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Sickle Crisis Precipitated by Pneumonia: A Diagnostic and Therapeutic Challenge

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Abstract

Sickle cell anemia (SCA) is a prevalent genetic disorder primarily affecting individuals of African descent and populations in malaria-endemic regions, with significant global public health implications. Sickle cell crises are their most common acute complication, characterized by episodes of intense pain and systemic manifestations that impair quality of life and impose a high healthcare burden. We present the case of a 19-year-old male diagnosed with SCA since the age of two, who developed a sickle cell crisis precipitated by right basal pneumonia. The patient exhibited sudden-onset, cyclic lumbar pain with progressive dyspnea. Initial management included multimodal pain control, volume optimization, and targeted antimicrobial therapy to achieve clinical stabilization. This case underscores the importance of a comprehensive approach to managing sickle cell crises, addressing both symptomatic relief and the prevention and treatment of complications. It also highlights the need for public health strategies promoting early diagnosis, access to disease-modifying therapies such as hydroxyurea, and interdisciplinary follow-up to mitigate the socioeconomic and clinical impact of SCA.

Keywords

Sickle Cell Anemia, Sickle Cell Crisis, Pain Management, Pneumonia, Hydroxyurea

1. Introduction

Sickle cell anemia (SCA) is an autosomal recessive genetic disorder caused by a point mutation in the HBB gene on chromosome 11, replacing glutamic acid with valine at the sixth position of the β-globin chain [1]. This alteration leads to the production of abnormal hemoglobin (HbS), which, under conditions of hypoxia, dehydration, or oxidative stress, polymerizes and distorts red blood cells, impairing their flexibility and morphology [1]-[3]. These sickle-shaped cells disrupt blood flow, cause endothelial damage, and contribute to the acute and chronic complications of the disease, known as sickle cell crises [4] [5].

SCA has historical roots in African regions where malaria is endemic, conferring a selective advantage against Plasmodium falciparum infection. This phenomenon supports the balanced polymorphism theory, suggesting that this mutation serves as an adaptive factor in these populations [3] [6]. However, SCA was not recognized in Western medical literature until 1910, when Dr. James B. Herrick first described a case in Chicago [2]. Since then, the disorder has been extensively studied due to its significant morbidity and mortality [7]. In 2006, the World Health Organization (WHO) declared it a global public health concern, highlighting the high pediatric mortality rates in resource-limited settings, particularly in sub-Saharan Africa, where mortality can reach up to 90% within the first years of life [3] [5].

Bacterial infections are among the most common triggers of sickle cell crises, exacerbating inflammatory responses through pathogen-associated molecular patterns (PAMPs) [7]-[9]. This highlights the importance of an integrated approach to managing these complications, including infection prevention through vaccination and antibiotic prophylaxis, alongside the early identification of acute decompensations [9].

The role of infections as a precipitant of vaso-occlusive crises (VOCs) and acute chest syndrome (ACS) has been well-documented in the literature. Pathogens such as *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Salmonella* spp. are particularly implicated, with viral infections, including influenza and parvovirus B19, also playing significant roles [5] [7]. These infections exacerbate the already heightened inflammatory state in SCD patients, further increasing the risk of VOCs and multi-organ damage [7]-[9].

Recent advancements in the understanding of infection-induced SCD crises have underscored the importance of individualized treatment protocols [3]. Novel therapeutic approaches, such as the use of hydroxyurea, which increases fetal hemoglobin levels and reduces the frequency of crises, and the exploration of gene

therapies, offer promising avenues for reducing disease burden [3] [5]. Furthermore, the development of rapid diagnostic tools for infectious agents allows for timely intervention, mitigating the severity of crises [6]-[9].

Sickle cell anemia remains a significant clinical and public health challenge, necessitating a multidisciplinary and global strategy to improve quality of life and reduce disease burden in affected communities.

2. Clinical Case

We report the case of a 19-year-old male patient diagnosed with sickle cell anemia (SCA) at the age of 2, undergoing treatment with hydroxyurea 500 mg every 12 hours and folic acid 5 mg daily, who presented to the emergency department with a three-day history of symptoms. The primary complaint was acute onset lumbar pain, described as stabbing and unrelated to physical activity, with an intensity of 7/10 on the visual analog scale. The pain radiated to the right lower limb (posterior region to the popliteal fossa), the right upper limb (to the forearm), and the anterior thoracic region, displaying cyclical characteristics, worsening at night, and unresponsive to acetaminophen 500 mg every 6 hours. The patient reported functional class deterioration accompanied by moderate exertional dyspnea for approximately one week. He denied fever, respiratory, urinary, or gastrointestinal symptoms. A significant history included severe pneumonia a year prior, which required advanced ventilatory support during hospitalization.

On initial physical examination, the patient was hemodynamically stable with a blood pressure of 119/64 mmHg, heart rate of 88 bpm, respiratory rate of 19 breaths/min, oxygen saturation of 97% on room air, and an axillary temperature of 36.8˚C. Notable findings included mucocutaneous pallor, hypochromic conjunctivae, and pale mucosa. Pulmonary auscultation revealed decreased breath sounds bilaterally, predominantly on the right side, without crackles or wheezes. Laboratory tests indicated severe anemia (Hb: 7.1 g/dL), leukocytosis (31,100/mm^3) with neutrophil predominance, mild thrombocytosis, and elevated mean corpuscular volume suggestive of active hemolysis. Acute-phase reactants were elevated (CRP: 12 mg/dL), while renal function, coagulation parameters, and electrolytes were within normal limits (**Table 1**). A computed tomography (CT) scan of the chest showed right basal consolidation syndrome with air bronchograms and pleural effusion, likely of parapneumonic origin (**Figure 1**). Empiric treatment with piperacillin-tazobactam 4.5 grams every 6 hours was initiated, given the patient's history and risk for Pseudomonas aeruginosa. Procalcitonin levels were 0.7 ng/mL, supporting the continuation of the antibiotic regimen. Blood cultures returned negative.

During the initial days of hospitalization, the patient continued to experience severe lumbar pain accompanied by generalized muscle and polyarticular pain, consistent with a sickle cell crisis. Analgesic management was adjusted with morphine 3 mg every 4 hours, achieving a favorable response. The dose of hydroxyurea was increased to 500 mg every 8 hours. Folic acid administration was

maintained, and goal-directed fluid management was implemented, including 2500 mL of Ringer's lactate infusion over 24 hours, with continued hydration based on clinical response.

On the fifth day of evolution, the patient experienced an exacerbation of pain, requiring intensified analgesic management using a multimodal regimen that included opioids, NSAIDs, and acetaminophen, ultimately achieving adequate pain control. Fluid management was optimized with adjusted infusion rates, contributing to the progressive resolution of the crisis. As an additional measure, respiratory incentive exercises were initiated to prevent pulmonary complications. These interventions stabilized the patient, leading to favorable clinical evolution and gradual resolution of the pain crisis. The combination of timely management with multimodal analgesic therapy, intensive fluid resuscitation, medication adjustments, and non-pharmacological support was pivotal in resolving the clinical presentation, emphasizing the importance of an integrated approach to sickle cell crises.

Table 1. Laboratory results.

	Value	Reference
Sodium	141 mEq/L	135 - 145 mEq/L
Potassium	4.25 mEq/L	3.5 - 5.2 mEq/L
Cloro	100.2 mEq/L	96 - 106 mEq/L
Calcium	9.4 mg/dL	8.5 - 10.2 mg/dL
Magnesium	2.1 mg/dl	1.7 - 2.2 mg/dL
Glycemia	89 mg/dL	70 - 110 mg/dL
Aspartate aminotransferase	37 U/L	4 - 40 U/L
Alanine aminotransferase	39 U/L	4 - 36 U/L
TP	12.8 seconds	Control 12.5 seconds
TTP	25.5 seconds	Control 25.8 seconds
Creatinine	0.61 mg/dL	0.6 - 1.1 mg/dL
BUN	10.2 mg/dL	7 - 21 mg/dL
C reactive protein	12 mg/dL	<5 mg/dL
Blood Count		
Hemoglobin	7.1 g/dL	12.5 - 16 g/dL
Hematocrit	31.2%	33 - 39%
Medium corpuscular value	102.5 fL	80 - 97 Fl
Leucocytes	31.100/mm^3	4.500 - 10.000/mm^3
Neutrophiles	21.770/mm^3	1.500 - 5.000/mm^3
Lymphocytes	6.220/mm^3	3.6 - 8/mm^3
Platelets	475,000/u/L	150,000 - 450,000/uL

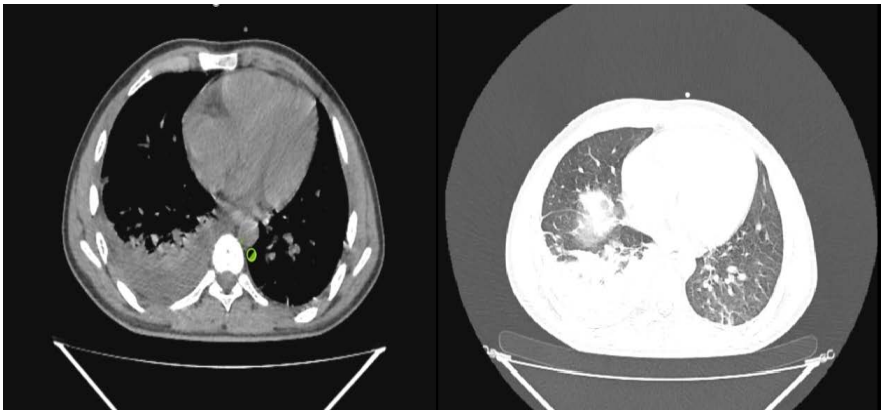


Figure 1. Plain Chest Computed Tomography. A right-sided pleural effusion is observed, associated with an air bronchogram and a right basal consolidative process. The mediastinal structures appear unremarkable.

Finally, on the eighth day of hospitalization, the patient was discharged due to favorable clinical progress and gradual resolution of the pain crisis. The adjusted hydroxyurea dose of 500 mg every 8 hours and folic acid 5 mg daily were continued. Clear instructions were provided for maintaining adequate oral hydration at home, using rescue analgesics as needed, and avoiding triggers for new crises. Follow-up was scheduled with complementary studies, including complete blood count and liver and kidney function tests, to evaluate hematological response and optimize management. The patient was referred to the hematology service for comprehensive follow-up, long-term treatment adjustment, and education about the condition, aiming to prevent future complications.

3. Discussion

Sickle cell anemia (SCA) is a genetic disorder that poses significant clinical challenges, particularly when complicated by acute vaso-occlusive crises often triggered by infections [1]-[3]. These crises, characterized by severe pain, organ dysfunction, and microvascular obstruction, demand early and multidisciplinary management [10]. The presented case highlights the complex interaction between infections and the underlying pathophysiological mechanisms in SCA, as well as the necessity of a comprehensive management approach.

3.1. Role of Infections in Crisis Pathophysiology

Infections play a pivotal role in triggering vaso-occlusive crises through immunological and pro-inflammatory mechanisms [5]. Pathogen-associated molecular patterns (PAMPs) activate the NLRP3 inflammasome, leading to the release of inflammatory cytokines such as IL-1β and IL-6 [11] [12]. These responses exacerbate oxidative stress, promote endothelial dysfunction, and facilitate hemoglobin S polymerization, altering erythrocyte morphology [3] [13]. The resulting sickle-shaped erythrocytes increase endothelial adhesion and microthrombus formation, contributing to vascular obstruction, tissue ischemia, and organ

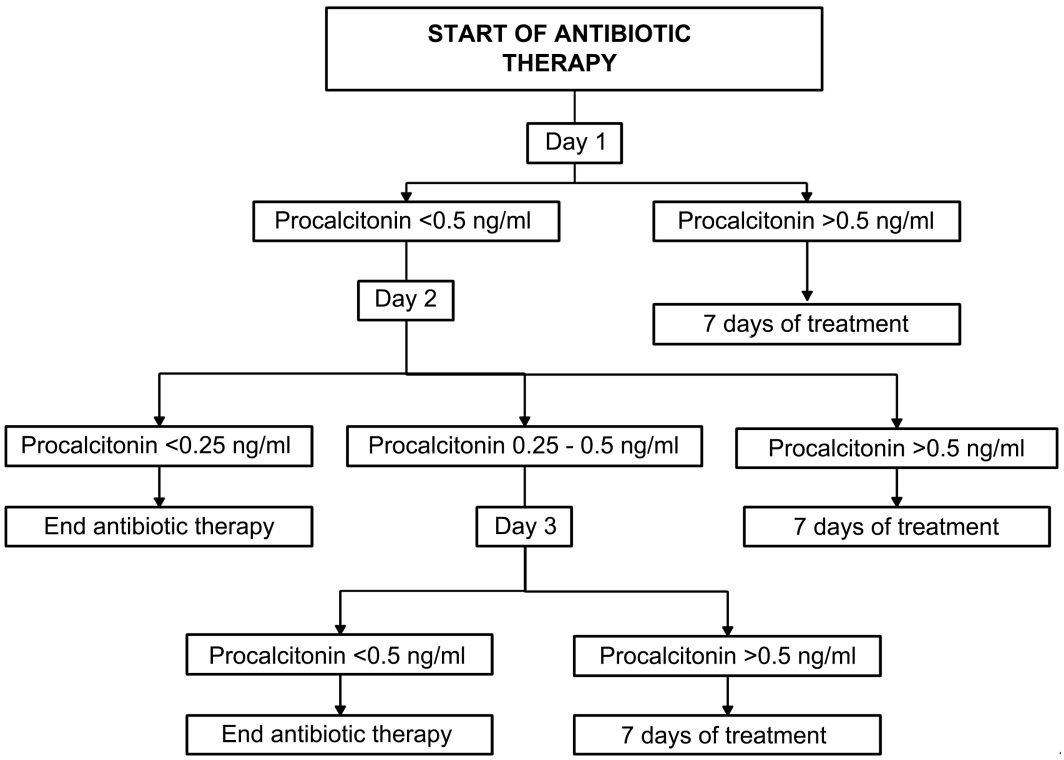
dysfunction [11] [13] [14].

3.2. Pharmacological Management

Prompt and appropriate management of underlying infections is critical to preventing crisis progression. In this case, the timely administration of piperacillin-tazobactam addressed the risk posed by encapsulated bacteria such as *Streptococcus pneumoniae* and *Haemophilus influenzae*, which are common in patients with functional asplenia [11] [15]. Early initiation of targeted antimicrobial therapy reduces the inflammatory burden and controls the infectious process, mitigating systemic impact [16].

Fluid management also plays a central role. Infection-exacerbated hypovolemia can precipitate hemoconcentration, favoring microthrombus formation [17]. In this case, Ringer's lactate infusion restored tissue perfusion and stabilized the patient. However, careful fluid resuscitation is essential to avoid complications such as acute chest syndrome, a severe pulmonary complication in SCA patients [15] [17] [18].

The use of biomarkers such as procalcitonin enhances the precision of antimicrobial management [19]. This marker distinguishes bacterial infections from non-infectious inflammatory processes, enabling therapeutic adjustments based on clinical progression [20]. Procalcitonin levels above 0.5 ng/mL, as observed in this case, justified the continuation of the antibiotic regimen, optimizing treatment while minimizing the risk of antimicrobial resistance [19] [20].



Algorithm 1. Antimicrobial therapy guided by procalcitonin levels. Adapted from Dilip *et al.*

3.3. Non-Pharmacological Interventions

Non-pharmacological strategies are equally vital in comprehensive management. Incentive spirometry and supplemental oxygen use are cost-effective interventions that enhance oxygenation, reduce the risk of atelectasis, and prevent pulmonary complications [13] [21] [22]. These measures, combined with antimicrobial therapy and pain management, significantly contribute to the patient's recovery.

3.4. Pain Management

Severe pain, a hallmark of vaso-occlusive crises, requires a stepwise and multimodal analgesic approach [8] [12] [13]. In this case, the use of opioids, nonsteroidal anti-inflammatory drugs (NSAIDs), and adjuvants enabled effective pain control. Adequate analgesia not only improves quality of life during hospitalization but also prevents complications associated with uncontrolled pain, such as prolonged immobility and tissue hypoxia [10].

3.5. Long-Term Perspectives

Beyond acute management, this case underscores the importance of preventive measures and interdisciplinary follow-up. Disease-modifying therapies, such as hydroxyurea, have demonstrated efficacy in reducing the frequency and severity of crises by decreasing hemoglobin S polymerization [23] [24]. Additionally, antimicrobial prophylaxis, vaccination against encapsulated pathogens, and patient education are essential to mitigate the long-term impact of the disease.

This case highlights the challenges of managing sickle cell anemia (SCA) exacerbations, particularly those involving severe pain crises triggered by multifactorial mechanisms, including infection and hemolysis. The interplay between infection, microvascular occlusion, and systemic inflammation necessitated a prompt, multidimensional approach combining aggressive analgesic therapy, targeted antimicrobial treatment, and precise fluid management. The delayed recognition of underlying complications, such as parapneumonic effusion, underscores the need for vigilance in evaluating secondary causes contributing to symptom severity. Key lessons include the importance of integrating pharmacological and non-pharmacological interventions, optimizing chronic treatment regimens, and providing comprehensive patient education to mitigate future crises.

4. Conclusion

This case underscores the pivotal role infections play in precipitating sickle cell crises and highlights the necessity of prompt and targeted management to mitigate their impact. Infections, such as the right basal pneumonia observed in this patient, exacerbate systemic inflammation, promote hemoglobin S polymerization, and contribute to vaso-occlusive complications. The timely administration of broad-spectrum antimicrobial therapy, guided by clinical and biomarker assessments like procalcitonin, was instrumental in controlling the infectious process and preventing further systemic deterioration. In addition to infection

management, the case demonstrates the importance of integrating aggressive pain control, individualized fluid therapy, and non-pharmacological interventions to stabilize patients during crises. Preventive strategies, including vaccination, prophylactic antibiotics, and patient education, are crucial to reducing the risk of infection-induced crises. This case reinforces the need for vigilance in identifying and addressing infections as a central component of managing sickle cell anemia exacerbations. A multidisciplinary approach that prioritizes infection prevention and early treatment can significantly improve patient outcomes and reduce the clinical and socioeconomic burden of the disease.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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