An enigmatic case presentation of Budd-Chiari syndrome with pulmonary embolism: An unusual syndrome with an uncommon complication

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1. Introduction

Budd–Chiari syndrome (BCS) can be specified as a pathophysiological process that results in an interruption or reduction of normal blood flow out of the liver at any level between the juncture of the inferior vena cava to the right atrium and the small hepatic veins. This definition excludes sinusoidal obstruction syndrome and hepatic outflow obstruction secondary to right-sided cardiac disease [1].

BCS is rare, especially in western countries, and is considered a potentially life-threatening condition. The prevalence of BCS is greatly determined by geographical differences. The clinical manifestation of BCS is heterogeneous, with manifestations ranging from acute liver failure to completely asymptomatic patients [1].

The triad of abdominal pain, ascites, and hepatomegaly is commonly present in patients with abdominal pain presenting in 61%, ascites in 83% and hepatomegaly in 67% of patients. Other clinical features include fever, pedal oedema, and truncal hepatic veins. Less common clinical manifestations include oesophageal bleeding (5%) and hepatic encephalopathy (9%) [2]. Up to 20% of patients are entirely asymptomatic [3]. BCS can be classified as being primary with obstruction due to an endoluminal aberration, secondary compression or invasion of an outside lesion [1].

In the West, primary BCS can be considered a rare hepatic presentation of an underlying prothrombotic condition [4]. The underlying prothrombotic condition is mostly undiagnosed when the hepatic venous outflow obstruction presents. Multicentre data illustrate that between 25% and 46% of patients have multiple coexisting prothrombotic conditions. Primary BCS is therefore regarded

Abbreviations: BCS, Budd–Chiari syndrome; PE, pulmonary embolism; CT, computed tomography; MRI, magnetic resonance imaging; BID, twice per day; V/Q, ventilation/perfusion; TIPS, transjugular intrahepatic portosystemic shunt; OLT, orthotopic liver transplantation; RCTs, randomized controlled trials; 3-D, three dimensions.

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Table 1
Biochemical test results and tumour marker levels.

| Test: | Result (normal range): |
|-------|------------------------|
| Haemoglobin | 11.8 (13.0–18.0) g/dL |
| WBC count | 8.7 (4.0–11.0) k/μL |
| Platelets | 150 (140–450) k/μL |
| PT | 21.6 (10.4–13.4) s |
| INR | 1.9 |
| aPTT | 33.4 (22.2–32.9) s |
| Lactic acid | 9.60 (0.4–2.0) mmol/L |
| FDP | 40 (<10 g/mL) |
| Serum total protein | 6.8 (6–8) g/dL |
| Albumin | 3.2 (3.5–5) g/dL |
| SGOT | 160 (15–37) U/L |
| SGPT | 170 (14–63) U/L |
| LDH | 280 (81–234) U/L |
| GGTP | 380 (5–55) U/L |
| ALP | 158 (46–116) U/L |
| HCG | <2 (=5 IU/L) |
| Cardiolipin IgG | <1.0 (=20 CU) Negative >20 Positive |
| Cardiolipin IgM | <2.6 (<=20 CU) Negative >20 Positive |
| LFT | (LA1 = 41.9 sLA2 = 36.2 sLA ratio = 1.16) |
| Glycoprotein antibody | (31.0–44.0) s (30.0–38.0) s (0.8–1.2) |
| Anti-β2 IgG | <6.4 (<=20 CU) Negative >20 CU Positive |
| Anti-β2 IgM | <1.1 (<=20 CU) Negative >20 CU Positive |
| Anti-double-strand DNA | <9.8 (<27 Negative <27 Intermediate 27–35 Positive >35) |
| AFP | 12 (0–40) ng/mL |
| BHCG | 1.20 (5–25) mU/mL |
| CA 125 | 21 (<35) U/mL |
| CA 19–9 | 0 (0–37) U/mL |
| CEA | 0.50 (<3) ng/mL |

**Fig. 1.** Enhanced CT scan of the abdomen.
a. Axial cut shows a heterogeneous parenchymal attenuation mainly affecting the right hepatic lobe with a filling defect involving the supra-hepatic and hepatic portion of the inferior vena cava (arrow).
b. Coronal cut shows extensive abdominal free fluid tracing into peri-hepatic and peri-pancreatic regions around the gallbladder fossa and Morison pouch as well as a dependent portion of the pelvis with a filling defect involving hepatic vein branches (arrow), consistent with acute Budd-Chiari syndrome.

as a result of a unique constellation of prothrombotic conditions [2].

We describe the case of a patient with BCS and fatal PE (pulmonary embolism) in line with the SCARE criteria [5]. This case considers the first example of co-occurrence of both diseases in a Middle Eastern region; moreover, this enigmatic presentation has never been described in the literature solely without identifiable underlying aetiology in a patient with no major prior medical history.

2. **Presentation of case**

A 20-year-old female of ethnic Arab race, with no known medical disorders, surgical intervention or family history of a similar condition, presented to our emergency room with sudden onset of acute lower abdominal pain referred to the epigastric region with radiation to both shoulders and 2 episodes of vomiting that lasted for approximately 2 h. The patient reported no history of allergy, medications or genetic diseases. Hypothermia, 35.9 °C (96.6 °F), and
Fig. 2. CT angiogram of the chest.

a. CT chest angiogram shows segmental and subsegmental arterial branches of both lower lung lobes; namely, the rig Sagittal reconstruction with 3-Dhht posteromedial basal and left posterior basal segments show filling defects (arrows) in keeping with an acute pulmonary embolism.

b. Sagittal reconstruction with 3-D maximum intensity projection image, that further delineate the endoluminal thrombosis (arrow).

c. CT scan of the chest 3-D volume-rendered reconstructing display technique, seen from the anterior aspect, demonstrates multi-isolated peripheral filling defects denoting an abnormal vascular tree of the pulmonary arteries (arrows).
marginal tachypnea, 23 breaths per minute, with normal oxygen saturation was noted in her vitals. Upon physical examination, she was signed for hepatomegaly. Her complete blood count was normal. However, her basic metabolic profile showed severely elevated liver enzymes (Table 1).

The patient had a contrast-enhanced CT of the abdomen (computed tomography), which showed heterogeneous parenchymal attenuation of enlarged liver with thrombosed hepatic veins as well as supra-hepatic and hepatic portions of the inferior vena cava in favour of BCS (Fig. 1). Later, the patient became hypotensive, 84/63 mmHg, and more tachyypnoeic despite a supply of 4 litres of IV fluid. The CT chest angiogram showed multifocal filling defects in keeping with an acute PE (Fig. 2). Moreover, multiple large mismatched V/Q (ventilation/perfusion) segmental defects were identified (Fig. 3).

The patient declined to undergo various non-invasive radiological interventions to resume hepatic venous flow. Subsequently, she was started on oxygen, total parenteral nutrition, and administration of antithrombotic agents, namely, Clexane [enoxaparin] 60 mg / 0.6 ml BID subcutaneous route. Her abdominal pain, hypothermia, and tachypnea resolved within 48 h.

Follow-up examinations revealed a gradual improvement of the clinical condition with better laboratory results. The patient was satisfied with the management plan and was discharged from the hospital within 1 week in dependable health. She was given an appointment for a further follow-up evaluation with the haematology clinic.

3. Discussion

BCS is the eponym used for referring to hepatic venous outflow obstruction [6]. In our patient, the diagnoses had primarily been enigmatic, especially with the high blood lactic acidosis (Table 1) that disguised our initial impression towards mesenteric ischaemia; however, after carrying out the enhanced CT scan of the abdomen, an existing thrombotic pathophysiology was revealed.

This rare obstruction can be accurately detected by non-invasive imaging, such as with Doppler ultrasonography, CT, or magnetic
resonance imaging (MRI) [6]. There are no data available regarding the diagnostic superiority of MRI over CT to diagnose this rare syndrome; however, MRI seems more useful in patients with renal impairment and younger patients given the avoidance of radiation. Currently, a liver biopsy is not necessary for the diagnosis of BCS.

In our instance, further deterioration was manifested including progressive tachycardia and hypotension. Moreover, fibrinogen degradation products appeared markedly high (Table 1). Therefore, a CT chest angiogram was conducted that revealed the presence of multiple pulmonary emboli. Unfruitfully, the literature data regarding the incidence, treatment, and effects of patients having BCS-related pulmonary emboli are lacking, and we urge conducting future studies.

Therapeutic options for BCS include medical management with anticoagulation therapy, decompressing therapies such as recanalization strategies (thrombolytic therapy, stenting, and angioplasty), surgical shunting and TIPS (transjugular intrahepatic portosystemic shunt). Lastly, OLT (orthotopic liver transplantation) is regarded as the ultimate treatment and salvage procedure for patients who are suffering from end-stage liver disease or have fulminant disease.

Devoid of RCTs (randomized controlled trials) comparing one treatment to another, it is unacceptable for any self-respecting physician to declare one treatment superior to another [7]. With advances in various non-invasive radiological interventions and techniques and a reasonably good midterm outcome, shunt surgery no longer remains the measure of care for BCS.

The natural history of BCS is not well known because there are no cohorts of untreated patients reported; nonetheless, with increasing therapeutic options becoming available over the past decades, the overall survival continues to increase, reaching five-year survival rates between 80% and 90% [2]. The basis of genetic defects can alter the complex mechanism of coagulation, favoring thrombosis in any district it arises, especially with multiple gene mutations. These patients at high risk of thrombosis in all districts should be studied, and efforts and protocols should be more proactive regarding patient diagnosis, treatment and follow-up to decrease mortality, morbidity, and recurrence [8].

Although similar reports in the literature are considered scant, a previous report by R.B. Bestetti et al. [9] discussed a similar co-occurrence of BCS and fatal PE caused by cardiac thrombosis associated with endomyocardial fibrosis. An additional report by Asrani et al. [11] discussed a similar condition of BCS and PE associated with fibrolamelar hepatocellular carcinoma and right atrial thrombus. Both reports supported the suggestion that BCS occurred secondary to the intracavitary thrombi and to the fibrotic pathogenesis, which mandated further investigation towards this poorly understood co-occurrence.

Formerly described subjects with BCS-related PE have been reported with other predisposing conditions, such as soft tissue sarcoma [10], hepatocellular carcinoma [11], restrictive cardiomyopathy [9], Crohn disease and oral contraceptives [12]. Despite all the clinical tests our patient had undergone and the exclusion of all possible underlying aetiologies, the mechanism behind the occurrence of such an immense thrombosis could not be identified.

Whereas the patient was not found to have any coagulation factor deficiency, all other assessment levels were nevertheless within normal limits, such as her inflammatory markers, antithrombin and platelet count. Nonetheless, a persistently normal blood eosinophil count was obtained, excluding the possibility of hypereosinophilic syndrome.

To increase the level of awareness, recent multicentre work has been established that has contributed to an increased understanding of BCS, enhancing the outcomes. Tremendous efforts must be taken in examining patients and determining which are adequate for specific therapies. Rivaroxaban, apixaban, and dabigatran are examples of unfamiliar anticoagulants that do not have adequate or appropriate data for employing them in the BCS. The advancement that some therapies show must efficiently be assessed. Thus, there is a vast need for more researchers to find the exact purpose of MRI for differentiating benign liver nodules with hepatocellular carcinoma in BCS patients [6].

4. Conclusion

BCS is an uncommon and potentially serious condition associated with hepatic venous outflow obstruction. Most patients have multiple underlying prothrombotic conditions, emphasizing the importance of a thorough work-up. All the same, solitary cases, such as in our patient, do not have a predisposing condition(s). Doppler ultrasound is often sufficient for documenting hepatic venous outflow tract obstruction, and other imaging methods, such as CT and MRI, are most frequently utilized for further details. Pulmonary embolism should be added among the listed complications of BCS. The management plan should be designed among a multidisciplinary team of hepatologists, interventional radiologists and transplant surgeons. The desired management outcomes can be ensured with early detection and the provision of better care.

Conflicts of interest

None.

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Ethical approval

As per the “Imam Abdulrahman Bin Faisal University (University of Dammam) Institutional Review Board,” case reports do not require ethical approval or patient consent, provided that there was no intervention and that no patient identifiers appear in the report. Therefore, neither ethical approval nor patient consent was required for this case report. However, Written informed consent was obtained from the patient. A copy of the consent form is available for review by the Editor of this journal.

Consent

Written informed consent was obtained from the patient. A copy of the consent form is available for review by the Editor of this journal. Consent for publication of the manuscript and the related patient information has been obtained by King Fahd Hospital of the University, Imam Abdulrahman Bin Faisal University.

Author contributions

A.M. Al-Sharydah wrote the original manuscript. Radiology image reporting was performed and interpreted by A.H. Al-Abdulwahhab. The revision of the final manuscript was performed by H.A. Abu AlOia. A.M. Al-Sharydah drafted the paper, and all authors read and approved the final manuscript.
Registration of research studies

Non applicable. This case report has no intervention or clinical trial on humans.

Guarantor

A.M. Al-Sharydah.

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