Case Report

Hemorrhagic Shock from Acute Variceal Bleeding Caused by Sarcoidosis: A Case Report

Mark Evert Haaksma[1], Sjoerd van der Bie[1], Ellert J. van Soest[2], Ben Vermin[1], Marco Goeijenbier[1,3]

Departments of [1]Intensive Care Medicine, [2]Gastro-enterology, Spaarne Gasthuis Hospital- Hoofddorp, [3]Department of Intensive Care Medicine, Erasmus MC, Rotterdam, The Netherlands

Abstract

Sarcoidosis is a disease of unknown etiology, characterized by noncaseating granulomas. Generally, the condition primarily manifests in the lungs. Extrapulmonary involvement is common, but localization in the gastrointestinal system is rare. Here, we present the case of a 37-year-old male who became increasingly hemodynamically unstable during the diagnostic workup for sarcoidosis due to acute variceal bleeding. The underlying mechanism was later attributed to portal hypertension caused by hepatic involvement of the disease. This case demonstrates the importance of considering variceal hemorrhage as a rare but life-threatening complication of gastrointestinal localization of sarcoidosis.

Keywords: Extrapulmonary sarcoidosis, upper gastrointestinal tract, portal hypertension, sarcoidosis, shock, variceal bleeding

Address for correspondence: Dr. Marco Goeijenbier, Department of Intensive Care Medicine, Spaarne Gasthuis, Haarlem, Netherlands.
E-mail: mgoeijenbier@spaarnegasthuis.nl

Submitted: 02-Dec-2023 **Revised:** 29-Mar-2024 **Accepted:** 18-Apr-2024 **Published:** 20-Jun-2024

INTRODUCTION

Sarcoidosis is a systemic inflammatory disease that can affect any part of the human body and is characterized by the occurrence of noncaseating granulomas. To date, its etiology is unknown. While pulmonary involvement is most common (in up to 90% of cases), gastrointestinal involvement is rare (in <10% of the cases).[1,2] Cirrhosis and portal hypertension can be clinical manifestations in <1% of cases;[3] however, given the low frequency of these complications, they may be easily missed by the treating physician. Here, we describe a rare case of variceal bleeding and hemorrhagic shock due to hepatic involvement of sarcoidosis in a young male patient.

The CARE Checklist was followed by the authors while preparing this case report.

Access this article online	
Quick Response Code:	Website: https://journals.lww.com/sjmm
	DOI: 10.4103/sjmms.sjmms_629_23

CASE REPORT

A 37-year-old male presented to the emergency department with dyspnea and left thoracic pain that exacerbated on inspiration. He did not have fever, night sweats, cough, palpitations, or chest pain on exertion. Prior medical history only revealed mild liver chemistry disturbances, which at the time were attributed to his recent weight gain.

Bloodwork revealed no signs of inflammation, mildly elevated calcium, and elevated lactate dehydrogenase. Given the high suspicion for pulmonary pathology, thoracic CT was performed. It revealed diffuse pulmonary consolidation [Figure 1], splenomegaly, and calcification of lymph nodes throughout the entire body. Under the strong suspicion of sarcoidosis, sIL-2R was tested and a positron

How to cite this article: Haaksma ME, van der Bie S, van Soest EJ, Vermin B, Goeijenbier M. Hemorrhagic shock from acute variceal bleeding caused by sarcoidosis: A case report. Saudi J Med Med Sci 2024;12:266-9.

emission tomography–computed tomography (PET-CT) was performed. With a value of 24,530 pg/ml, sIL2r was strongly elevated, while the PET-CT demonstrated disseminated metabolic activity in the lungs, liver, spleen, lymph nodes, and bone marrow [Figure 2]. The patient was scheduled for diagnostic excision of an axillary lymph node. Further bloodwork revealed pan-hypopituitarism, potentially through cerebral localization of sarcoidosis, for which hydrocortisone was started as the first step of the treatment process.

After an uncomplicated lymph node excision, the patient became progressively hypotensive and passed melena. He was admitted to the ICU under suspicion of an ulcerative bleed and was started on vasopressor therapy and continuous proton pump inhibitor infusion. Extensive laboratory analysis was performed [Table 1]. The following day, gastroscopy was performed and revealed an actively bleeding varix [Figure 3], upon which the procedure

Table 1: Bloodwork at admission and directly after variceal bleed

Parameters	Reference values	At admission	After variceal bleed
Hemoglobin	8.5–11.0 mmol/L	4.3	6.2
Hematocrit	0.40–0.50 L/L	0.21	0.28
Platelets	150–400×10^9/L		159
Leukocytes	4.0–10.0×10^9/L	18.8	19.6
Factor I (fibrinogen)	2.0–4.0 g/L	1.0	
APTT	22–30 s	25	
INR	0.95–1.17	1.4	
pH (art)	7.35–7.45	7.42	7.41
PO_2 (art)	10.0–13.3 kPa	10.0	17.9
PCO_2 (art)	4.7–6.4 kPa	3.7	4.9
Bicarbonate (art)	21.0–28.0 mmol/L	18.2	23.5
Base excess	−3.0–3.0 mmol/L	−5.7	−0.9
Sodium	135–145 mmol/L	148	155
Potassium	3.5–5.1 mmol/L	4.4	3.5
Chloride	96–107 mmol/L	122	126
Urea	2.5–6.4 mmol/L	8.9	8.9
Creatinine	64–104 umol/L	78	72
eGFR (CKD-EPI)	>60 mL/min/1.73 m^2	>90	>90
Bilirubin total	3–20 umol/L	8	
Gamma GT	0–55 IU/L	106	
Alkaline phosphatase	0–115 IU/L	582	
ASAT	0–35 U/L	121	
ALAT	0–45 U/L	38	
LD	0–248 U/L	355	
CK	0–171 U/L	28	
Albumin	35–55 g/L	20.5	
Calcium	2.15–2.55 mmol/L	1.74	
Magnesium	0.70–1.00 mmol/L	0.84	0.91
Phosphate	0.70–1.50 mmol/L	0.82	0.98
Lactate	0.5–1.7 mmol/L	6.1	1.5
Glucose	3.5–7.8 mmol/L	5.3	8.4

APTT – Activated partial thromboplastin time; INR – International normalized ratio; eGFR – Estimated glomerular filtration rate; CKD-EPI – Chronic kidney disease-epidemiology collaboration; GT – Glutamyl transferase; ASAT – Aspartate amino transferase; ALAT – Alanine amino transferase; CK – Creatine kinase; LD – Lactate dehydrogenase

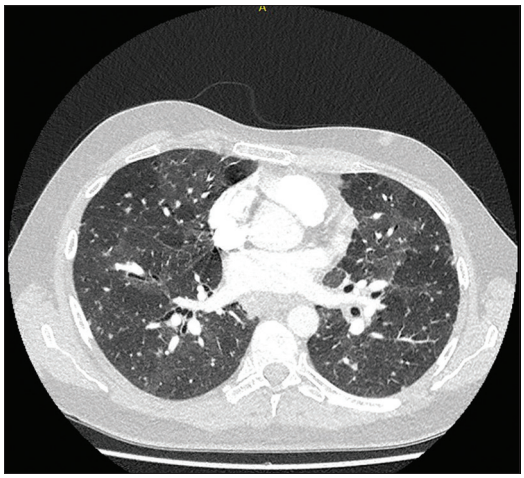

Figure 1: Transverse chest computed tomography showing diffusely consolidated lung tissue

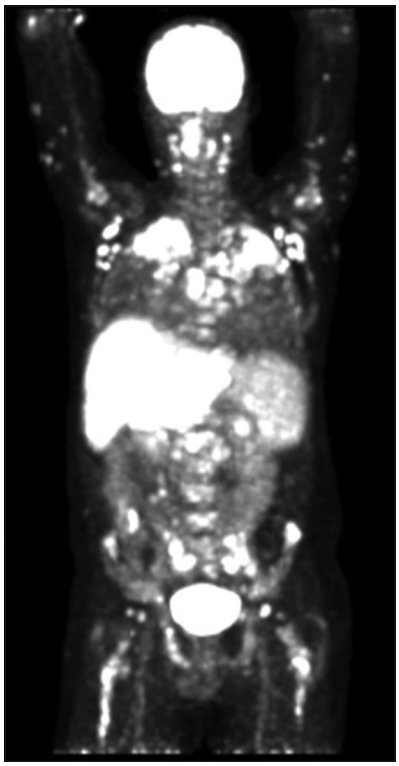

Figure 2: Positron emission tomography–computed tomography demonstrating disseminated metabolic activity in lungs, liver, spleen, lymph nodes and bone marrow

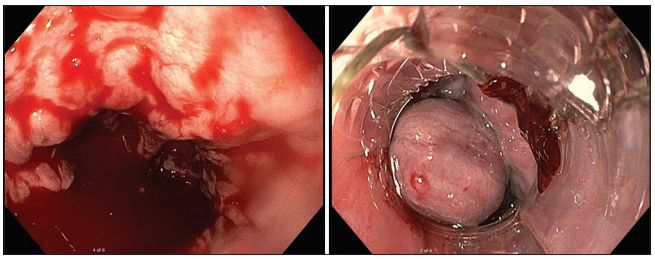

Figure 3: Left image: Endoscopy of the esophagus with severe active bleeding. Right image: Endoscopy of the esophagus showing a ligated varix

was ended to prepare for intubation before proceeding. During pre-oxygenation, the patient started to repeatedly vomit large amounts of blood. After a failed attempt to place a Sengstaken balloon, continuous suction briefly provided improved visibility, which allowed for successful intubation. Subsequently, the gastroscopy was continued, and actively bleeding varices could be ligated. During the procedure, four units of packed red cells, four units of fresh frozen plasma, four units of thrombocytes, 1000 cc 0.9% sodium chloride, and 2g of calcium gluconate were transfused [Table 1]. The patient was started on ceftriaxone prophylaxis and continuous octreotide and pantoprazol perfusion.

After three days, the patient remained hemodynamically stable and he was extubated. A week later he was discharged. Follow-up and subsequent treatment were to occur at a tertiary academic hospital, given the severity and complexity of the disease, with yet-to-be confirmed but suspected cerebral localization of granulomas. Later, a histological diagnosis of sarcoidosis was made.

DISCUSSION

The present case illustrates the importance of recognizing extrapulmonary manifestations of sarcoidosis, especially those of the gastrointestinal system that result in portal hypertension and acute upper gastrointestinal variceal bleeds. Including this rare but potentially fatal complication of sarcoidosis in the differential diagnosis of a hemodynamically unstable patient with a prior history of the disease could lead to earlier identification, treatment, and safer intervention. As such, we aimed to summarize the pathophysiology of variceal bleeding in patients with sarcoidosis and provide a brief outline of the current treatment recommendations.

Sarcoidosis can manifest anywhere in the body including, although less frequently, the gastrointestinal system. An even more rare occurrence is cirrhosis and portal hypertension as consequences of hepatic involvement of the disease. The underlying pathophysiology is not fully understood, with several hypotheses postulated, of which the most straightforward is through the obstruction of hepatic venous outflow by granulomas, similar to the mechanism of portal hypertension in cirrhosis. However, there is also evidence for the presence of arteriovenous shunts within the granulomas potentially also contributing to the rise of portal pressure.[4] Another hypothesis is that granulomas in the portal circuit restrict flow, and thus increase presinusoidal pressure.[5] Regardless of the exact cause, the final common pathway is elevation in the portal venous system, which leads to an increase in esophageal vein size, and subsequently, risk for spontaneous bleeds from them.

Fast and deliberate treatment is vital, given the poor prognosis of patients with variceal hemorrhage. The first step is securing the airway to prevent aspiration. Hemodynamic instability is initially treated with bolus infusions of isotonic crystalloids. Transfusion strategy in severe ongoing bleeding is identical to trauma patients in a 1:1:1 ratio for red blood cells, plasma, and platelets.[6] This remains the case even in the presence of disturbed coagulation panels, as they are poorly representative of true hemostatic balance given variable pro- and anticoagulant effects of cirrhosis.[7] Subsequent permissive hypotension and avoidance of volume overload are important to reduce the risk of rebound portal hypertension and rebleeding.[8,9]

Pharmacological intervention in upper GI bleeds includes proton pump inhibitors, antibiotics, somatostatin (analogs), and less frequently, vasopressin (analogs). While proton pump inhibitors have not been proven to improve clinical outcomes in cirrhosis, current guidelines still advocate their use in treating patients with hypothesized upper gastrointestinal bleeding of still unknown cause.[10] In proven variceal hemorrhage, they have no role.[11] Prophylactic antibiotics are the only option that reduce overall mortality, rebleed, and infections, and thus should be administered as soon as possible.[12] Typically, ceftriaxone is the antibiotic of choice for a duration of up to 7 days. Somatostatin (analogs) prevent rebleeding and help achieve hemostasis, but have no proven benefit on mortality.[13] Vasopression (analogs) have potent vasoconstrictive properties on the splanchnic system, but are considered third-line therapeutic regime given the increased frequency of adverse events. Endoscopic treatment consists of ligation of bleeding varices. If prompt endoscopy is not possible, balloon tamponade devices, such as the Sengstaken or Linton tube can be used.

The disease progression of hepatic sarcoidosis is poorly documented and highly variable. This entails that treatment indication, its timing, and choice of therapeutic drug are just as unclear. To date, no randomized controlled trials are available that compare agents and their efficacy. As such, current treatment strategies are based on retrospective studies.

The available evidence suggests that corticosteroids generally form the first line of treatment, typically started around 20–40 mg prednisone daily.[14] Other treatment options include antimetabolites (e.g., azathioprine and

methotrexate), alkylating agents (e.g., cyclophosphamide) biologic agents (e.g., infliximab) or a combination of these with corticosteroids.[15,16] The goal of the treatment is to limit sarcoidosis-related symptoms and to prevent disease progression and loss of hepatic function. Whether normalization of liver chemistry disturbances during treatment is related to better long-term outcomes is unclear.

CONCLUSION

Variceal hemorrhage is a rare but life-threatening complication of gastrointestinal localization of sarcoidosis. It should be considered in the differential diagnosis of patients presenting with upper gastrointestinal bleeding.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

Peer review

This case report was peer-reviewed by two independent and anonymous reviewers.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Fauci AS, Braunwald E, Isselbacher KJ, Wilson JD, Martin JB, Kasper D, *et al*. Harrison's Principles of Internal Medicine. 14th ed. New York, New York, United States: McGraw-Hill; 1997. p. 1406.
2. Vardhanabhuti V, Venkatanarasimha N, Bhatnagar G, Maviki M, Iyengar S, Adams WM, *et al*. Extra-pulmonary manifestations of sarcoidosis. Clin Radiol 2012;67:263-76.
3. Blich M, Edoute Y. Clinical manifestations of sarcoid liver disease. J Gastroenterol Hepatol 2004;19:732-7.
4. Maddrey WC, Johns CJ, Boitnott JK, Iber FL. Sarcoidosis and chronic hepatic disease: A clinical and pathologic study of 20 patients. Medicine (Baltimore) 1970;49:375-95.
5. Mistilis SP, Green JR, Schiff L. Hepatic sarcoidosis with portal hypertension. Am J Med 1964;36:470-5.
6. Weeder PD, Porte RJ, Lisman T. Hemostasis in liver disease: Implications of new concepts for perioperative management. Transfus Med Rev 2014;28:107-13.
7. Tripodi A, Mannucci PM. The coagulopathy of chronic liver disease. N Engl J Med 2011;365:147-56.
8. Villanueva C, Colomo A, Bosch A, Concepción M, Hernandez-Gea V, Aracil C, *et al*. Transfusion strategies for acute upper gastrointestinal bleeding. N Engl J Med 2013;368:11-21.
9. Cerqueira RM, Andrade L, Correia MR, Fernandes CD, Manso MC. Risk factors for in-hospital mortality in cirrhotic patients with oesophageal variceal bleeding. Eur J Gastroenterol Hepatol 2012;24:551-7.
10. Sreedharan A, Martin J, Leontiadis GI, Dorward S, Howden CW, Forman D, *et al*. Proton pump inhibitor treatment initiated prior to endoscopic diagnosis in upper gastrointestinal bleeding. Cochrane Database Syst Rev. 2010;2010:CD005415.
11. Gralnek IM, Camus Duboc M, Garcia-Pagan JC, Fuccio L, Karstensen JG, Hucl T, *et al*. Endoscopic diagnosis and management of esophagogastric variceal hemorrhage: European Society of Gastrointestinal Endoscopy (ESGE) guideline. Endoscopy 2022;54:1094-120.
12. Chavez-Tapia NC, Barrientos-Gutierrez T, Tellez-Avila FI, Soares-Weiser K, Uribe M. Antibiotic prophylaxis for cirrhotic patients with upper gastrointestinal bleeding. Cochrane Database Syst Rev 2010;2010:CD002907.
13. Gøtzsche PC, Hróbjartsson A. Somatostatin analogues for acute bleeding oesophageal varices. Cochrane Database Syst Rev. 2008 Jul 16;2008(3):CD000193.
14. Beegle SH, Barba K, Gobunsuy R, Judson MA. Current and emerging pharmacological treatments for sarcoidosis: A review. Drug Des Devel Ther 2013;7:325-38.
15. Sedki M, Fonseca N, Santiago P, Diaz L, Garcia-Buitrago M, Mirsaeidi M, *et al*. Hepatic sarcoidosis: Natural history and management implications. Front Med (Lausanne) 2019;6:232.
16. Graf C, Arncken J, Lange CM, Willuweit K, Schattenberg JM, Seessle J, *et al*. Hepatic sarcoidosis: Clinical characteristics and outcome. JHEP Rep 2021;3:100360.