ACTA MÉDICA PORTUGUESA
A Revista Científica da Ordem dos Médicos

CASO CLÍNICO

Acute Chest Syndrome and Critical Illness-Associated Cerebral Microbleeds in Sickle Cell Disease: A Case Report

Síndrome Torácico Agudo e Microhemorragias Cerebrais Associadas a Doença Crítica em Doente com Doença Falciforme: Relato de Caso

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Acta Med Port (In Press) ▪ https://doi.org/10.20344/amp.23392

ABSTRACT

A 33-year-old woman with sickle cell disease presented with severe lumbar pain. Initially stable, she experienced rapid deterioration within the first 24 hours, developing respiratory failure, fever, and impaired consciousness. Chest imaging revealed extensive bilateral infiltrates, and laboratory tests showed severe anemia, thrombocytopenia, and elevated inflammatory markers. She required mechanical ventilation, exchange transfusions, and antibiotics. Parvovirus B19 infection was confirmed. After nine days, she improved, but neurological recovery was delayed. Magnetic resonance imaging revealed cerebral microhemorrhages consistent with critical illness-associated cerebral microbleeds. She was discharged after a 34-day hospitalization. This case highlights two severe and potentially life-threatening complications of sickle cell disease, namely acute chest syndrome and critical illness-associated cerebral microbleeds, underscoring the importance of early recognition and aggressive management.
Keywords: Acute Chest Syndrome; Anemia, Sickle Cell/complications; Cerebral Hemorrhage; Parvoviridae Infections; Parvovirus B19, Human

RESUMO

Uma mulher de 33 anos com anemia falciforme apresentou-se com dor lombar intensa. Inicialmente estável, evoluiu com rápida deterioração nas primeiras 24 horas, desenvolvendo insuficiência respiratória, febre e alteração do estado de consciência. Imagiologicamente, apresentava infiltrados pulmonares bilaterais extensos e os exames laboratoriais evidenciaram anemia grave, trombocitopenia e elevação dos marcadores inflamatórios. Necessitou de ventilação mecânica, exsanguineotransfusões e antibioterapia. Confirmou-se infeção por parvovírus B19. Após nove dias, apresentou melhoria clínica, mas mantinha disfunção neurológica. A ressonância magnética cerebral revelou microhemorragias cerebrais compatíveis com microhemorragias associadas a doença crítica. Teve alta após 34 dias de internamento. Este caso destaca duas complicações graves e potencialmente fatais da anemia falciforme, a síndrome torácica aguda e microhemorragias cerebrais associadas a doença crítica, sublinhando a importância do reconhecimento precoce e da abordagem terapêutica agressiva.
Palavras-chave: Anemia Falciforme/complicações; Hemorragia Cerebral; Infecções por Parvoviridae; Parvovírus B19 Humano; Síndrome Torácica Aguda

INTRODUCTION

Sickle cell disease (SCD) is a genetic hematologic disorder characterized by the presence of hemoglobin S, leading to sickle-shaped red blood cells and multiple complications.[1] Among these, acute chest syndrome (ACS) is one of the most frequent and life-threatening, accounting for approximately 25% of SCD-related deaths.[2] Acute chest syndrome is defined by new radiographic pulmonary infiltrates with fever and/or respiratory symptoms.[1] In adults, about 78% of ACS episodes result from a vaso-occlusive crisis which can lead to bone marrow infarction and the release of fat emboli into the pulmonary circulation.[3,4] Mortality rises with age, from 4.3% to 9% in adults.[5,6]

Additionally, critical illness-associated cerebral microbleeds (CICM) is a rare and newly recognized complication in critically ill patients, often with acute respiratory failure. It is characterized by microbleeds primarily in the subcortical white matter, corpus callosum, and less commonly in the cortex, deep and periventricular white matter, basal ganglia, and thalami. Pathogenesis remains unclear, but hypoxemia may contribute, as similar microbleeds have been observed in high-altitude exposure. Despite few reported cases, CICM carries high mortality and significant long-term neurological sequelae.[7]

CASE REPORT

A 33-year-old woman with SCD (HbSC) presented to the emergency department with severe lumbar pain refractory to morphine. She was hemodynamically stable, afebrile, with an oxygen saturation of 100% on room air, and a Glasgow Coma Scale (GCS) of 15. Laboratory results (Table 1) showed anemia, reticulopenia, low haptoglobin, elevated LDH, and HbS levels above 30%. Chest radiography showed no infiltrates. Lumbar pain was non-focal, with no skin or joint complaints. She denied recent contact with children or immunocompromised individuals possibly infected with parvovirus B19.

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Revisto por/*Reviewed by*: Maria Bourbon de Aguiar Branco Ruão.
Recebido/*Received*: 17/05/2025 - **Aceite/*Accepted*:** 02/09/2025 - **Publicado *Online*/*Published Online*:** 19/11/2025

Given a suspected vaso-occlusive crisis, she was admitted for pain management with intravenous lidocaine and tramadol, alongside intensive hydration.

Within 24 hours, her condition deteriorated significantly, presenting with an impaired consciousness, fever, productive cough with gold sputum and respiratory failure (PaO_2/FiO_2 ratio of 118). Chest radiography showed extensive bilateral pulmonary infiltrates (Fig. 1). Repeat laboratory tests (Table 1) revealed a marked hemoglobin drop, thrombocytopenia and elevated inflammatory markers. Chest computed tomography (CT) showed extensive consolidations in the lower lobes, contiguous posterior consolidations in the middle and upper lobes, scattered ground-glass opacities, and signs of right humeral head necrosis, with no signs of pulmonary embolism (Fig. 2). Echocardiography revealed mild signs of right ventricular dysfunction suggestive of acute pulmonary hypertension. The patient was intubated for mechanical ventilation and treated with oxygen, ceftriaxone and azithromycin. She performed two exchange transfusions (targeting HbS < 15%), which significantly reduced HbS from 44% at admission to 12%, leading to an immediate benefit on microcirculation and regression of hypoxia. Parvovirus B19 infection was confirmed (positive IgM and viral load), while blood cultures and bronchial lavage (BL) cultures and a multiplex polymerase chain reaction panel for pneumonia from BL, were negative.

Clinical improvement was observed after nine days, allowing sedation withdrawal and extubation. However, the patient remained minimally responsive, opening her eyes spontaneously, localizing pain but not vocalizing (GCS 10), responding to voice but not following commands. Brain CT and electroencephalogram were unremarkable. Magnetic resonance imaging (MRI) revealed numerous cerebral microhemorrhages on T2*, symmetrically involving the juxtacortical white matter, corpus callosum, internal and external capsules, and cerebellar peduncles, without restricted diffusion (Fig. 3). A lumbar puncture was not performed because the clinical presentation was not suggestive of central nervous system infection—there were no meningeal signs, seizures, or sudden focal neurological deficits. In addition, non-invasive diagnostic tools were prioritized, and the MRI findings adequately explained the neurological status.

Three days after extubation, the patient was transferred to the general ward. Throughout the 34-day hospitalization, she exhibited a gradual recovery of consciousness. At discharge, she had clinical improvement with resolution of hypoxia, normalization of laboratory results, and a GCS of 15, albeit with mild residual psychomotor slowing. The patient's final diagnoses were ACS and CICM.

At six-month follow-up, the patient maintained a GCS 15 but reported persistent concentration and memory difficulties, consistent with mild cognitive impairment.

DISCUSSION

Acute chest syndrome presents a diagnostic challenge due to its clinical similarity to pneumonia and its potential for rapid progression to respiratory failure within 24 hours and multiorgan failure.[6] Prompt recognition and a multidisciplinary approach are crucial to prevent irreversible lung damage and improve outcomes. Some predictors of poor prognosis are adult age, neurological symptoms, need for mechanical ventilation, abrupt hemoglobin drop, and thrombocytopenia.[4,8] Acute chest syndrome is strongly associated with painful vaso-occlusive episodes involving the chest, spine and abdomen, which may lead to shallow breathing to avoid discomfort, atelectasis, and worsening hypoxia, thereby exacerbating red blood cell sickling. Additionally, vaso-occlusive episodes can lead to bone marrow ischemia and necrosis (evidenced by humeral head necrosis on CT), with a subsequent fat embolization into the pulmonary circulation, causing mechanical pulmonary vaso-occlusion.[4] Possible etiologies of ACS in this patient include vaso-occlusive pain crisis, bone marrow fat embolism, Parvovirus B19 infection and hypoventilation due to pain and opioid use. Bronchoalveolar lavage to identify lipid-laden macrophages and confirm fat embolism was not performed due to the technical challenges of performing the procedure in an invasively ventilated patient, as well as the fact that it would not have changed therapeutic management. Parvovirus B19 likely contributed to aplastic anemia and thrombocytopenia by targeting erythroid progenitor cells and disrupting bone marrow function. Furthermore, this virus has been linked to ACS, by exacerbating anemia, triggering hemolysis, promoting endothelial injury, and increasing sickled erythrocyte adhesion, leading to pulmonary and bone marrow infarction.[9]

Critical illness-associated cerebral microbleed was first described in 2017 in critically ill patients with respiratory failure requiring mechanical ventilation and has been reported in SCD.[7,10] It is a distinct microbleed phenomenon in the cerebral white matter, with MRI findings that may overlap with fat embolism, but limited diffusion restriction supports CICM,[7] as in this case. Treatment is supportive and long-term effects remain uncertain. The largest reported cohort (12 patients), reported 41% mortality and persistent neurologic deficit in 71% of survivors.[10]

This case underscores two severe SCD complications: ACS and CICM, both diagnostic and therapeutic challenges, especially when concomitant. Early recognition, aggressive multidisciplinary management, and prompt intervention are

crucial to improving patient outcomes. While CICM remains an underdiagnosed phenomenon in critically ill patients, requiring further research to clarify its pathogenesis and long-term consequences, increasing clinician awareness may facilitate earlier detection and better care strategies.

ACKNOWLEDGMENTS

The authors declare that generative artificial intelligence tools (e.g., ChatGPT, OpenAI) were used to assist in language editing and formatting, under the supervision of the authors. All scientific content was conceived and validated by the authors.

AUTHOR CONTRIBUTIONS

MJM: Study design, data collection, writing and critical review of the manuscript.
EC: Data collection, critical review of the manuscript.
MAC, SR: Critical review of the manuscript.
RM: Image acquisition, critical review of the manuscript.
All authors approved the final version to be published.

PROTECTION OF HUMANS AND ANIMALS

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the Helsinki Declaration of the World Medical Association updated in October 2024.

DATA CONFIDENTIALITY

The authors declare having followed the protocols in use at their working center regarding patients' data publication.

PATIENT CONSENT

Obtained.

COMPETING INTERESTS

The authors have declared that no competing interests exist.

FUNDING SOURCES

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

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Table 1 – Laboratory results at admission and after 24 hours

Parameter	Reference range	On admission	24 hours later
Hemoglobin (g/dL)	12 - 16	8.6	4.3
Hemoglobin S (%)	--	44	--
Reticulocytes (×10^6/μL, %)	0.8 - 4	0.06 (1.86%)	0.0036 (0.22%)
Haptoglobin (mg/dL)	30 - 200	< 10	< 10
LDH (U/L)	135 - 214	367	938
Total bilirubin (mg/dL)	0.1 - 1.1	0.73	0.91
Leucocytes (x10^3/μL)	3.6 - 11	8.3	12.24
Platelets (x10^3/μL)	150 - 450	241	78
CRP (mg/dL)	< 0.5	0.15	22

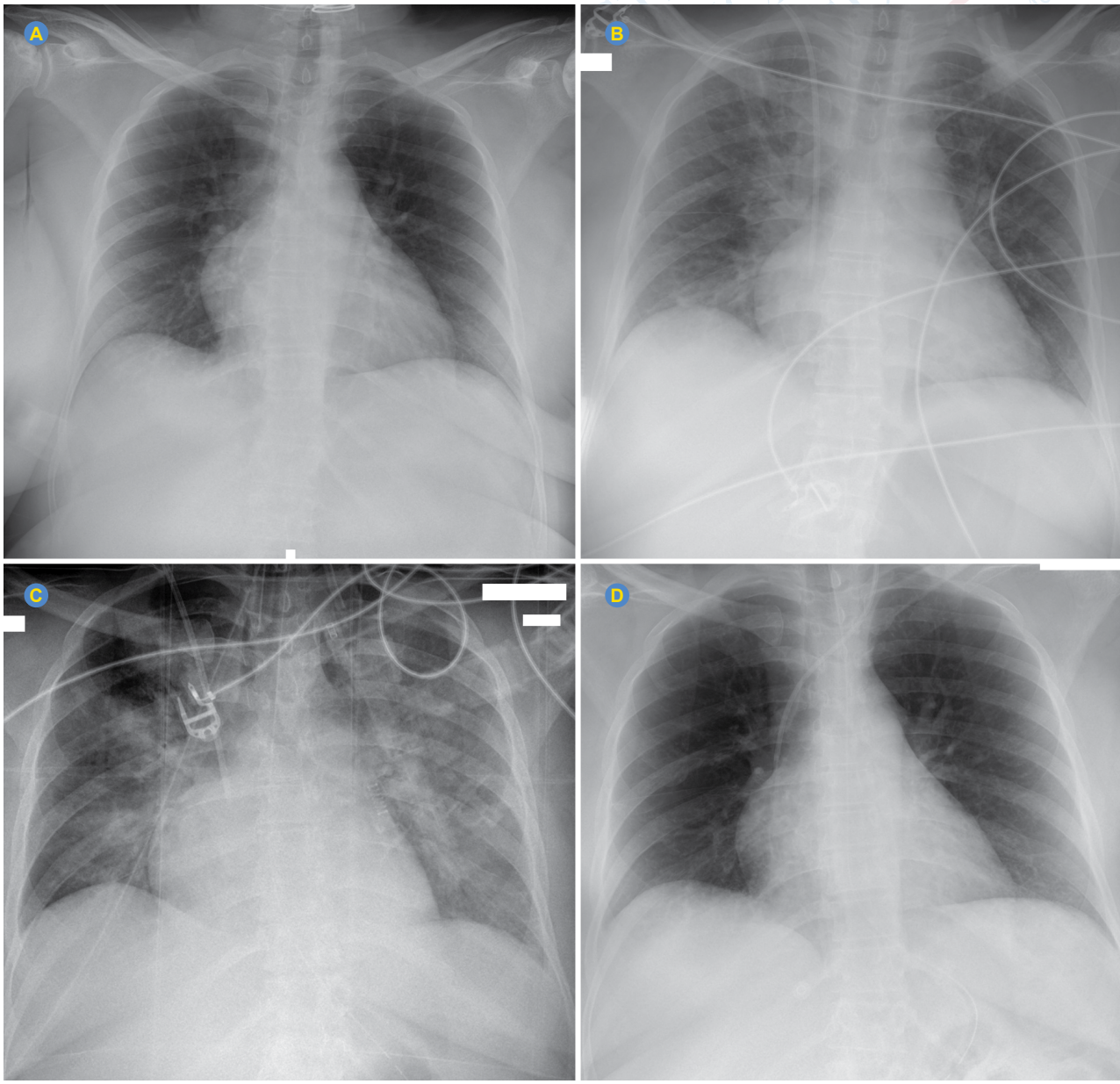

Figure 1 – Chest radiography images (A) at admission, (B) 24 hours after admission demonstrating bilateral opacities, (C) worsening after 48 hours, and (D) normal at discharge

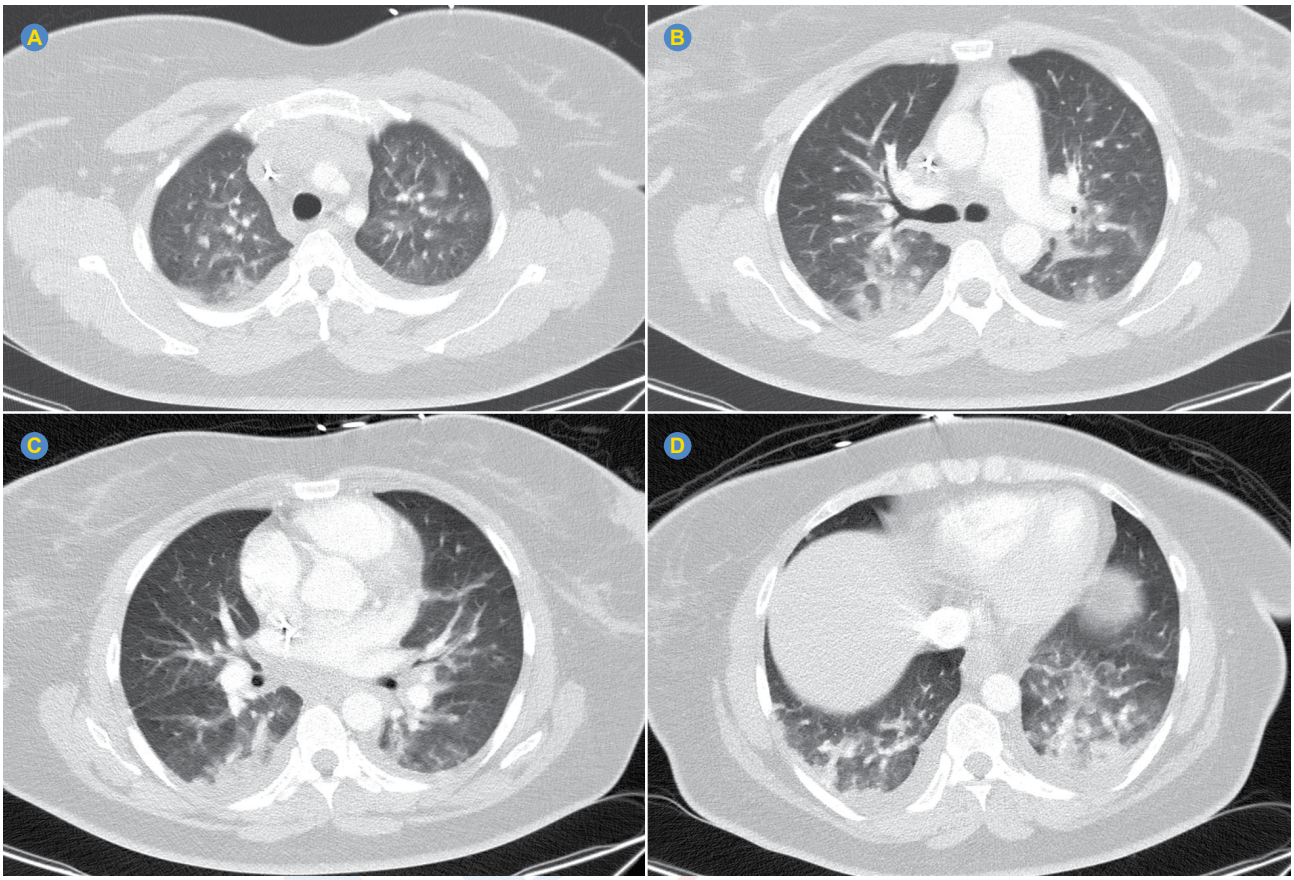

Figure 2 – Chest CT image obtained with the lung window setting shows extensive consolidations in the lower lobes, contiguous posterior consolidations in the middle and upper lobes and scattered ground-glass opacities

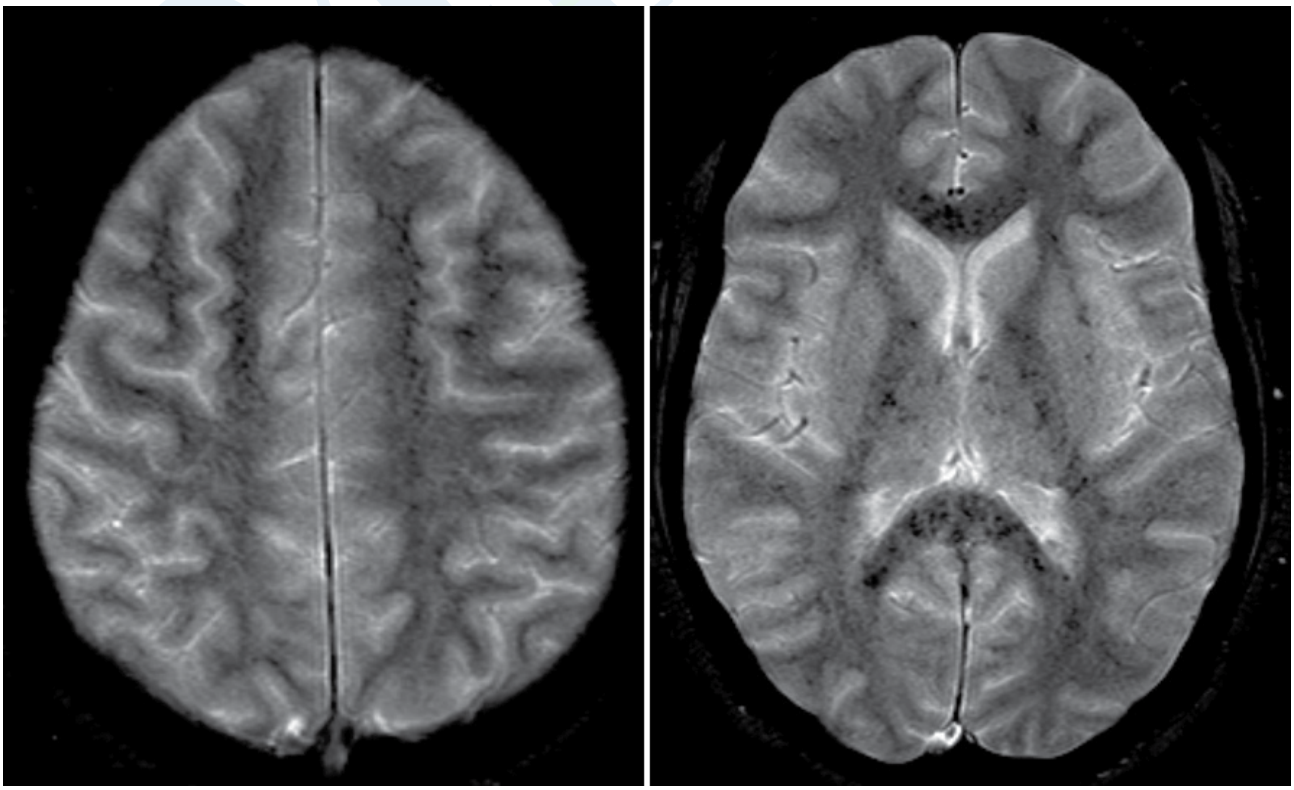

Figure 3 – Axial T2* images demonstrating uncountable diffuse punctate cerebral microbleeds, symmetrically involving the juxtacortical white matter, corpus callosum, internal capsules and cerebellar peduncles (not shown)