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Case Report

Integrated Treatment of Sickle Cell Disease Patient with Associated Thyroid Complications

Atul Desai[1,*], Kavita Desai[1], Hemshree Desai[1], Rutvij Desai[2], Kajal Purohit[3], Chirag Desai[3]

[1]Dhanvantari Clinic, Ayurveda Healthcare and Research Centre, Vyara, Gujarat, INDIA.
[2]Manila Central University, Caloocan, Kalakhang Maynila, PHILIPPINES.
[3]Department of Pharmacology, ROFEL Shri G M Bilakhia College of Pharmacy, Vapi, Gujarat, INDIA.

ABSTRACT

According to several studies, the prevalence of hypothyroidism in SCA patients ranges from 2 to 6%. In India, there is no regular practice for screening for hypothyroidism, despite the negative effects it can have on people with sickle cell anemia. In this case report, we present a case exhibiting the impact of integrated therapy on the clinical response of a 35-year-old woman suffering from sickle cell disease and thyroid disorder. She is suffering from sickle cell disease but considering her complications she was prescribed hydroxyurea for critical complications 11 years prior. After adhering to treatment for more than 6 years she started complaining of weight fluctuation, mood swings and palpitation and experienced sickling-induced complications. She was diagnosed with a thyroid disorder in 2019. She was started on thyroxine and hydroxyurea but her complications and issues did not resolve. Considering her unresolved problem she developed hypothyroidism-associated complications and visited the clinic. With prior knowledge and consent, the 300 mg T-AYU-HM Premium integrated treatment was initiated along with thyroxine. The Hydroxyurea treatment was discontinued. Throughout the treatment, the patient's general health continued to improve. The TSH which was once 150 on the day of the visit increased to 38.87. The RBC was also improvised from 3.83 million/mm^3 to 4.29 million/mm^3. Over two years, the patient showed significant improvements in her symptoms and balancing of thyroid function. This strategy was safer, less expensive and has therapeutic potential for treating sickle cell anemia with thyroid disorder. No adverse reactions were noted.

Keywords: Hydroxyurea, Hypothyroidism, Sickle cell anemia (SCA), T-AYU-HM Premium.

Correspondence:
Dr. Atul Desai
Ayurvedic Physician, Dhanvantari Clinic, Ayurveda Health Care and Research Centre, Vyara, Gujarat, INDIA.
Email: dratuldesai@gmail.com

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INTRODUCTION

Hemoglobinopathies can be effectively prevented by carefully balancing strategies for disease prevention and management. Considering sickle-cell anemia is an autosomal recessive trait, there is no cure currently available. However, the illness and its symptoms can be controlled with a high fluid intake, a nutritious diet, folic acid supplements and painkillers. India is significantly affected by SCD, with approximately 40,000 sickle homozygous births annually.[1,2] The primary obstacles to mapping the condition and giving sickle cell anemia treatment to the tribal people of India include language problems, healthcare access issues and lack of knowledge. Prenatal and premarital screening has been the subject of numerous campaigns and they will be beneficial. A program like this will undoubtedly alter the way that tribes view and handle sickle cell patients.[3,4]

The 300mg T-AYU-HM Premium herbo-mineral pill is intended for use as an effective anti-sickling agent. The herbomineral formulation demonstrated antioxidant and anti-sickling properties in vitro. The formulations have already been investigated with published scientific data on acute, sub-chronic, immunomodulatory activity studies in experimental animals. The retrospective clinical trial on sickle cell patients and pediatric case series to evaluate safety and effectiveness also reported. The references for above mentioned claim are already cited in the work to justify the authenticity.[5-8]

Thyroid failure in Sickle Cell Disease (SCD) patients is not well understood, while the majority of afflicted individuals have had numerous transfusions that are consistent with severe iron overload. Significant iron deposition has been seen in the thyroid gland in some autopsy reports of individuals, indicating that transfusional hemosiderosis and subsequent cellular damage to the thyroid gland may be the cause of the primary thyroid failure. Not many case reports regarding the management of thyroid complications in sickle cell patients are available on the literature database.[9,10]

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CASE PROFILE

This case study is done to enhance the information about integrative treatment options in sickle cell disease patients with thyroid complications. In this case study, a patient with severe sickle cell disease and thyroid complications is shown the results of an integrated treatment approach combining Ayurvedic and modern medicine. The patient was treated at the Dhanvantari Clinic, an Ayurvedic Health Care and Research Centre located in Vyara, Gujarat. The patient granted consent to exchange data such as vital signs, laboratory results and imaging investigations, which would be published to update evidence-based treatment in the context of the present hemoglobinopathies.

PATIENT INFORMATION

A 35-year-old female Mrs X from a rural area of Mandvi, Gujarat with a critical financial condition presented to the clinic with a complaint of weakness, palpitations, fatigue, puffiness, abdominal colic, loss of appetite, headache, generalized pain, body ache, backache, joint pain, irregular periods. Her medication history consists of T. Folic (Folic Acid) and T. Hydra (Hydroxyurea) since 2009 and she adhered to the same since then. She had received 12 units of blood transfusion and the last one was in 2011. She was diagnosed with a thyroid disorder in 2019 and started on thyroxine. She is married and has 2 children and during delivery, she was required 4 units of blood transfusion. The Preliminary assessment revealed that the patient had swelling, splenomegaly, jaundice and pallor on the day of the visit. Her vitals were BP: 104/68 mmHg, SpO2 98%, Pulse Rate 82 bpm, Weight 47.6 kg. On preliminary examination, hypothyroidism-associated complications appeared which require further confirmation. Therefore, further laboratory investigation has been prescribed for a better understanding of the condition. Diagnostic evaluations included thyroid function tests (T3, T4 and TSH), complete blood count and clinical assessments of symptoms and physical health.

Primary Condition

Sickle Cell Disease (SCD) Characterized by chronic hemolysis, vaso-occlusive crises and potential organ damage. Thyroid Dysfunction: Likely hypothyroidism, Symptoms of hypothyroidism may include fatigue, pallor, puffiness and generalized weakness. Spleenomegaly: Likely secondary to SCD, given the history of hemolysis and the body's compensatory response to chronic anemia. Present day 6/5/2022 laboratory parameters are mentioned in Table 1.

Follow-Up Treatments

Based on her laboratory investigation and clinical presentation Tab. Thyroxin 50 mg and Tab. T-AYU-HM Premium has been prescribed for 30 days with non-pharmacological measures like drinking plenty of water, avoiding stress, avoid hard activities if any. Based on her one-month response continuation of treatment was suggested mentioned in Table 2 for treatment follow-up to monitor clinical improvement and conditions meantime her clinical investigations were also performed at certain time intervals to assess the effectiveness of ongoing treatment.

DISCUSSION

Thyroid issues might present as a major comorbidities for sickle cell anemia patients. Both disorders may have complicated interactions that impact a patient's overall health and course of treatment. There are possible etiological reasons responsible for which a sickle cell disease patient might acquire hypothyroidism. The possible reasons behind acquiring thyroid disorders are prolonged stress; continuous inflammation-associated sickling episodes, nutritional deficiency, medication side effects and many more which can be identified with proper observations. The present case where the patient presented with swelling, splenomegaly, jaundice, pallor, low blood pressure, weakness and irregular periods suggested the primary appearance of hypothyroidism-associated complications. Based on a literature search the patient was receiving hydroxyurea and the literature suggested that irregular monitoring and such complications of

Table 1: Patient laboratory investigation at first visit on 06/05/2022.

Test	Values	Test	Values
Hb(g/dL)	7.92	T3 (ng/dL)	0.58
RBC (million/mm^3)	3.82	T4 (ng/z)	1.6
WBC (cells/mm^3)	5840	TSH (ng/dL)	150
Platelet (cells/µL)	145000	ESR (mm/hr)	19
MCHC (g/dL)	31.55	CRP (mg/L)	1.1
MCH (pg/cell)	20.73	RBS (mg/dL)	92
MCV (µm^3)	65.70	Eosinophil (cells/Mcl)	05
PCV (%)	25.10	Basophils (K/cumm)	00
Neutrophil (cells/Mcl)	64	Monocytes (Mcl)	03
Lymphocytes (µL)	28		

Table 2: Follow up treatment profile of patient.

Sl. No.	Date	Symptoms	Medicines
1	23-6-2022	Headache	T.T-AYU-HM Premium BID, T.Thyronorm 100.
2	10-8-2022	Pain, puffiness, irregular cycles, insomnia, anxiety.	T.T-AYU-HM Premium BID, T.Thyronorm 100.
3	16-8-2022	Splenomegaly, pallor, body ache, backache.	T.T-AYU-HM Premium T. Thyronorm 100.
4	7-12-2022	Swelling	T.T.AYU-HM Premium, T. Thyronorm 100.
5	28-1-2023	Heavy menstrual bleeding, headaches, abdominal colic.	T. T.AYU-HM Premium, T. Marical. D, Yuktikrutbala drop, Arogyavardhini ras.
6	25-9-2023	No complaints	T. Thyronorm 100, Cap. Nurite active.
7	12-3-2024	No complaints	T.T-AYU-HM Premium BID.
8	18-5-2024	No complaints	T.T-AYU-HM Premium BID.
Tab. Thronorm (Thyroxine), Tab. MaricalD (Calcium, Vit D3 and Magnesium), Cap Nutrite actrive (L-Methylfolate with Pyridoxine and Mecobalamin), BID- bis in die.			

Table 3: Laboratory evaluations of patient during treatment period.

Test	10/8/22	28/1/23	18/05/24
Hb (g/dL)	9.4	8.24	9.46
RBC (million/mm^3)	3.91	3.59	4.29
WBC (cells/mm^3)	5900	4890	5830
Platelet (cells/µL)	189000	168000	196000
MCHC (g/dL)	31.6	32.56	31.63
MCH (pg/cell)	24.6	22.95	22.05
MCV (μm^3)	76.6	70.47	69.69
PCV (%)	29.7	25.30	29.9
Neutrophil (cells/Mcl)	70	59	66
Eosinophil (cells/Mcl)	03	06	05
Basophils (K/cumm)	00	00	00
Lymphocytes (µL)	27	30	26
Monocytes (Mcl)	00	05	00
ESR (mm/hr)		13	12
CRP (mg/L)			2.46
Reticulocytes (cells*$10^{9/}$/L)			4.8
Corrected Reti.Cou (%)			3.25
Retic.Production Index			1.62
IRF-Immature Retic. Fraction			23.5
T3 (ng/dL)T4 (ng/dL)TSH (ng/dL)	T3- 75.1T4-3..56TSH->100	T3- 0.57T4-2.8TSH->110	T3- 1.35T4-49.42TSH-38.78
SpO2 (%)	100	100	100
PR (bpm)	70	80	85
BP (mmHg)	101/65	102/64	110/71
Weight (Kg)	45.700	47.300	45.120

thyroid can occur may be due to autoimmune thyroid disease or long-term treatment of hydroxyurea-associated endocrine complications.[9]

The case highlights the complexities of managing thyroid dysfunction in a patient with sickle cell anemia, who was on long-term hydroxyurea therapy. Hydroxyurea is the primary long-term disease-modifying therapy for Sickle Cell Anemia (SCA) approved formulation.[9-11] It functions as a ribonucleotide reductase inhibitor and increases the expression of Fetal Hemoglobin (HbF), which prevents the sickling of red blood cells. Decades of research have shown that hydroxyurea significantly reduces mortality and morbidity in sickle cell anemia patients, improves complications.[11]

Hydroxyurea's possible role in inducing thyroid dysfunction can be attributed to its tyrosine kinase inhibitor activity, which interferes with normal thyroid hormone regulation. Tyrosine kinases are enzymes that play a role in cell signaling, including signaling pathways involved in thyroid function regulation. By inhibiting tyrosine kinase activity, hydroxyurea may interfere with the normal regulation of thyroid hormone synthesis and secretion. This disruption can lead to elevated levels of thyroid hormones. Prolonged exposure to hydroxyurea might exacerbate these effects, leading to elevated Thyroid Stimulating Hormone (TSH) levels and altered T3 and T4 levels.[12]

Other possible reasons are the risk of developing hypothyroidism due to mechanisms such as recurrent hemolysis, vaso-occlusive crises, micro-vasculature obstruction, iron overload from frequent blood transfusions and red blood cell entrapment. These mechanisms lead to thyroid gland damage, altering thyroid hormone levels and potentially resulting in hypothyroidism, which can delay physical and sexual development and affect the quality of life.[13]

The results of the thyroid function test are variable in sickle cell anemia patient, which suggests that additional diagnostic evaluations are necessary to improve therapeutic outcomes. It's critical to rule out any potential effects that comorbidities may have on sickle cell disease patients' thyroid function. The SS genotype of the male patients also correlates with clinically substantial reductions in endogenous T3 levels and elevations in TSH in sickle cell disease cases. Furthermore, elevated TSH-releasing hormone levels may be linked to sickle cell disease, causing aberrant TSH accumulation that ultimately results in thyroid dysfunction.[12-14]

Furthermore, in patients with iron deficiency and subclinical hypothyroidism, combined treatment with levothyroxine and iron supplements demonstrated better effects than either factor alone. Previous study reported that Iron overload has been associated with multiple endocrine abnormalities.[15,16]

Repetitive sickling episodes may induce endothelial dysfunction and thereby eventually lower the thyroid volume might also be one of the possible reasons behind hypothyroidism in sickle cell disease patients. Literature reveals 10% and 12% of incidences of subclinical hypothyroidism and primary hypothyroidism, respectively, in sickle cell disease cases.[17,18]

A low level of thyroid hormone suppresses the activity of bone marrow and thereby decreases the synthesis of red blood corpuscles. In sickle cell anemia, sickling-induced destruction of red blood corpuscles causes various organ-based complications. Endothelial dysfunction, bone marrow suppression due to drugs like hydroxyurea, Pregnancy induced complications also require attention while discussing various etiological factors. Therefore, there are many possible factors present that can lead to acquired thyroid in patients. Regular thyroid checks while receiving hydroxyurea are also considered important for those who receive treatment for longer periods. Early diagnosis of thyroid symptoms in sickle cell patients may prevent the development of further complications.

The Integrated treatment with T-AYU-HM™ Premium provided adequate management in sickle cell patients as observed in Table 3 suggested sustained red blood corpuscles and hemoglobin levels. The ingredients in formulation individually already established for their mechanism on maintaining thyroid disorders.[19-23] The treatment works well in coordination with thyroxine as there was a remarkable improvement in thyroid hormone levels mentioned in Table 3. To prevent further thyroid complications hydroxyurea was discontinued and only above mentioned integrated treatments were prescribed. The inflammatory markers also appeared improving which might also indicate that no inflammation-associated complications, no sickling-induced complications, or no coagulation-related complications were observed as well as experienced and reported by the patient. The integrated Yuktikrutbala drop is prescribed to enhance overall strength and vitality.[24] The Arogyavardhini Ras is prescribed to balance doshas and improve metabolic functions.[25] During the 2 years patient hasn't reported any untoward complications or problems while continuing the integrated treatment. There is a dire need to look forward to multidisciplinary care with regular monitoring, preconception counselling, integrated treatment consideration and timely adjustment of dose and dosage form.

CONCLUSION

This case study underscores the importance of monitoring thyroid function in SCA patients undergoing long-term hydroxyurea therapy. The potential for hydroxyurea to induce thyroid dysfunction necessitates careful management and regular assessment of thyroid hormone levels. Whereas other etiological parameters suggest individualised monitoring and treatment plan require for patient. Not much such kind of complexities cases are reported or discussed the present study revealed, integrated

treatment approach has managed the patient remarkably well with improvement in thyroid function, no sickling complication, no blood transfusion, no hospitalization and importantly no untoward complications definitely require more attention. Therefore, further researches are requiring establishing systematic integrated treatment plan for such kind of cases.

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ETHICAL APPROVAL

Patient consent has been received and mentioned already in case introduction.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

SCD: sickle cell disease, **SCA:** Sickle cell anemia, **TSH:** Thyroid stimulating hormone, **HbF:** Fetal hemoglobin, **CRP:** C-reactive protein. **ESR:** Erythrocyte sedimentation rate, **RBC:** Red blood corpuscles, **WBC:** White blood cells.

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