ISSN: 2754-4931

Journal of Gastroenterology & Hepatology Reports

SCIENTIFIC Research and Community

Case Report

Open Access

Unveiling the Uncommon: Cocaine-Induced Budd-Chiari Syndrome - A Rare Medical Puzzle

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ABSTRACT

Cocaine, a potent stimulant derived from coca plant leaves, is well-documented for its adverse cardiovascular effects. Among these complications, thrombosis has gained prominence as a significant concern, leading to thrombotic events in various vascular beds throughout the body, highlighting cocaine's systemic pro-thrombotic impact. However, its role in hepatic vascular disorders remains relatively underrecognized. This case report details the clinical presentation of a 23-year-old male with Budd-Chiari syndrome linked to cocaine use disorder, emphasizing the critical need for healthcare providers to recognize hepatic vascular disorders as possible outcomes of cocaine abuse.

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Received: November 27, 2023; **Accepted:** December 04, 2023; **Published:** December 11, 2023

Abbreviations
CTB: Computed Tomography Brain
CTA: Computed Tomography Angiogram
JAK 2: Janus Kinase 2
AFP: Alpha-fetoprotein
CEA: Carcinoembryonic Antigen
CA 19-9: Carbohydrate Antigen 19-9
Hep A/B/C: Hepatitis A/B/C
HIV: Human Immunodeficiency Virus
EBV: Epstein-Barr Virus
CMV: Cytomegalovirus
IVC: Inferior Vena cava

Case Report

A 23-year-old man was admitted to the hospital with complaints of abdominal distension, epigastric pain, and chest pain.

The patient had no known comorbidities, was not on regular medication, and had a history of smoking 30 cigarettes per day since the age of 15. Additionally, he consumed two glasses of wine daily. He was in a heterosexual, monogamous relationship and had no previous hospital admissions. The patient also had a history of cocaine use, which included oral, intranasal, and intravenous routes, but he did not share needles. He had been using cocaine until the onset of symptoms about 1 week prior to presentation. It's worth noting that his most recent blood tests, conducted one month prior, were negative for hepatitis B, hepatitis C, and HIV.

Family history revealed that his father had died at the age of 70 due to a haemorrhagic stroke, and his mother had succumbed to breast cancer at the age of 65.

On examination, the patient exhibited tachycardia with a heart rate of 110 beats per minute, regular pulse with no radio-femoral delay and a blood pressure of 150/90 mmHg in both arms. The patient was agitated, and cardiac examination revealed normal heart sounds without murmurs and did not have raised Jugular Venous Pressure or lower limb swelling. Chest examination was unremarkable. Abdominal examination revealed distention with tender hepatomegaly but no splenomegaly.

An electrocardiogram (ECG) revealed sinus tachycardia without ST changes. The urine drug screen tested positive for cocaine and its metabolites. Additionally, a chest X-ray (CXR) did not indicate any cardiomegaly or lung parenchymal abnormalities.

While in the emergency department, the patient had a generalized tonic-clonic seizure that responded to intravenous Midazolam. CTB and CTA scans of the head showed no evidence of infarction or haemorrhage. Abdominal ultrasound (U/S) demonstrated mild to severe ascites and hepatomegaly. A contrast-enhanced CT scan of the abdomen further confirmed the presence of ascites and demonstrated the occlusion of hepatic veins.

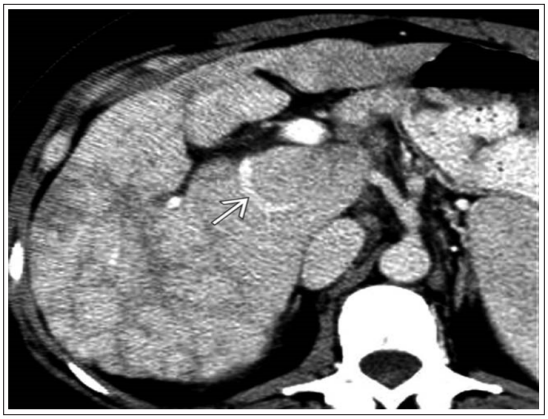

Figure 1: (Right) Axial CECT shows caudate hypertrophy, a large caudate collateral vein, ⇒ and peripheral atrophy and heterogeneity. The hepatic veins were occluded.
N.B- these images are not of the patient in the case study and have been taken from Budd-Chiari Syndrome | Radiology Key [1].

Liver function tests showed elevated alkaline phosphatase (300 U/L) and gamma-glutamyl transferase (GGT) (400 U/L) levels with normal transaminases. Full blood count and kidney function tests were within normal ranges.

Diagnostic abdominal paracentesis was performed, revealing a serum ascitic albumin gradient (SAAG) of 1.3 g/dL and a total protein concentration of 2.8 g/dL, consistent with portal hypertension. The ascitic fluid analysis showed 50 neutrophils and normal cytology. Coagulation studies were normal.

The Colour Doppler ultrasound findings raised concerns about hepatic vein obstruction, suggesting Budd-Chiari syndrome. Following informed consent from the patient, a liver biopsy was conducted, revealing sinusoidal dilation, hepatic congestion, portal expansion, and mild bile ductular proliferation upon hematoxylin and eosin staining. These pathological features further confirmed the diagnosis of Budd-Chiari syndrome.

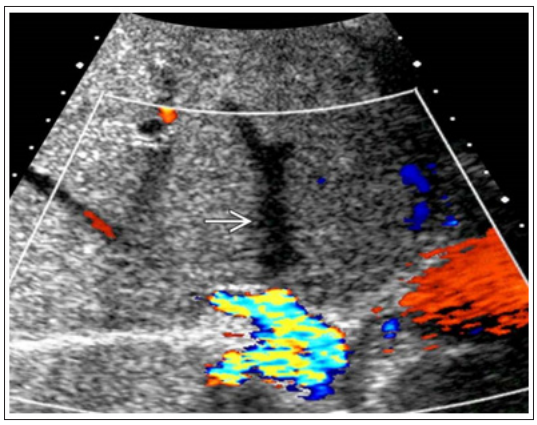

Figure 2: Transverse color Doppler ultrasound of the liver in a 48-year-old reveals a lack of flow within the right hepatic vein.
N.B- these images are not of the patient in the case study and have been taken from Budd-Chiari Syndrome | Radiology Key [1].

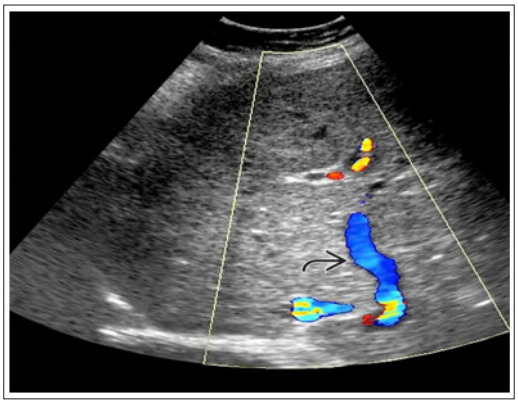

Figure 3: Color Doppler ultrasound in the same patient demonstrates a large intrahepatic collateral vein ↗ bypassing the occluded hepatic veins.
N.B- these images are not of the patient in the case study and have been taken from Budd-Chiari Syndrome | Radiology Key [1].

Subsequently, the patient underwent screening for other potential causes of Budd-Chiari Syndrome, including myeloproliferative disorders, malignancy, and hypercoagulable states. The results showed a negative JAK2 mutation, no evidence of solid organ malignancy on CT scans, and negative tumour markers such as AFP, CEA, and CA19-9. Thrombophilia screening yielded negative results, and repeat tests for infective hepatitis, including Hep A/B/C, HIV, CMV, and EBV, also returned negative findings.

He was initial treated with therapeutic paracentesis, albumin infusion, and diuretics but yielded no improvement. On the third day, therapeutic low molecular weight heparin and warfarin was started. All symptoms resolved within two weeks. Repeat colour Doppler studies showed resolution of hepatic vein occlusion and ascites and warfarin was continued for total of 3 months.

Discussion

This case report presents a rare manifestation of Budd-Chiari syndrome induced by cocaine, resulting in the onset of abdominal pain, hepatomegaly, and ascites accompanied by a Serum Ascites Albumin Gradient (SAAG) exceeding 1.1 g/dL, indicative of non-cirrhotic portal hypertension. To the best of our knowledge, this is the first documented case of Budd-Chiari syndrome directly linked to cocaine use. The diagnosis was definitively established via a liver biopsy, revealing sinusoidal dilation, hepatic congestion, and bile ductular proliferation.

Remarkably, initial therapeutic interventions, including paracentesis, albumin infusion, and diuretics, failed to yield any discernible improvement. Nevertheless, the implementation of anticoagulation therapy, involving low molecular weight heparin and a vitamin K antagonist, resulted in the resolution of clinical symptoms and evidence of vascular occlusion, as ascertained through repeated Doppler studies.

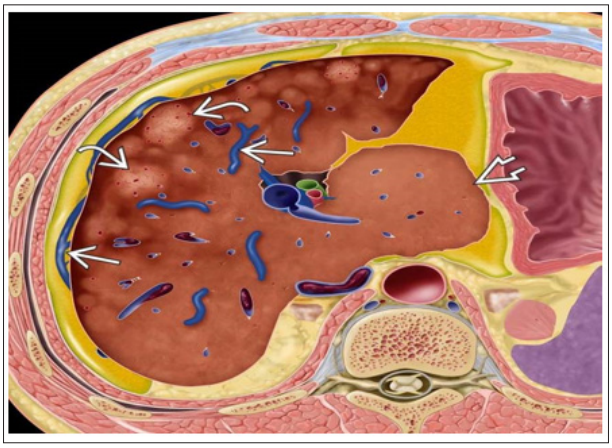

Figure 4: Axial Anatomical Illustration of Budd-Chiari Syndrome-Budd-Chiari syndrome demonstrates ascites, venous collaterals, heterogeneous hepatic parenchyma due to centrilobular necrosis, and hypervascular regenerative nodules. Note the sparing of the caudate lobe with hypertrophy, as well as the thrombosed IVC [1].

Cocaine-induced veno-occlusive disease of the liver is a rare entity characterized by hepatic vascular occlusion. This case underscores the need to consider substance abuse-related hepatopathies, especially in young patients with atypical liver disease presentations.

Cocaine, once used as a local anaesthetic, is now avoided due to its strong addictive properties. It acts as a potent local anaesthetic by blocking voltage-gated sodium channels, raising the threshold for nerve axon excitability, reducing neuroconduction and centrally it inhibits the reuptake of both norepinephrine and serotonin [2].

Adverse effects associated with cocaine use, particularly in the arteries encompass cardiac issues such as sudden cardiac death, acute myocardial infarction, myocarditis, dilated cardiomyopathy, and dissections of coronary/aortic and carotid arteries [3]. The major cerebrovascular effects of cocaine consist of ischemic and haemorrhagic strokes [4, 5]. The clinical phenotype of cocaine hepatotoxicity is usually acute hepatic necrosis.

Cocaine-induced Hepatotoxicity occurs through two mechanisms: the conversion of cocaine into the harmful metabolite norcocaine (NC) through P450 metabolism and the constriction of central liver veins, which leads to severe hepatic inflammation and tissue necrosis [6].

The vascular effects of cocaine have been extensively studied, with the majority of research focusing on the acute and more common arterial thrombosis, which carries a higher associated mortality rate compared to venous thrombosis [7]. However, it is important to recognize the potential significance of cocaine-induced venous thrombosis, as illustrated in our case report. This is particularly crucial when considering life-threatening conditions such as Budd-Chiari syndrome that can result from it. While our case represents a rare instance of Budd-Chiari syndrome linked to cocaine-induced venous thrombosis, studies have increasingly highlighted a greater occurrence and prevalence of venous thrombosis among individuals with a history of cocaine abuse [8].

The intricate physiological process of cocaine-induced accelerated thrombosis includes endothelial damage promoting an increase in fibrinogen and Von Willebrand factor resulting in the aggregation of platelets and, ultimately, the formation of blood clots [3]. Cocaine also induces a heightened inflammatory response in the immune system, accompanied by reduced levels of natural anti-inflammatory markers like interleukin-10 and increased pro-inflammatory cytokines (e.g., tumour necrosis factor alpha, Interleukin 1β) all contributing to vascular disease [3, 9]. Additionally, cocaine usage leads to quicker clot formation, enhanced platelet activation, and an increase in the activity of plasma plasminogen activator inhibitor (PAI-1), all of which are associated with an elevated risk of thrombus formation [10-12]. While the clotting mechanisms used to describe arterial thrombosis can also apply to venous thrombosis, the comparatively lower occurrence of the latter condition sparks curiosity about uncovering additional elements that might contribute to the development of cocaine-related venous thrombosis. The recognition of these elements is vital for anticipating and addressing this condition. Suggested mechanisms include the potential direct harm caused by cocaine to the veins, which could be exacerbated by the citric acid used to dissolve the drugs, as well as the local anaesthetic properties of cocaine, adulteration of cocaine with vasoactive substances such as quinine, procaine phencyclidine, antihistamine, methamphetamine, decreased circulation due to inactive muscle pumps when a person is intoxicated, damage to the endothelial lining caused by injections, and elevated levels of blood clotting factors resulting from infections introduced through injections [13-16].

At present, there exist no established specific management protocols for Cocaine-induced venous thrombosis, and these cases are typically managed in accordance with provoked venous thrombosis guidelines within the context of cocaine usage. It is essential to underscore that the prevention of secondary complications and the mitigation of disease progression in individuals with cocaine use disorder necessitate two critical measures: discontinuation of cocaine use and cessation of cigarette smoking. It is noteworthy that abstaining from cocaine or reducing its usage can significantly contribute to the reduction of endothelial-1 damage, underscoring the importance of these interventions in clinical practice [17-18].

In conclusion, Cocaine-induced veno-occlusive liver disease, albeit rare, presents a significant threat to patient survival. Timely recognition and the application of appropriate therapeutic measures, including anticoagulation therapy, can lead to favourable patient prognosis. This case serves as a compelling reminder of the critical importance for healthcare providers to maintain a high level of vigilance in identifying and understanding the hepatic vascular consequences linked to cocaine abuse, particularly when confronted with patients afflicted by cocaine use disorder who present with abdominal pain and distension.

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