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Delayed Hydroxyurea Use in Adult Female Sickle Cell Anaemia: A Missed Long-Term Management Opportunity

Saeed M Kabrah[1*]
[1]Department of Clinical Laboratory Sciences, Faculty of Applied Medical Sciences, Umm Al-Qura University, Makkah, Kingdom of Saudi Arabia

Author Designation: [1]Associate Professor

*Corresponding author: Saeed M Kabrah (e-mail: smkabrah@uqu.edu.sa).

Abstract **Objectives:** Sickle Cell Anaemia (SCA) is a lifelong haemoglobinopathy marked by chronic haemolysis, recurrent vaso-occlusive crises (VOCs), and progressive organ damage. Hydroxyurea is a well-established disease-modifying therapy; however, its use in adults remains inconsistent, particularly in regions with limited access to specialised care. **Case Presentation:** We describe a 35-year-old Saudi woman with homozygous SCA who presented with acute back and limb pain unresponsive to standard analgesia. She reported frequent admissions and transfusions but had never received hydroxyurea. On admission, she was tachypneic with oxygen desaturation (SpO_2 80%) and borderline hypotension. Laboratory evaluation revealed normocytic anaemia (Hb 8.2 g/dL), elevated lactate dehydrogenase (317 U/L), reticulocytosis (6.12%), and severe vitamin D deficiency (7 ng/mL). Hydroxyurea (500 mg/day) was initiated in conjunction with folic acid and vitamin D supplementation. At the two-week follow-up, her pain score improved from 6/10 to 3/10, her energy levels increased, oxygen saturation stabilised, and laboratory monitoring demonstrated reduced haemolysis with stable haemoglobin levels. **Discussion and conclusion:** This case illustrates how delayed initiation of hydroxyurea represents a missed therapeutic opportunity in adult SCA, particularly among women beyond childbearing age. The timely use of hydroxyurea, combined with the correction of comorbidities such as vitamin D deficiency, can improve quality of life. Standardised pathways and systematic reassessment are urgently needed to ensure consistent adult SCA care.

Key Words Sickle Cell Anaemia, Hydroxyurea, Vaso-occlusive Crisis, Case Report, Saudi Arabia

INTRODUCTION

Sickle Cell Anaemia (SCA) is a hereditary haemoglobinopathy that continues to cause a significant health burden in regions such as sub-Saharan Africa and the Middle East, where the sickle cell gene is more prevalent due to consanguineous marriage customs [1]. In Saudi Arabia, particularly in the Eastern and Southwestern regions, the disease is notably common, and premarital screening programmes have been implemented to reduce transmission through public health interventions [2-4].

Despite improvements in early diagnosis and paediatric care, adult patients with SCA remain vulnerable to significant morbidity and mortality, especially when long-term, disease-modifying therapies are underutilized. Vaso-Occlusive Crises (VOCs), chronic haemolytic anaemia, and progressive end-organ damage are hallmark complications [5-7]. Hydroxyurea, the first-line disease-modifying agent for SCA, reduces the frequency of VOCs, hospitalizations, and transfusion needs while promoting foetal haemoglobin (HbF) production [6,8]. However, real-world evidence shows its use is frequently delayed or avoided in adult patients, particularly among women of reproductive age, due to concerns about teratogenicity, inadequate counselling, and fragmented care [9,10].

This case report highlights a critical clinical and systemic gap in the delayed initiation of hydroxyurea in a symptomatic adult SCA female, despite multiple indicators supporting early intervention. It demonstrates how missed opportunities in commencing hydroxyurea therapy in adults with known SCA can arise from a combination of provider-related hesitancy, system-level limitations, and fragmented follow-up. This highlights the need for enhanced care pathways to address these challenges. Although the complications of SCA have been widely documented, individual case reports remain valuable for illustrating treatment gaps, monitoring biochemical trends during crises, and evaluating responses to interventions in real-world settings [9,11].

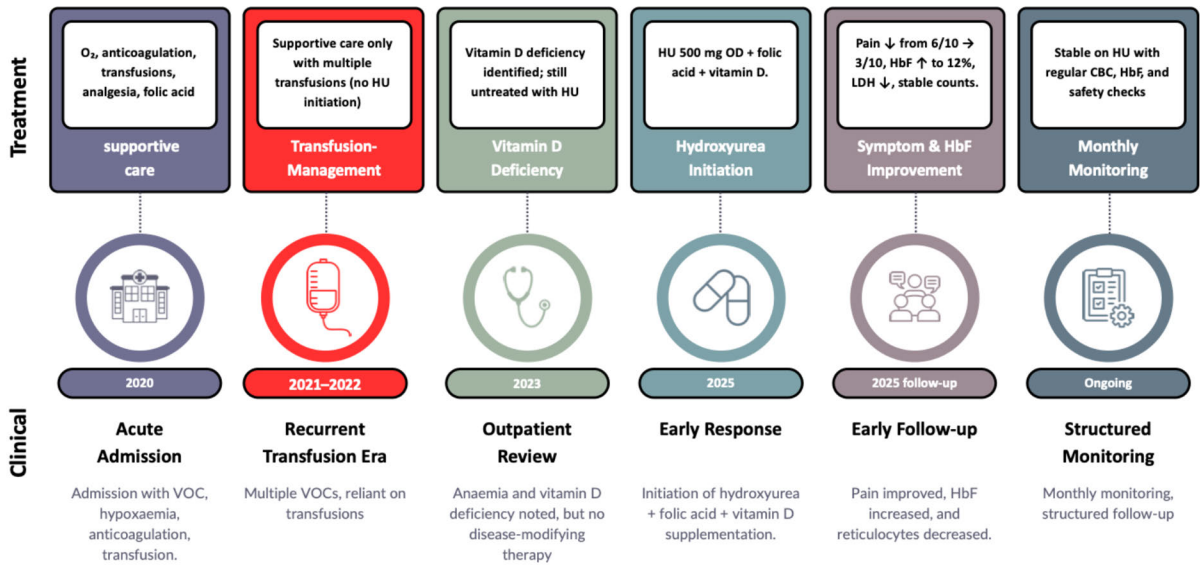

Figure 1: Clinical Course and Treatment Timeline of a 35-Year-Old Female with Sickle Cell Anaemia

The current study presents the case of a 35-year-old Saudi woman with longstanding SCA who had not previously been treated with hydroxyurea, despite a history of multiple transfusions and recurrent VOCs. Her presentation also revealed comorbid vitamin D deficiency, normocytic anaemia, and an elevated haemolysis marker profile, offering a multifactorial insight into her chronic symptoms. What makes this case noteworthy is the combination of delayed hydroxyurea initiation, absence of iron overload despite frequent transfusions, and the correction of modifiable comorbidities, all within the context of transitioning from crisis-oriented to preventive care.

The case also situates itself within broader themes in the literature, including studies by Sabina *et al.* [6] and Barton *et al.* [8], which have described both the benefits and the underuse of hydroxyurea therapy in adult populations. By examining the diagnostic process, therapeutic initiation, and early response, this report contributes to the growing body of evidence that underscores the importance of timely hydroxyurea intervention. Clinicians should maintain a high index of suspicion for under-treated sickle cell patients, particularly adults who have aged out of paediatric care pathways. Regular assessment for hydroxyurea eligibility, even in clinically stable patients, is crucial to avoid therapeutic delays that may worsen prognosis and quality of life.

Case Presentation

Patient Description

The patient was a 35-year-old O^+ Saudi woman, married, and the mother of one child. She was a known case of homozygous SCA (HbSS genotype) diagnosed in early childhood. At the time of presentation, she was not on any disease-modifying therapy and had no history of hydroxyurea use (Figure 1).

Case History

Her medical history was significant for frequent admissions with VOCs, usually managed with supportive measures and intermittent blood transfusions (Figure 1). The most recent transfusion occurred three weeks before this presentation, during an admission at a peripheral hospital. She had not attended regular haematology follow-up and reported persistent fatigue, musculoskeletal pain, and reduced functional capacity, which she attributed to her chronic anaemia. There was no history of stroke, thromboembolism, or avascular necrosis. Past surgical history included a laparoscopic cholecystectomy for gallstone disease. She denied fever, cough, chest pain, abdominal discomfort, or urinary symptoms at this visit.

This schematic timeline illustrates the clinical trajectory and treatment pathway of a 35-year-old woman with homozygous Sickle Cell Anaemia (SCA). In November 2020, she was admitted with a vaso-occlusive crisis (VOC), hypoxaemia, and suspected acute chest syndrome/pulmonary embolism, managed with oxygen, anticoagulation, transfusions, and supportive care. During 2021–2022, she experienced multiple recurrent crises requiring repeated transfusions, but no disease-modifying therapy was initiated. By August 2023, outpatient review confirmed persistent anaemia and severe vitamin D deficiency, though hydroxyurea had still not been prescribed. In January 2025, hydroxyurea (500 mg once daily) was initiated in conjunction with folic acid and vitamin D supplementation. At two-week follow-up in 2025, the patient reported symptomatic improvement with reduced pain scores (VAS 6/10 → 3/10), increased foetal haemoglobin (HbF), decreased reticulocytes, and improved biochemical markers. She continues under ongoing structured monthly monitoring, including full blood counts, haemoglobin electrophoresis, and safety assessments, with no further hospitalisations reported in the first month of therapy.

Physical Examination

Upon examination, she appeared pale and mildly distressed due to pain, but was alert and oriented. She was afebrile with a temperature of 36.2 °C. Her pulse was 92–108 beats per minute, and her blood pressure was 118/74 mmHg. The respiratory rate was elevated at 22 breaths per minute, and oxygen saturation was 80% on room air, which improved to 99% with 5 L/min of oxygen administered via face mask. Chest auscultation revealed bilateral basal crepitations extending to the mid-zones. The cardiovascular assessment revealed a regular rhythm with normal heart sounds and no murmurs. Abdominal examination revealed no tenderness, masses, or hepatosplenomegaly. Neurological examination was unremarkable, and there were no clinical signs of deep vein thrombosis.

Results of Pathological Tests and Other Investigations

Initial laboratory investigations at admission (November 19, 2020) demonstrated a normocytic, normochromic anaemia with a haemoglobin level of 9.3 g/dL, haematocrit of 28%, and a reduced red cell count of 3.01×10^{12}/L (Table 1). The white blood cell count was significantly elevated at 17.75×10^{9}/L, reflecting an acute vaso-occlusive episode, while the platelet count was normal at 363×10^{9}/L. Red cell distribution width (RDW) was increased at 15.5%, indicating anisocytosis, and the reticulocyte count was 6.12%, consistent with an active marrow response to haemolysis. Lactate dehydrogenase (LDH) was markedly elevated at 317 U/L, corroborating ongoing haemolysis. Serum ferritin levels were within the normal range at 258 ng/mL, indicating neither iron deficiency nor iron overload, despite her history of multiple transfusions.

Haemoglobin electrophoresis (Table 1) confirmed homozygous SCA (HbSS genotype), with HbS at 85.6%, HbA at 1.6%, HbF at 9.3%, and HbA2 at 3.5%. The moderately elevated HbF was considered a protective factor, although it was insufficient to prevent recurrent crises. Biochemical evaluation revealed a serum albumin level of 24 g/L, which is reduced from the normal reference range, suggesting a negative acute-phase

Table 1. Longitudinal Laboratory Follow-up in a 35-Year-Old Woman with SCA

Parameter (unit)	Reference Range	Initial (19-Nov-2020)	Last (13-Jan-2025)	Clinical Implication
Haemoglobin (g/dL)	12 – 16	9.3	8.0	Chronic anaemia, slightly worsened
WBC ($\times10^{9}$/L)	4.0 – 10.0	17.75	8.2*	VOC leukocytosis → resolved
RBC ($\times10^{12}$/L)	3.8 – 4.8	3.01	2.5	Ongoing haemolysis
HCT (%)	36 – 46	28.0	23.0	Reduced oxygen delivery
MCV (fL)	85 – 95	93.0	92.1	Normocytic pattern
MCH (pg)	27 – 32	30.9	32.2	Normochromic pattern
Platelets ($\times10^{9}$/L)	150 – 400	363	336	Stable; no thrombocytopenia
RDW (%)	11.6 – 14.0	15.5	15.2	Mild anisocytosis
MPV (fL)	6.2 – 12.5	10.1	7.5	Lower with hydroxyurea, possible marrow effect
LDH (U/L)	98 – 192	317	382.7	Elevated during haemolysis
Sodium (mmol/L)	135 – 150	136	136	Normal throughout
Potassium (mmol/L)	3.5 – 5.0	3.6	3.75	Stable within normal limits
HbA (%)	95 – 98	1.6	1.3	Absent in HbSS; confirms diagnosis
HbA2 (%)	1.5 – 3.5	3.5	3.0	Within expected range
HbF (%)	0 – 2	9.3	12.0*	Increased with hydroxyurea; protective
HbS (%)	0	85.6	83.0*	Slight decline with therapy
Vitamin D3 (ng/mL)	>30	7.0	28.6	Corrected with supplementation
Ferritin (ng/mL)	20 – 300	258	240	Stable, no iron overload
Reticulocytes (%)	0.5 – 2.0	6.12	3.5	Decreased after hydroxyurea, reflecting reduced haemolysis
Pain Score (VAS, 0–10)	–	6/10	3/10	Clear improvement
Serum Albumin (g/L)	35-52	24	41.5*	Initially low (possible acute-phase response or nutritional insufficiency); normalised on follow-up
ALT (U/L)	<40	38	35	Stable; no hepatocellular injury
AST (U/L)	<40	36	34	Stable
ALP (U/L)	44 – 147	90	88	Within normal
Blood Urea Nitrogen (mg/dL)	7 – 20	11	13	Stable renal function
Creatinine (mg/dL)	0.6 – 1.1	0.7	0.8	Stable renal function
Total Bilirubin (mg/dL)	0.2 – 1.2	3.2	2.8	Persistently elevated; chronic haemolysis
Serum Glucose (mg/dL)	70 – 110	92	95	Normal
Amylase (U/L)	<100	45	42	Stable
Lipase (U/L)	<60	32	30	Stable
Magnesium (mmol/L)	0.7 – 1.0	0.9	0.88	Stable
Sodium (mmol/L)	135 – 150	136	137	Normal
Potassium (mmol/L)	3.5 – 5.0	3.6	3.8	Normal
Chloride (mmol/L)	96 – 106	102	103	Normal
CK (U/L)	<200	120	110	No evidence of muscle injury
CK-MB (U/L)	<25	18	16	No myocardial damage
LDH (U/L)	98 – 192	317	220	Elevated initially, decreased with hydroxyurea

response or nutritional insufficiency. Total bilirubin was elevated at 3.2 mg/dL, reflecting chronic haemolysis.

Liver enzymes (ALT 38 U/L, AST 36 U/L, ALP 90 U/L) and renal parameters (urea 11 mg/dL, creatinine 0.7 mg/dL) were within acceptable limits. Electrolytes remained normal, with sodium levels at 136 mmol/L and potassium levels at 3.6 mmol/L. Amylase, lipase, creatine kinase, and CK-MB were also within reference ranges. Vitamin D3 was profoundly deficient at 7 ng/mL, consistent with her musculoskeletal complaints.

At follow-up on January 13, 2025 (Table 1), laboratory monitoring revealed persistent anaemia, with a haemoglobin level of 8.0 g/dL and a haematocrit of 23%, although the white blood cell count had normalised to 8.2×10^{9}/L. Platelet count remained stable at 336×10^{9}/L. Reticulocytes had decreased to 3.5% and LDH to 220 U/L, indicating reduced haemolytic activity after initiation of hydroxyurea. Haemoglobin electrophoresis showed HbS 83.0% with a corresponding rise in HbF to 12.0%, consistent with the expected pharmacological effect of hydroxyurea. Serum albumin improved to 41.5 g/L, within the normal range, suggesting resolution of the acute-phase response. Vitamin D3 normalized to 28.6 ng/mL after supplementation. Liver and renal function remained stable, with bilirubin showing a mild improvement to 2.8 mg/dL.

Pain assessment was performed using a validated Visual Analogue Scale (VAS) at both admission and follow-up (Table 1). At baseline, the patient reported a pain score of 6/10, consistent with significant but manageable discomfort. Following initiation of hydroxyurea and vitamin D therapy, the score improved to 3/10 at the two-week review, indicating a clinically meaningful reduction in symptom burden.

Overall, the laboratory and clinical findings support a diagnosis of homozygous SCA with recurrent VOCs and chronic haemolysis, compounded by severe vitamin D deficiency. Longitudinal follow-up demonstrated stabilisation of haematological indices, correction of nutritional deficiencies, and a favourable early response to hydroxyurea.

Table 1 summarises the haematological, biochemical, and clinical parameters of the patient at admission (November 19, 2020) during a vaso-occlusive crisis and at the most recent follow-up (January 13, 2025) after initiation of hydroxyurea therapy. Reference ranges are provided for comparison. The data illustrate persistent anaemia, resolution of initial leucocytosis, an improved reticulocyte count, and an increasing HbF level with hydroxyurea therapy. Biochemical markers, including renal and hepatic function, remained stable, with serum albumin and vitamin D corrected by supplementation. Pain was assessed using the Visual Analogue Scale (VAS), showing improvement from 6/10 to 3/10 at follow-up.

Treatment Plan

At the time of her initial admission in November 2020, the patient presented with a VOCs complicated by hypoxaemia, leucocytosis, and biochemical evidence of haemolysis (Figure 1). She was managed acutely with oxygen supplementation, therapeutic anticoagulation (Clexane), intravenous fluids, analgesia, and folic acid. Broad-spectrum antibiotics were administered empirically, given her increased susceptibility to infection, though no sepsis was documented. Pain was managed with paracetamol and NSAIDs, with escalation to opioids as needed. Following stabilisation, she continued to be monitored through supportive care and received intermittent blood transfusions during subsequent admissions in 2021–2022, without introduction of disease-modifying therapy.

By August 2023, during the haematology clinic review, the patient was clinically stable but continued to experience recurrent VOCs. Laboratory workup demonstrated chronic anaemia, adequate iron stores, and severe vitamin D deficiency. Despite these findings, hydroxyurea had not yet been commenced, and management remained supportive.

In January 2025, after a multidisciplinary review, a proactive treatment strategy was adopted in line with contemporary haematological guidelines for adult sickle cell disease. Hydroxyurea was initiated at 500 mg orally once daily for the first time. The decision was based on her history of frequent VOCs, chronic haemolysis, and transfusion dependence. Prior to initiation, the patient received structured counselling regarding the benefits of hydroxyurea, the need for routine monitoring of complete blood count, renal and hepatic function, and reproductive considerations. Folic acid 5 mg daily was prescribed concurrently to support erythropoiesis.

Given her severe vitamin D deficiency (7 ng/mL), she was commenced on cholecalciferol 50,000 IU weekly for eight weeks, followed by a maintenance dose. Serum albumin, initially low at 24 g/L, was also targeted with nutritional counselling and later normalized to 41.5 g/L by follow-up. Supportive recommendations included maintaining adequate hydration, avoiding recognised triggers of VOC, such as cold exposure and overexertion, and promptly recognising warning signs.

Follow-up was arranged two weeks after hydroxyurea initiation, where her pain score improved from 6/10 to 3/10 on a VAS. Reticulocyte counts decreased from 6.12% at baseline to 3.5%, and HbF increased from 9.3% to 12.0%, demonstrating an early biochemical response to therapy. Monthly haematology follow-up was planned to continue monitoring haematological indices, HbF response, and potential cytopenias, alongside evaluation of renal and hepatic safety.

In summary, her treatment plan evolved from reactive, transfusion-based management to a structured disease-modifying approach incorporating hydroxyurea, nutritional correction, and longitudinal monitoring. This strategy aimed to reduce the frequency of VOCs, limit transfusion requirements, and improve quality of life through proactive, guideline-based care.

Table 2 provides a structured timeline of the patient's care pathway, from presentation to follow-up and outcomes.

Table 2: Timeline of Clinical Management and Follow-up

Visit / Date	Event / Intervention	Notes
November 19 2020 (Admission)	Presentation with VOC; suspected ACS/PE; admitted at 31+6 weeks' gestation with back and chest pain, tachypnoea, and hypoxaemia	GCS 15, SpO_2 80% RA → 98% on O_2; WBC 17.75 ×10^9/L, Hb 9.3 g/dL, retics 6.12%, LDH 317 U/L; HbS 85.6%, HbF 9.3%; started therapeutic anticoagulation (Clexane), analgesia, folic acid
Late Nov 2020	Doppler US (no DVT), Echocardiogram (EF 75%, PASP 40 mmHg)	No right ventricular strain; PE not excluded; managed as VOC/possible ACS
2021–2022	Multiple transfusions for VOC; supportive management only	No initiation of hydroxyurea during this period
Aug 2023 (Clinic)	Stable between crises; not on HU	CBC: Hb 8.2 g/dL, WBC 7.9, Plt 406; ferritin 258 ng/mL; vitamin D deficiency (7 ng/mL) identified
Jan 2025 (Clinic)	Initiation of Hydroxyurea 500 mg OD, Folic acid, Vitamin D replacement	First time on disease-modifying therapy; baseline VAS 6/10 for pain
Jan 2025 (2-week FU)	Symptom reassessment	Pain VAS improved from 6/10 → 3/10; HbF increased to 12%, retics decreased to 3.5%; albumin improved to 41.5 g/L
Ongoing 2025	Monthly haematology follow-up planned	Monitor CBC, reticulocytes, HbF response, renal/liver profile, iron status, and screen for cytopenias

Expected Outcome

Based on her initial laboratory investigations and clinical presentation in November 2020, the primary treatment goals were centred on stabilising acute vaso-occlusive pain, correcting hypoxaemia, and mitigating the risk of complications such as acute chest syndrome or thromboembolism. At baseline, she demonstrated normocytic, normochromic anaemia (Hb 9.3 g/dL, Hct 28%), elevated reticulocyte count (6.12%), and raised LDH (317 U/L), all consistent with ongoing haemolysis. Biochemical evaluation revealed significant vitamin D deficiency (7 ng/mL) and hypoalbuminaemia (24 g/L), both of which were anticipated to contribute to musculoskeletal pain, fatigue, and reduced functional capacity. Haemoglobin electrophoresis confirmed HbSS disease, with markedly elevated HbS (85.6%) and a modestly protective level of HbF (9.3%).

Given this baseline profile, the anticipated outcome of hydroxyurea initiation at 500 mg once daily was a measurable reduction in haemolytic activity, reflected by a decline in reticulocyte count and LDH levels, alongside an increase in HbF percentage. Clinically, this was expected to translate into fewer and less severe VOC episodes, stabilization of haemoglobin concentration, and reduced dependence on blood transfusions. Correction of vitamin D deficiency with high-dose supplementation was expected to improve musculoskeletal health, enhance energy levels, and reduce background chronic pain. Folic acid supplementation aimed to support erythropoiesis in the context of ongoing haemolysis.

Additionally, from a systems perspective, the introduction of structured follow-up and close haematology supervision was expected to shift her care from crisis-oriented, transfusion-dependent management toward preventive, longitudinal disease control. The overarching goal was to improve her quality of life, reduce hospitalizations, and provide a foundation for long-term organ protection by adopting a proactive, guideline-driven treatment strategy.

DISCUSSION

This case highlights the complexities of managing adult SCA patients, particularly in the continuity of care, and the proactive use of disease-modifying therapy is inconsistent. The patient, despite a longstanding diagnosis of SCA, was not commenced on hydroxyurea until her mid-thirties, following recurrent VOCs and multiple transfusions. The delay in initiating hydroxyurea reflects a combination of systemic and physician-related factors, including: fragmented follow-up care, provider hesitancy related to female reproductive age, and a persistent reliance on transfusion-based crisis management rather than guideline-directed preventive therapy [11-13]. Such delays are well-documented in the literature and underscore ongoing barriers to the translation of evidence into clinical practice.

Hydroxyurea remains the cornerstone of pharmacological management in SCA, with substantial evidence supporting its role in reducing pain crises, hospitalizations, and transfusion requirements by stimulating HbF production [9, 11]. In this instance, despite the occurrence of frequent VOCs and the administration of transfusions over several years, hydroxyurea was not offered. This omission suggests that concerns regarding fertility, limited physician awareness, or systemic inertia within the healthcare system may have contributed to therapeutic inertia. Notably, by the time treatment was considered, the patient had already completed childbearing, thereby eliminating a common barrier often cited as a reason for delaying the initiation of treatment [14]. This highlights the need for structured protocols to reassess eligibility for hydroxyurea in adults, particularly in women who are beyond childbearing or who have clear indications for therapy. The patient was also advised to maintain adequate hydration, avoid known VOC triggers (e.g., cold exposure, overexertion), and monitor for early signs of complications [15, 16].

Another significant feature of this case was the identification of severe vitamin D deficiency, which was corrected with supplementation. Vitamin D deficiency is increasingly recognized as a prevalent condition in SCA and may exacerbate chronic musculoskeletal pain, contribute to fatigue, and diminish quality of life [17]. Its correction in this patient coincided with both improved biochemical indices and a reduction in pain scores. This underscores the importance of incorporating metabolic and nutritional

screening into the routine care of adult patients with SCA, rather than focusing exclusively on haematological parameters. Inadequate attention to such comorbidities often reflects a system that is geared toward crisis management rather than comprehensive, preventive care [18].

Laboratory follow-up demonstrated a consistent picture of chronic haemolysis, with normocytic, normochromic anaemia, elevated LDH, and high reticulocyte counts at baseline. Following initiation of hydroxyurea, a measurable biochemical response was observed, characterised by a reduction in reticulocytes and LDH, alongside an increase in HbF from 9.3% to 12.0%. The absence of significant iron overload despite multiple transfusions was a noteworthy finding, suggesting either careful transfusion practices or favourable iron handling in this patient [19]. Furthermore, preserved renal and hepatic function, alongside improved albumin levels, reflect a degree of systemic resilience despite years of suboptimal long-term therapy. These findings raise questions about potential protective genetic modifiers and adaptive mechanisms that may influence disease trajectory in some adult SCA patients [20].

Ultimately, this case highlights the broader significance of patient education, shared decision-making, and timely specialist referral [16]. The patient's willingness to initiate hydroxyurea only came after clear counselling on its safety and benefits, reflecting how communication gaps between healthcare providers and patients can perpetuate under-treatment. Integrating structured education programmes and multidisciplinary care models may therefore improve therapy uptake and adherence in adult SCA populations [21,22]. Additionally, the use of a validated VAS to monitor pain provided an objective measure of symptomatic benefit, reinforcing the value of incorporating patient-reported outcomes into routine care [23, 24].

In summary, this case not only demonstrates the clinical benefits of hydroxyurea once initiated but also highlights the consequences of delayed therapy and unrecognised comorbidities in adult SCA. Improved long-term management of similar cases requires a systematic reassessment of therapy eligibility, routine screening for metabolic deficiencies such as vitamin D deficiency, and enhanced patient–provider communication to overcome barriers to disease-modifying treatment.

This report describes a single patient, which restricts the generalisability of the findings. The short-term follow-up period limits our ability to evaluate the long-term effects of delayed hydroxyurea initiation on organ function, disease progression, or overall survival. Some laboratory and clinical data were not available at every time point, which may obscure fluctuations in disease activity or treatment response. Furthermore, while this case documents the clear benefits of hydroxyurea once initiated, it cannot establish causal relationships or quantify the long-term risks of delayed treatment.

This case highlights the need for further research into the impact of delayed hydroxyurea initiation on long-term outcomes, including end-organ damage, transfusion burden, and quality of life. Larger cohort studies and prospective registries could provide evidence to guide the earlier initiation of treatment in adult populations. From a clinical perspective, there is an urgent need for policies that ensure systematic reassessment of therapy eligibility, routine monitoring of metabolic deficiencies, and the development of standardised care pathways for adult SCA. Educational initiatives targeting both healthcare providers and patients may help overcome misconceptions about hydroxyurea, particularly in women beyond childbearing age. At a systems level, tracking treatment initiation times and integrating adult SCA management into national health strategies could help reduce variability in care and prevent missed opportunities for disease modification.

CONCLUSIONS

This case demonstrates the practical consequences of delayed hydroxyurea initiation in an adult SCA patient, despite longstanding indications, such as recurrent VOCs, transfusion dependence, and chronic anaemia. Once therapy was commenced, the patient showed early clinical and biochemical improvement, including reduced pain scores, stabilization of haematological indices, and an increase in HbF. The concurrent correction of vitamin D deficiency further contributed to symptomatic relief, emphasizing the importance of addressing metabolic comorbidities alongside disease-modifying therapy.

The delay in initiating hydroxyurea therapy highlights persistent system-level and provider-related barriers, particularly for women of reproductive age**,** who may be excluded or overlooked. This highlights the need for protocols that mandate regular reassessment of therapy eligibility, especially once childbearing is complete. In parallel, routine screening for vitamin D and other nutritional deficiencies should be incorporated into the care of adults with SCA to optimize their functional outcomes and quality of life.

The crucial lesson from this case is that timely initiation of hydroxyurea, coupled with proactive monitoring and supportive interventions, can reduce the disease trajectory, even in adulthood. For clinicians, the essential finding is to move beyond crisis-oriented care toward structured preventive management. For healthcare systems, strengthening education, continuity of care, and multidisciplinary follow-ups is essential for reducing treatment gaps.

In conclusion, this patient's journey highlights the risks associated with delayed intervention and the benefits of timely comprehensive management. Early recognition of missed opportunities and commitment to proactive therapy can substantially improve the quality of life and long-term outcomes in adults with SCA.

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