



## Budd-Chiari Like Syndrome in a Dog: Hematology, Biochemistry, Histopathology and CT Scan Angiography Findings

[A case report]



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**A**NINE months old mix breed dog was presented by lethargy, symptoms of abdominal pain, mild respiratory distress and abrupt onset of massive and hemorrhagic ascites that responded to medical treatments partially. The dog had a history of car accident three months earlier. Mild non-regenerative microcytic anemia, hypoalbuminemia, hypoproteinemia, elevated liver enzymes, mild pulmonary edema and high protein transudate in abdominal cavity were detected. Abdominal ultrasonography demonstrated hepatomegaly and intra-abdominal fluid collection. Histopathological examination of the liver biopsy showed a diffuse sinusoidal distension with some area of hepatocyte necrosis. The histopathological findings, together with increased level of liver enzymes, and moderate panhypoproteinemia, high protein transudate and abdominal pain were all in favor of the diagnosis of post-sinusoidal hypertension secondary to obstruction of hepatic venous outflow (Budd-Chiari-like syndrome). CT angiography confirmed a massive thrombosis in caudal vena cava and pulmonary artery. Unfortunately, 24 hours after CT scan study the patient was spontaneously expired. However, because the owner did not give his consent for the autopsy, the detailed data is not acquired. In conclusion, obstruction of venous blood flow and Budd-Chiari like syndrome must be considered in dogs with ascites, hepatomegaly, and symptoms abdominal pain.

**Keywords:** Budd-Chiari Syndrome, Thrombosis, Dogs.

### Introduction

In human medicine, Budd-Chiari syndrome (BCS), veno-occlusive disease (VOD), and congestive hepatopathy (CH) are three similar syndromes caused by hepatic venous outflow obstruction. The obstruction level in these disorders is different. In BCS the level of obstruction is from hepatic veins to the superior end of inferior vena cava. In VOD the venous obstruction is in sinusoids and terminal venules, and in CH the venous obstruction is seen at the level of heart [1]. BCS in human is an uncommon

disorder characterized by congestive hepatopathy and is caused by blockage of hepatic veins. The classic triad of the BCS is ascites, hepatomegaly and abdominal pain, which can present as acute or chronic [2]. Based on the origin of the obstructive lesion, BCS is classified as primary or secondary. In primary BCS, the cause originates from intravascular thrombosis, as this is the main cause of hepatic vein obstruction in human, and if obstruction is the result of extravascular compression or tumor invasion, secondary BCS is considered. [3] Obstruction of hepatic veins

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can cause sinusoidal dilatation, increase of sinusoidal pressure, reduction of sinusoidal blood flow, liver congestion, interstitial fluid filtration through the liver capsule and finally abdominal pain and ascites[4, 5]. In this situation, hypoxic damage of hepatocytes, non-inflammatory centrilobular cell necrosis, and reperfusion injury is expectable[6, 7]. In veterinary medicine, the mechanical obstruction of the post-sinusoidal hepatic veins, the caudal vena cava (CVC) cranial to the liver and the right atrium are described as Budd-Chiari like syndrome[8]. Different etiology such as kinking of the CVC as idiopathic or due to trauma,[9] tethering of the CVC by a fibrous band in a dog with history of trauma[10], wrapping of the pericardium around the CVC following trauma[11], CVC obstruction associated with a contagious invasion of an adrenal pheochromocytoma[12, 13], or due to intracardiac tumor[14], Budd-Chiari like syndrome due to cor triatriatum dexter and hiatal hernia as congenital disorders[15, 16], CVC obstruction in a dog following fibrous reaction around a needle foreign body in the CVC[17] was reported in dogs with Budd-Chiari like syndrome. As mentioned previously, clotting disorders are as the main cause in BCS development in human, however clotting disorders and clot formation are not explained in dogs with Budd-Chiari like syndrome. The case described here had clinical and paraclinical signs related to both Budd-Chiari like syndrome and pulmonary disorders that both of them were probably associated to intravascular thrombosis or a thrombosis-like lesion.

#### *Case presentation*

A 9 months old dog weighing 7 kg was examined because of abrupt onset of ascites and painful abdomen. The dog had a history of severe trauma and multiple bone fracture and cholangiohepatitis three months ago. The results of initial diagnostic evaluation included serum biochemistry and hematology showed mild nonregenerative anemia, neutrophilia, lymphopenia, mild azotemia, increased level of liver enzymes, and mild panhypoproteinemia. The urine analysis was unremarkable. Abdominal ultrasonography demonstrated hepatomegaly and intra-abdominal fluid collection. More than 3 liters fluid was aspirated from peritoneal cavity. The analysis of the peritoneal fluid showed a hemorrhagic ascites (RBC: 100000/microliter) with high protein (Total protein: 3.77-5.20 g/dl and albumin: 1.6-2.0 g/dl in different

days) and low nucleated cells (600 nucleated cells/microliter). Common causes of ascites, including heart failure, and protein-losing enteropathy were ruled out. Considering high liver enzyme activities, hemorrhagic ascites and hypoalbuminemia, liver failure were noted as differential diagnosis. Conservative treatment with prednisolone (0.5 mg/kg every day), vitamin E (100 IU every day), furosemide (0.5 mg/kg every 12 hours), spironolactone (0.5 mg/kg every 12 hours), ursodeoxycholic acid (10 mg/kg every 24 hours divided in two doses) and pantoprazole (1 mg/kg every 24 hours) was applied and two weeks later, the peritoneal fluid formation rate was reduced and serum liver enzymes activities and serum albumin level were improved (Tables 1 and 2), however the patient showed severe weight loss despite a good appetite. For more evaluation, liver biopsy and histopathology examination were recommended.

In histopathology study, severe and diffuse congestion was seen in the liver (Figure 1). Histopathological findings as well as other signs and symptoms were all consistent with a diagnosis of Budd-Chiari-like syndrome. Plain and post contrast helical CT scan images were taken using Siemens Somatom Spirit Dual Slice CT Scanner. The patient underwent two phasic helical CT (Boluses of 4 mL/kg (600 mg/kg) of 300 mg I/mL iohexol (Omnipaque 300; GE Healthcare) were administered via peripheral intravenous catheters. CT images were acquired once immediately after the beginning of the contrast injection in order to capture the pulmonary artery phase and then 30s after administration) (130 kV, 70 mA, pitch=1.0)[19]. Injection of iodinated non-ionic contrast media. There was an intravascular hypo-attenuating obstructive filling defect appreciated in the anatomical region of the right main pulmonary artery (measuring about 1.31 cm in diameter) at the level of T6 to T7 which had advanced to the segmental arteries. An additional hypo-attenuating obstructive filling defect was visualized in the intrathoracic segment of the CVC at the level of T9 creating almost 50% luminal stenosis.

Furthermore, a same lesion as a non-enhanced obstructive lesion was seen in thoracic CVC (about 1cm in diameter) at the level of T9 (Figure 2). Based on surveys of the CT images by several expert and proficient radiologists, intravascular thrombosis was the most likely lesion seen in the CT angiography (Figure 2). In addition,

some degree of pulmonary edema and dyspnea were seen in the patient (Fig. 3). The liver was enlarged. No sign of primary or metastatic neoplastic lesion was detected in the abdominal and thoracic organs. Unfortunately 24 hours after CT scan study the patient was spontaneously expired. However, because the owner did not give his consent to the necropsy, the detailed necropsy data is lacking.

### Discussion

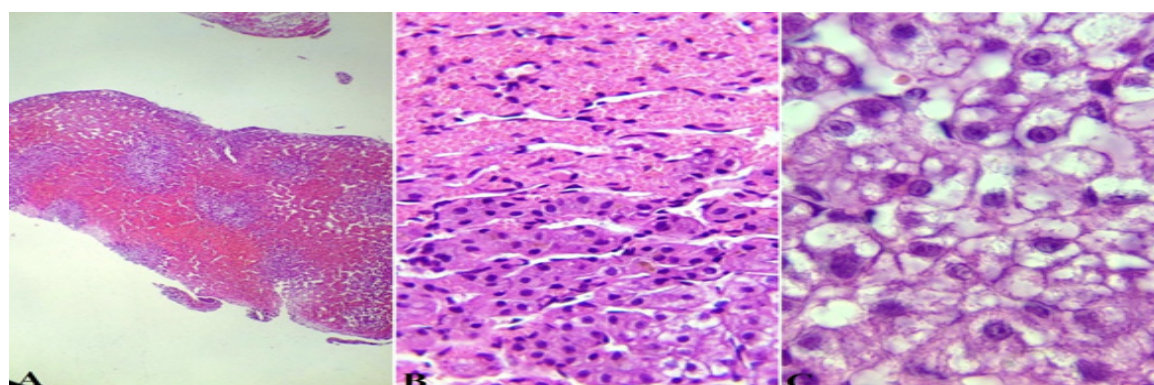
Based on the protein content, the abdominal transudative effusion can be divided into high protein and low protein effusions (more or less than 2.5 gr/l protein). Portal (presinusoidal) hypertension due to liver disease such as hepatic cirrhosis, portosystemic shunt or vascular anomalies, and severe hypoalbuminemia (<1.0-1.5 g/dL) are important causes of low protein transudates development[20]. However,

**TABLE 1. Different hematology parameters before and after medication**

	WBC	Seg.	Lym.	Band	Hct	RBC	Hg	MCV	MCHC	Plt
First day	24.1	23.14	0.96	0	33	5.66	10.6	59.5	31.9	229
20 days after beginning of medication	15.6	14.82	0.15	0.63	22	4.39	8.5	52.2	37.9	168
Reference Range[18]	5-14.1 $\times 10^3 / \mu\text{l}$	2.9-12.0 $\times 10^3 / \mu\text{l}$	0.4-2.9 $\times 10^3 / \mu\text{l}$	0.0-0.45 $\times 10^3 / \mu\text{l}$	35-57 $\times 10^3 / \mu\text{l}$	5.5-8.5 $\times 10^6 / \mu\text{l}$	11.9-18.9 g/dl	66-77 fl	32-36.3 g/dl	100-621 $\times 10^3 / \mu\text{l}$

**TABLE 2. Different serum biochemical parameters before and after medication**

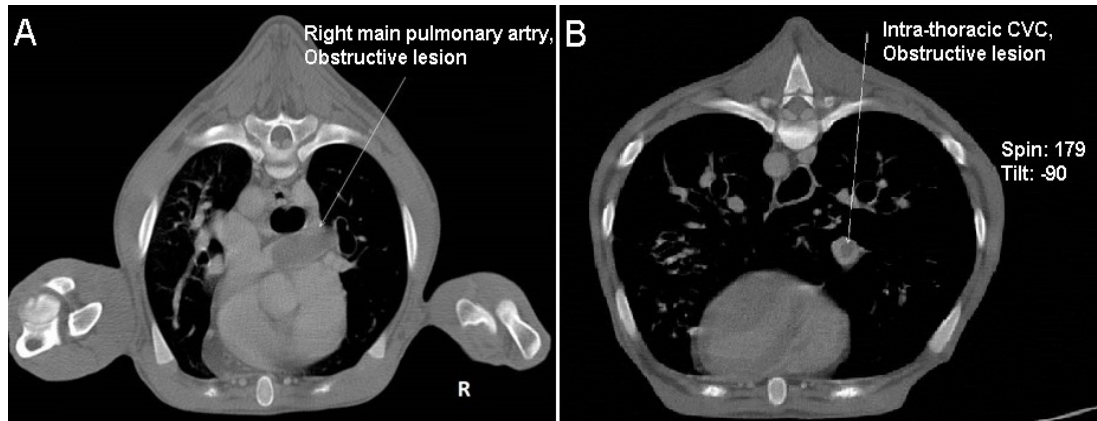
	SGOT	SGPT	ALP	GGT	Urea	Creatinine	Tp	Alb	Glucose	Sodium	Potassium
First day	319	900	421	4.3	87.9	0.91	4.73	2.1	106	138	4.1
20 days after beginning of medication	245	548	481	7.8	66	1.13	6.5	3.1	110	139	4.3
Reference Range[18]	13-15 IU/L	10-109 IU/L	1-114 IU/L	0-10 IU/L	17-59 mg/dl	0.5-1.7 mg/dl	5.4-7.5 g/dl	2.3-3.1 g/dl	76-119 mg/dl	142-152 mmol/L	3.9-5.1 mmol/L



**Fig. 1. Representative H & E-stained liver sections.**

**A:** Diffuse and severe centrilobular congestion without significant inflammation in liver parenchyma and loss of hepatocytes in hepatic cords and their substitution by erythrocytes (magnification,  $\times 40$ ).

**B:** Sinusoidal dilatation and congestion (magnification,  $\times 400$ ). **C:** Cellular swelling (hydropic degeneration) of hepatocytes as enlarged cells with clear cytoplasm (magnification,  $\times 1000$ )



**Fig. 2.** Contrast- enhanced transverse CT scan findings.

- A). Contrast- enhanced transverse CT scan obtained during the arterial phase showed a hypodense obstructive lesion in the main right pulmonary artery at the level of T6 to T7 extending to the further to the associated segmental arteries.
- B). Contract- enhanced transverse CT scan obtained during arterial phase revealed a hypodense obstructive lesion in the intrathoracic segment of the CVC at the level of T9 with a 50% stenosis. Intravascular thrombosis was the most likely lesion seen in the CT angiography (Arrow)



**Fig. 3.** Focal peribronchial increased soft tissue attention at the dorsal aspect of the left caudal lung lobe (Arrow) consistent with pulmonary edema.

hypoalbuminemia by itself is inadequate to cause considerable transudation, because in addition to albumin, globulins are also effective in creating oncotic pressure, and can partly compensate the low oncotic pressure due to hypoalbuminemia. Furthermore increased lymphatic drainage, reduced intravascular hydraulic pressure, and reduced interstitial oncotic pressure are other compensatory processes for increased transudation in patients with hypoalbuminemia[21]. In the present study, there was a mild hypoalbuminemia at the time of admission; however it does not seem that the ascites was caused by the hypoalbuminemia. The nucleated cell count in low protein transudates is  $< 1,500/\mu\text{l}$  to  $< 5,000/\mu\text{l}$  (appropriate to protein

content)[22]. Post-sinusoidal hypertension and sinusoidal hypertension are important causes of high protein transudate development[22]. Congestive heart failure in dogs and caudal vena cava obstruction can cause post-sinusoidal hypertension, and some disorders within the liver affecting sinusoids or central vein such as chronic active hepatitis can cause sinusoidal hypertension[20]. The nucleated cell count in high protein transudates is  $< 5,000/\mu\text{l}$  [22]. In the present study, there was a high protein transudate (Tp: 4.1gr/dl), with low nucleated cell count (600 cell/  $\mu\text{l}$ ). In human, an ascitic fluid red blood cell (RBC) count  $\geq 10,000$  cell/ $\mu\text{l}$  is defined as hemorrhagic ascites [23]. Some neoplastic lesions such as hepatocellular carcinoma and hepatoma



and some non-neoplastic disorders such as trauma and Budd-chiari syndrome are different etiologies of hemorrhagic ascites in human[23, 24]. The presence of hemorrhagic ascites in cirrhotic patients had a poor prognosis[23]. In the present study the red blood cell count in abdominal fluid was about 100000 cell / $\mu$ l, and the patient showed a progressive microcytic anemia. In addition to iron deficiency, microcytic anemia can be seen in dogs with multiple acquired porto-systemic shunts which is related to an unknown defect in mobilization of iron stores[20]. With attention to echocardiography and laboratory results heart failure and heart worm disease were ruled out. On the basis of clinical signs and symptoms and laboratory and Ultrasonography results post-sinusoidal hypertension and early stages of liver failure were considerable in the dog. Prescribing a hepatic failure treatment protocol during three weeks could decrease the abdominal effusion formation, decrease liver enzyme activities, increase the serum albumin level, and improve pain abdomen and clinical signs. However progressive weight loss in spite of a good appetite and abdominal fluid formation were present. Histopathology study on liver biopsy showed a diffuse sinusoidal distension without significant inflammation in liver parenchyma, loss of hepatocytes in hepatic cords and their substitution by erythrocytes which was well-matched with post-sinusoidal hypertension and secondary sinusoidal distension. In some area, cellular swelling (hydropic degeneration) of hepatocytes as enlarged cells with clear cytoplasm was present which, most likely, was developed by hypoxia (Fig.1).

Acute cell swelling is a major pathologic event that can be caused by hypoxia and ischemia in different tissues[25].

In human, necrosis and disappearance of hepatocytes in hepatic cords and their replacement by erythrocytes are histopathological features observed in the patient with Budd-chiari syndrome. Also, severe hepatic fibrosis as either veno-portal cirrhosis (when fibrous bridging is seen between hepatic vein and portal tract), or veno-centric cirrhosis (when fibrous bridging between hepatic veins and portal tract is minimal) may develop in patients with this. However, the main histopathological features in patients with cardiac failure are sinusoidal congestions

in liver and peri-cellular and sinusoidal fibrosis and fibrosis around central veins[26, 27, 28]. The clinical and para-clinical signs such as abdominal pain, ascites, hepatomegaly, abdominal transudative effusion with high protein, panhypoproteinemia, microcytic anemia in the patient were compatible with Budd-chiari like syndrome. Ascites, hepatomegaly, and abdominal pain constitute the classic triad of the Budd-Chiari syndrome in human. The most important cause of Budd-Chiari syndrome in human is intravascular thrombosis that is never reported in Budd-Chiari like syndrome in dogs. A complete CT scan and CT angiography of thoracic and abdominal cavity showed no neoplastic lesion; however there were intravascular lesions in pulmonary artery and caudal vena cava. The texture of the lesions was completely compatible with thrombosis. The respiratory distress could be caused by pulmonary artery thrombosis and mild pulmonary edema. Adult respiratory distress syndrome (ARDS), or non-cardiogenic pulmonary oedema and hypoxia could be associated with pulmonary thromboembolism[29]. Furthermore there is a possibility of Hepatopulmonary syndrome (HPS) in this patient. HPS seen in some patients with BCS consists of intrapulmonary vascular dilatation and impaired oxygenation in the setting of liver dysfunction and/or portal hypertension[30].

### **Conclusion**

Obstruction of venous blood flow and Budd-Chiari like syndrome must be considered in dogs with ascites, hepatomegaly, and painful abdomen. Like in BCS in human, thrombosis or thrombosis-like lesion may be involved in Budd-Chiari like syndrome development in dogs. Furthermore, spontaneous formation of intravascular thrombosis in other vessels and partial obstruction of them may cause other clinical signs independent to Budd-Chiari like syndrome.

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### *Conflict of Interest*

The authors declared that no conflict of interest.

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