites resolved and laboratory parameters normalized.

CASE PRESENTATION

A 3-month-old boy came to the Emergency Department of Dr. Soetomo General Academic Hospital, Surabaya with complaints of an enlarged abdomen since the age of 2.5 months and currently

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getting bigger. At the previous hospital, an ultrasound examination revealed intestinal abnormalities. The patient was referred with the diagnosis of ascites + transaminitis + hypoalbuminemia. The navel seemed to protrude out, previously accompanied by fever for 7 days, often vomiting if drinking more than 10 ml. There were no complaints of swelling and no jaundice. According to the parents, the patient defecates normally with a brownish-yellow color and there is no history of pale stool. The urine color in the diapers was clear as usual. There were no similar complaints in the family. Vomiting and constipation were absent.

The patient is the first child, born spontaneously at 37 weeks gestation, cried immediately, birth weight of 2570 grams, body length of 48 cm, and head circumference of 30 cm. The patient consume breast milk and formula milk since the age of 2 days until now. Routine immunization history is complete according to age, including hepatitis B0, BCG, OPV1, DPT-Hb-Hib1, OPV 2, PCV 1, and rotavirus. Growth and development were normal for age.

The general condition of the patient appeared moderately ill. Consciousness was compos mentis. Anthropometric examination revealed a body weight of 6000 grams, body length of 60 cm, head circumference of 32 cm, and abdominal circumference of 48 cm. Vital signs were stable. Physical examination revealed a jaundiced sclera, Abdominal examination revealed a non-tender, distended abdomen with a dull percussion and a positive peritoneal thrill with an umbilical hernia. The size of the hepar and lien were difficult to evaluate.

Laboratory examination showed elevated liver function tests (AST 133 U/L, ALT 118 U/L, and GGT 184.3 U/L), bilirubin (total 1 mg/dL, direct 0.7 mg/dL), PPT 23.8 sec, APTT 32.4 sec. and hypoalbuminemia (2.48 g/dL). The complete routine blood test showed Hb 9.4 g/dL, Wbc 8.08 × 10^3/µL, and Platelet 209 × 10^3/µL. LDH 486 U/L, blood glucose 117 mg/dL, sodium 134 mmol/l, potassium 4.5 mmol/l, chloride 109 mmol/l, BUN 5.6 mg/dL, serum creatinine 0.4 mg/dL, and procalcitonin 0.24 ng/mL. Work up anemia showed serum iron 54.3 Ug/dL, TIBC 230, and Ferritin 190.44 ng/mL. Thyroid hormones showed TSH 6,424 µUl/mL and FT4 0.89 ng/dL. Serologic examination showed non-reactive IgG CMV, non-reactive IgM CMV, non-reactive IgG Toxoplasma, non-reactive IgM Toxoplasma, IgG Rubella gray-zone, and non-reactive IgM Rubella. Hepatitis serology markers were negative. The blood culture results were sterile.

Urine examination showed a light yellow color, clear, specific gravity 1.003, pH 5, negative protein, negative glucose, negative ketones, negative bilirubin, negative erythrocytes, normal urobilinogen, negative leukocytes, negative nitrite, squamous epithelium 0.29/Lp, hyaline cylinders 0/Lp, fungi 0.216/Lp, ACR <30 mg/gCr, PCR <0.15, albumin 10 mg/L.

The patient underwent ascites puncture. The ascitic fluid analysis showed LDH 128 U/L, albumin 1.27 g/dL, PMN# 0.000 × 10^3/µL, MN# 0.010 × 10^3/µL, glucose 105 mg/dL, total protein 2.11 g/dL, LDH 127.07 U/L, RBC 0.000 × 10^3/µL. Gene Expert TB ascites fluid was negative, and gram culture and aerobic bacteria ascites fluid were sterile (Figure 1).

FIGURE 1. Ascites fluid

Abdominal X-ray showed there was ground glass opacity in the abdominal cavum up to the abdominal cavum accompanied by floating material intestinal gas. Hepatic and splenic shadows are not visible. The contour of the right and left kidney is not clear. There is no radioopaque shadow along the urinary tract. The right and left psoas shadows are symmetrical. The corpus, pedicle, and intervertebral spatium appear good. Abdominal X-ray revealed ascites (Figure 2).

The results of abdominal ultrasound include normal liver size, sharp angles, flat edges, echo intensity parenchyma was normal and homogeneous, no visible dilation of IHBD/EHBD, v.porta/v.hepatica looks normal, with no visible nodules/cysts/masses. The gall bladder is non-fasting GB, with no stones/nodules/sludge. The spleen is normal size, echo intensity of parenchyma appears normal, no mass/cyst. The pancreas is normal in size, echo intensity of parenchyma appears normal, no dilation of duc-

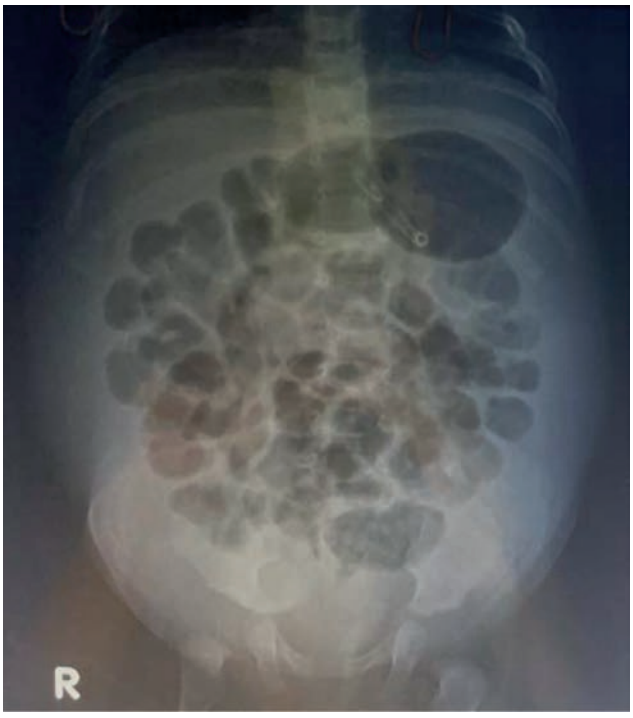

FIGURE 2. Abdominal X-ray showed ascites

tus pancreaticus, and no mass/cyst/calcification. Right kidney: normal size, echo intensity of the cortex appears normal, sinus cortex boundaries are clear, no ectasis of the pelvicalyceal system, no stones/cysts/masses. The left kidney is normal in size, the echo intensity of the cortex appears normal, the sinus cortex boundaries are clear, there is no ectasis of the pelvicalyceal system, no stones/cysts/masses. Echo intensity of extraluminal free fluid in the abdominal cavum and pelvic cavum is seen. An abdominal ultrasound examination revealed ascites (Figure 3A). An abdominal ultrasound at the previous hospital revealed free fluid in the abdominal cavum with a depth of 1.80 cm from the skin surface with parenchymal liver abnormalities and cholecystitis (Figure 3B). The liver, pancreas, spleen, and kidney were normal. Echocardiography showed a small ASD Secundum (0.4 cm diameter) - L to R shunt with an ejection fraction of 82%.

Magnetic Resonance Cholangiopancreatography (MRCP) showed extraluminal fluid intensity in the abdominal cavum to the pelvis accompanied by a floating bowel picture. The Liver is enlarged with midclaviculo-craniocaudal length +/- 9.6 cm, normal intensity, flat edges, sharp corners, biliary system appears normal, v.porta/v.hepatica normal, no hypo/hyperintense nodules. The gall bladder is normal in size, with no wall thickening, and no stones. The pancreas, spleen, and kidneys are normal in size, normal in intensity, and have no stones/masses/cysts. MRCP showed ascites and hepatomegaly, but the gallbladder and biliary tract were within normal limits (Figure 4).

Percutaneous liver biopsy revealed no bile duct proliferation was found in the portal tract. There

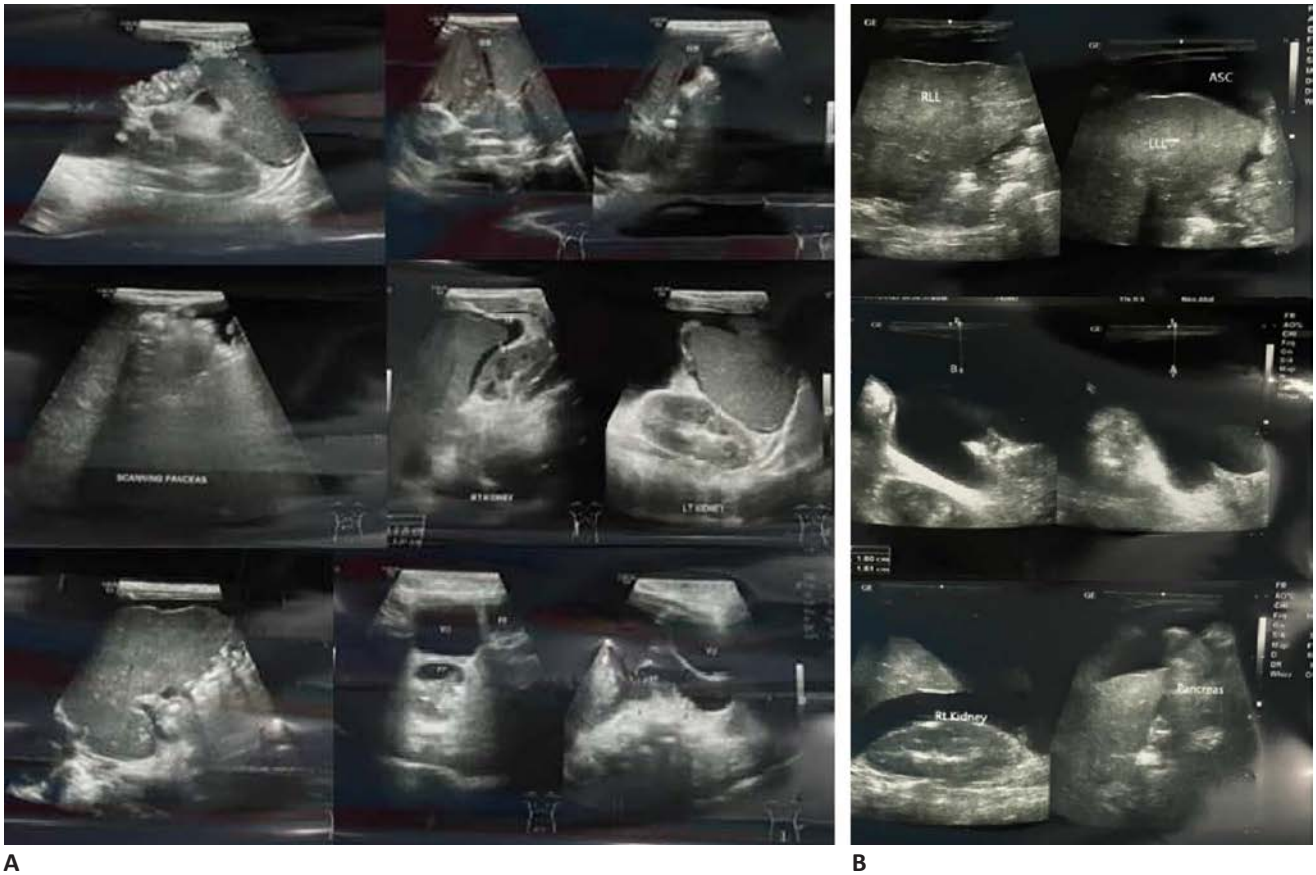

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FIGURE 3. Abdominal ultrasound examination revealed ascites (A. in admission; B. in the previous hospital)

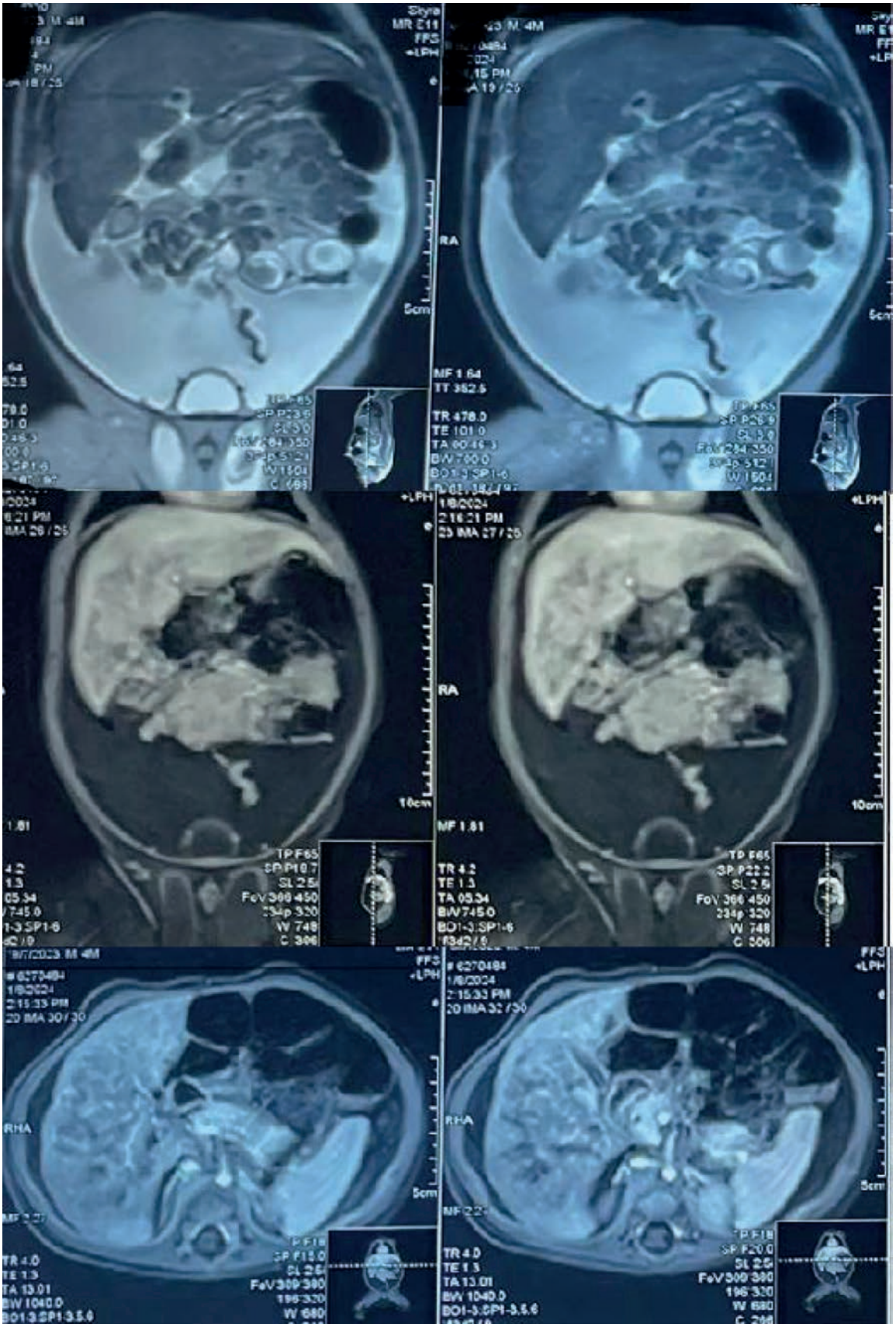


FIGURE 4. MRCP showed ascites and hepatomegaly

were foci of polymorphonuclear and mononuclear inflammatory cell distribution among hepatocytes. There were no dilated canaliculi. There was no cholestasis. Hepatic lobules consisting of cloudy degenerated hepatocytes were seen. There are no signs of malignancy. No fibrosis was found (F0).

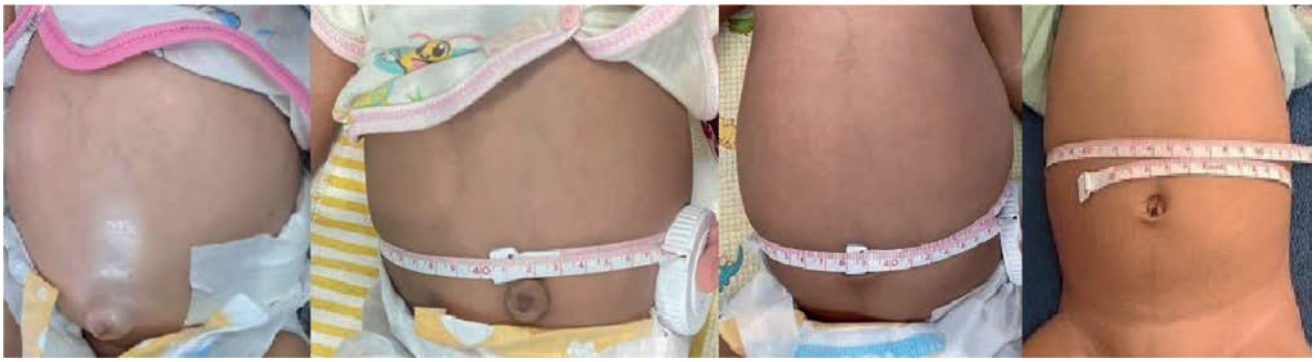
The patient received antibiotic injection, furosemide injection, spironolactone orally, and methyl-

prednisolone 2 mg/kg BW/day in divided doses orally. The patient also received sodium intake restriction, an albumin, and an FFP transfusion. After 22 days of treatment, the patient's condition improved and the abdominal circumference decreased to 40 cm. The laboratory parameters showed Hb 12.1 g/dL, Wbc 6.740 × 103/µL, Plt 684 × 103/µL, AST 62 U/L, ALT 32 U/L, alkali phosphatase 143 ng/mL, albumin 5.76 g/dL, APTT 24 sec, PPT 11.6 sec. There was an improvement in ascites and decreased abdominal circumference after treatment (Figure 5).

An abdominal ultrasound was assessed performed? after 7 days of treatment and found to have improved ascites (relatively much reduced compared to the previous ultrasound. After 14 days of treatment, an abdominal ultrasound showed no extraluminal free fluid echo intensity in the cavum abdomen and pelvis. The liver, gall bladder, pancreas, and right and left kidneys were within normal limits. No ascites were found on abdominal ultrasound examination (Figure 6).

DISCUSSION

Ascites is defined as a pathological accumulation of fluid within the peritoneal cavity [3]. Neoplasms such as intra-abdominal cysts, hepatobiliary disorders, cardiac disorders, serositis, and metabolic diseases can cause ascites [1]. However, cystic lesions usually presenting as fluid-filled masses are often found as ascites [3]. However, the ascites that occurs in neonates is divided into 3 classifications, namely urinary, chylous, and bilious ascites. Urinary ascites occur mostly in boys due to urinary tract obstruction. Chylous ascites is the accumulation of lipid-rich lymph in the peritoneal cavity due to obstruc-



A B C D

FIGURE 5. Abdominal circumference evaluation after treatment (A. The day of admission 48 cm; B. After 7th day of treatment 43 cm; C. After 14th day of treatment 40.5 cm; after 22nd day of treatment 40 cm)

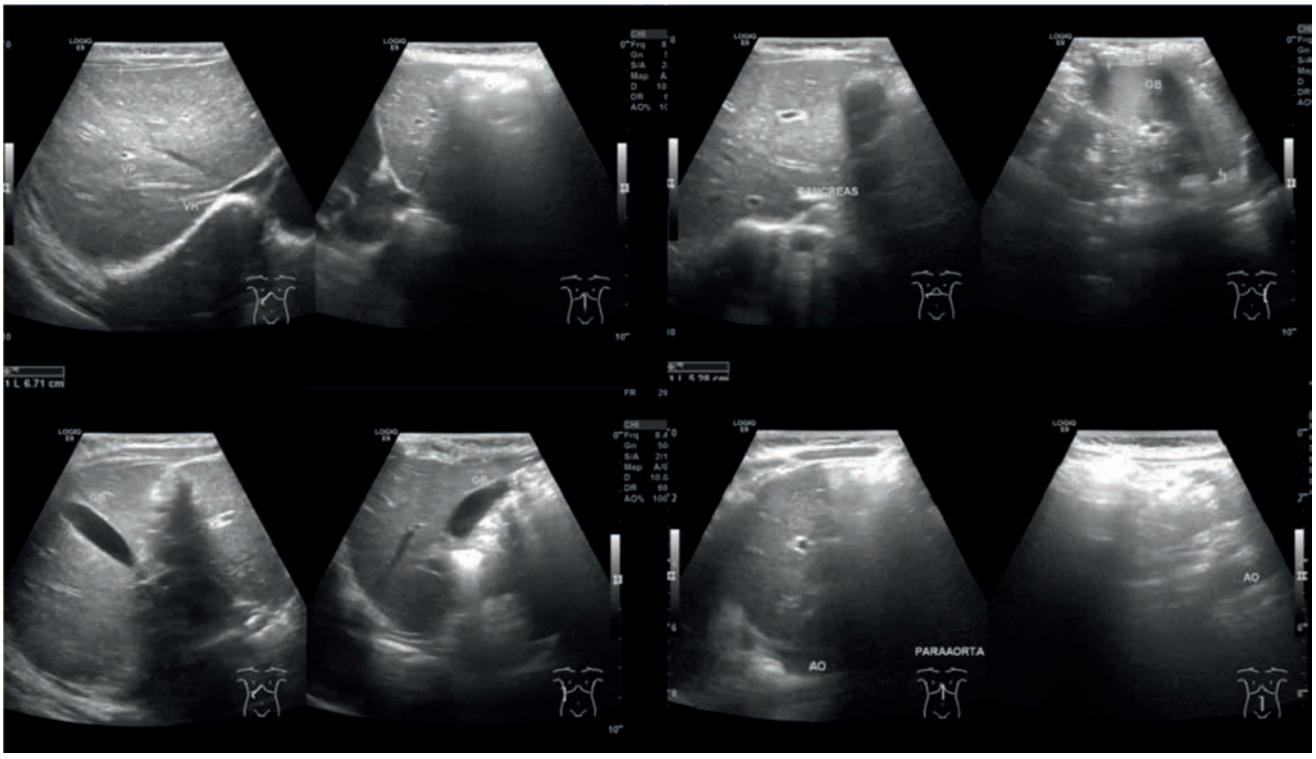


FIGURE 6. The abdominal ultrasound evaluation after treatment revealed normal

tion of the lymphatic system caused by congenital abnormalities of the lymphatic ducts. Biliary ascites in neonates occur due to spontaneous perforation of the bile ducts [4]. Ascites can result from a disturbance in the balance of hydrostatic and oncotic pressures that regulate splanchnic, portal, and hepatic blood and lymphatic flow [2].

Diagnostic paracentesis is indicated in children with newly diagnosed ascites to examine the ascitic fluid for cell counts, protein levels, and culture. The best single test to classify ascites into portal hypertension (SAAG >1.1 g/dl) and non-portal hypertension (SAAG <1.1 g/dl) is the serum ascites albumin gradient (SAAG) [1]. Diagnostic paracentesis should especially be performed if ascites accumulate rapidly, or there is a clinically evident infection, encephalopathy, or increasing abdominal pain [2]. In this case, the accumulation of ascitic fluid was rapid and the patient had a history of fever. In this case, diagnostic paracentesis was performed with the result of SAAG 1.13 which showed portal hypertension. A disturbance in the balance of hydrostatic and oncotic pressures that regulate splanchnic, portal, and hepatic blood and lymph flow leads to ascites. Ascites develop secondary to vaso-splanchnic dilation in liver cirrhosis. Nitric oxide-mediated vasodilation decreases arterial blood volume leading to sympathetic nervous system activation and renal sodium retention via the renin-angiotensin-aldosterone system and antidiuretic hormone (ADH) secretion. Sodium retention leads to expansion of extracellular volume and ascites accumulation in portal hypertensive conditions. Portal hypertension also increases splanchnic capillary pressure leading to excess lymph formation [2].

Laboratory tests including liver function tests, albumin, coagulation factors, serum urea nitrogen, creatinine, and urinalysis should be performed in the evaluation for ascites etiology [2]. In this case, renal function and urinalysis results were within normal limits. Liver function tests revealed slight elevation of transaminase enzyme levels, hypoalbuminemia, and prolongation of coagulation factors. Ascites may occur even in the absence of cirrhosis [2]. As in this case, liver biopsy results showed no cirrhosis despite decreased albumin levels and prolonged coagulation factors. In the diagnosis of liver disease, a liver biopsy plays an important role. A liver biopsy helps confirm the specific type of liver disease. In addition, liver biopsies can be used to help assess the severity of the liver disease [5]. The limitation of liver biopsy in this case is that it is performed after the ascites have improved, therefore the results obtained may be that the liver cells have returned to repair, and the liver biopsy does not show any fibrosis in the liver.

The presence of a few injured cells or a group of inflammatory cells may indicate mild liver parenchymal injury in liver histopathology. The presence of more than five inflammatory foci or apoptotic bodies per 10 fields with multiple necroinflammatory foci is considered moderate. Severe liver parenchymal injury may show confluent necrosis and stromal collapse [5]. In this liver biopsy, foci of polymorphonuclear and mononuclear inflammatory cell distribution were found among the hepatocytes, and liver lobules consisting of turbid degenerated hepatocytes were found, but no necroinflammatory foci were found.

Management of non-cirrhotic ascites depends on the underlying aetiopathology [1,2]. The basic principle of the management of ascites is that the benefits of medical or surgical therapy should be greater than the potential risks. If not treated promptly or appropriately, ascites can lead to respiratory distress, increased risk of infection, gastrointestinal bleeding, renal failure, encephalopathy, and death [2].

In liver disease, diuretics monotherapy or dual therapy and salt restriction are used to treat mild to moderate ascites in children, especially if hyponatremia is present [1]. In this case, the patient has a sodium intake restriction. In ascites, sodium restriction is recommended to 1-2 mEq sodium/kg/day, or 1-2 g sodium a day. However, sodium restriction is not necessary for exclusively breastfed infants as breast milk contains low levels of sodium [2].

Diuretic drugs were administered to achieve a negative sodium balance as one of the management of ascites. Spironolactone is given to increase the excretion of sodium chloride and water at a dose of 0.5-1 mg/kg/day in 2-3 divided doses. Furosemide is given to inhibit the reabsorption of sodium and chloride and increase the excretion of water and sodium at a dose of 0.5 and 2 mg/kg/day. The patient received furosemide injection and spironolactone orally. The administration of spironolactone and furosemide accelerates the improvement of ascites, especially in portal hypertension [2].

Portal hypertension is an increase in portal venous pressure greater than 5 mm Hg, most commonly caused by cirrhosis. Portal hypertension is triggered by increased intrahepatic resistance due to the presence of liver fibrosis. The release of vasodilating agents such as nitric oxide leads to splanchnic vasodilation, reduction in arterial blood volume, activation of the renin-angiotensin-aldosterone system, and sodium and water retention, eventually leading to ascites [6].

In this case, oral methylprednisolone 2 mg/kg BW/day in divided doses was delivered orally. The mild liver parenchymal injury was found in a liver biopsy. Studies have shown that the efficacy of glucocorticoid treatment is mainly related to the timing of glucocorticoid administration, while the underly-

ing disease and possible complications should be assessed. Certain parameters that may benefit more from glucocorticoid therapy include ALT levels >1,000 U/L, total serum bilirubin within 10~20×ULN, no obvious signs of infection, no predisposition to liver and kidney syndrome, and an exaggerated immunologic response [7]. In this patient, an immunoreactive response was suspected because of the progressive development of ascites with the onset of fever.

The patient also received an albumin transfusion due to hypoalbuminemia and an FFP transfusion due to prolonged coagulation factor. Albumin plays a role in the maintenance of intravascular oncotic pressure. Albumin (0.5-1g/kg dry weight) should be administered to maintain intravascular volume balance if the serum concentration falls below 2.5 g/dL. After administration of albumin transfusion, diuretic drugs can be administered to achieve maximal diuresis [2].

In cases of unresponsive ascites or children with large amounts of ascites, a large volume paracentesis (LVP) with infusion of albumin should be performed [1]. In this case, abdominal paracentesis was not performed because of the improvement of ascites and decrease in abdominal circumference, followed by improvement in liver function tests, albumin, and coagulation factors.

Immune injury is considered the first blow in the "three-hit theory" of liver failure. Stopping the immune injury process in time to prevent excessive immune response can reduce or reverse the condition. As anti-inflammatory and immunosuppressive agents, glucocorticoids inhibit the phagocytosis of macrophages and can suppress the production of inflammatory cytokines, thereby suppressing further injury to liver cells. [7-9].

CONCLUSION

Successful steroid therapy in infants with ascites, followed by abnormalities in liver function tests, hypoalbuminemia, and prolongation of blood coagulation factors, has been reported. Mild inflammatory mechanisms in liver tissue may play a role in the development of ascites. Steroid administration may be considered for unexplained ascites if liver inflammatory markers are elevated, especially if previously associated with fever.

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