Medical Research Archives

ESMED
European Society of Medicine

OPEN ACCESS

Published: July 10, 2023

Citation: Zottmann FS, Gebrin LC, et al., 2023. SC Hemoglobinopathy: A Rare Case Report on a Late Diagnosis in a 45-Year-Old Female, Medical Research Archives, [online] 11(7). https://doi.org/10.18103/mra.v11i7.1.4112

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DOI
https://doi.org/10.18103/mra.v11i7.1.4112

ISSN: 2375-1924

CASE REPORT

SC Hemoglobinopathy: A Rare Case Report on a Late Diagnosis in a 45-Year-Old Female

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ABSTRACT:
Sickle cell hemoglobinopathy SC is considered a rare type of sickle cell disease. Patients with this condition may present vaso-occlusive phenomena, but in a milder form when compared to the SS variant, which is considered the classic and most common among them. This case report has the objective to present the case of a 52-year-old patient with this rare form of hemoglobinopathy, which accounts for 30% of the individuals with sickle cell disease SS. The patient had a late diagnosis, with only one episode of arthralgia due to a vaso-occlusive crisis. This report also describes the patient's clinical progression, treatment, and life expectancy based on the literature, but mainly focusing on the patient's current clinical condition after seven years of follow-up. It is important to conduct epidemiological studies about hemoglobinopathies, especially the rare forms, to obtain more information about the incidence/ prevalence of the disease and its clinical manifestations as the early diagnosis is crucial for better prognosis and quality of life for the patient.

Introduction:

Hemoglobin (Hb), a protein present in erythrocytes, has the main function of transporting oxygen from the lungs to peripheral tissues[1]. It is composed of two alpha (α) globin chains and two beta (β) globin chains, forming a quaternary structure[1,2]. Each globin chain is associated with a heme prosthetic group containing an iron atom (Fe2+), allowing the oxygen molecule.This mechanism involves interactions established between two abnormal hemoglobin variants, such as the erythrocyte dehydration process leading an increase in HbS levels which causes a polymerization process[13,20] and gives the erythrocyte a sickle shape and increases its rigidity, culminating in hemolysis. to bind to blood cells[3]. HbS is the most common Hb disorder, with a worldwide prevalence of 55,000 new babies born with the finding every year[2]. Tln addition, it hinders the passage through the blood microcirculation due to the abnormal increase in adherence of the major hematological parameters: erythrocytes, leukocytes and platelets, as well as an increase in the activation of leukocytes and platelets, causing vaso-occlusion and ischemic injury in various organs and tissues[4, 13] as a result of the elevated blood viscosity, which leads to thrombotic events[13]. This mechanism can lead to pain, necrosis, and dysfunction, in addition to permanent organ damage[1]. However, some people have genotypes that produce a lower amount of HbS or an elevation of fetal Hb (HbF), which can reduce the severity of the disease and the intensity of symptoms. This occurs because these alterations hinder the formation of polymers and the sickling of erythrocytes, reducing the chance of obstruction of blood vessels[1]. In the SC form of the disease, there is no presence of normal hemoglobin (HbA) and the levels of HbS and HbC (another type of anomalous Hb) are close[1, 13]. The goal of this work is to present a case report of SC hemoglobinopathy in a patient in the 4th decade of life, who was diagnosed late, considering the characteristics of the case, as well as the treatment and management measures used in the patient and the obstacles found that contributed to the diagnosis being made with the patient at an advanced age.

Case report:

A 52-year-old afro-descendant female patient was diagnosed with SC hemoglobinopathy at the age of 45 after investigation of a single episode of arthralgia due to vaso-occlusive crisis, accompanied by anemia. At the time of diagnosis, she had moderate macrocytic anemia and the other blood count parameters were normal. Her hemoglobin electrophoresis showed the following levels of hemoglobin S: 49.2% and C: 43.1%. Since then, she has been using hydroxyurea 500 mg/day and folic acid 5 mg/day, which keep her hemoglobin above 9 g/dL, and she is asymptomatic from the point of view of anemia. The patient was instructed to undergo annual follow-up with an ophthalmologist and to practice physical exercises accompanied by a physical education teacher. Except for the slight skin pallor, the other physical examination data were normal in all clinical evaluations in these seven years after diagnosis, including absence of splenomegaly, musculoskeletal disease, and ophthalmological impairment.

Table 1 shows ours patient's hemogram results before starting the treatment

Parameter	Result	Reference values
Red blood cell count	2,6	3,9 - 5,2 million/ mm³
Hemoglobin	9,6	12,0 - 16,0 g/dL
Hematocrit	26,0	35,0 - 49,0 %
MCV	101,2	80,0 - 101,0 fL
MCH	37,4	26,9 - 34,0 pg
MCHC	36,9	31,0 - 37,0 g/dL
RDW	14,4	11,50 - 15,5%
White blood cell count	5.600	3.500 - 11.300 mm³
Neutrophils	2.990/ 53,4%	1.800 - 7.000 mm³
Lymphocytes	1.854/ 33,1%	1.000 - 5.000 mm³

Monocytes	549/ 9,8%	80 - 1.200 mm³
Eosinophils	157/ 2,8%	0 - 600 mm³
Basophils	50/ 0,9%	0 - 200 mm³
Platelets	343.000	15.000 - 450.000 mm³

Source: elaborated by the authors

Discussion:

As seen in the case report, the patient had a late diagnosis at the age of 45, after a vaso-occlusive crisis marked by an isolated episode of arthralgia. This can be explained by certain factors, such as: the development of hemoglobinopathy SC, a milder variant of sickle cell disease[5] that manifests its symptoms later[1], originating the condition with the vaso-occlusive crisis[5], as in the case of the patient. Furthermore, another extremely relevant factor for this case is that at the time of the patient's birth, it was not possible to screen for hemoglobinopathies through neonatal screening tests, because it was only introduced in Brazil in 1976[6], years after the patient's birth. Considering the presented clinical picture: afro-descendant, macrocytic anemia, and isolated episode of arthralgia due to a vaso-occlusive crisis, sickle cell disease was suspected. Therefore, a hemoglobin electrophoresis test was requested and performed to clarify the diagnosis, confirming hemoglobinopathy SC.

It is observed a prevalence of 3.7% of hemoglobinopathies in the adult population in Brazil[3], with 2.2% being sickle cell diseases[7], and 30% of this value being hemoglobinopathy SC[2], a milder form and rare subtype of sickle cell diseases[18,19]. The clinical manifestations of hemoglobinopathy SC appear later, with the most common being acute pain crises, vaso-occlusive events, and cholelithiasis[5]. In the case, the patient had the acute pain crisis due to the vaso-occlusive crisis.

Table 2[5,13,16] shows the most complications of SC hemoglobinopathy in comparison to the complications presented by the patient.

Main complications associated with hemoglobinopathy SC	**Complications presented by the patient.**
Proliferative retinopathy	-
Splenic sequestration	-
Vaso-occlusive crisis	+
Osteonecrosis	-
Renal complications (microalbuminuria, necrosis of the renal papillae, renal infarction)	-
Genitourinary complications (seen in male patients, like priapism, erectile dysfunction)	-
Hepatobiliary disease	-
Stroke	-
Thrombosis	-
Acute chest syndrome	-
Hemolytic anemia	+

Source: elaborated by the authors

The use of hydroxyurea, folic acid[1], and guidance on lifestyle, including hydration (risk of vaso-occlusive crisis), diet (folate), exposure to cold (risk of sickle cell crisis), oral hygiene (risk of infection), and moderate physical activity, contributed to the patient not experiencing a worsening of the condition[9], as hydroxyurea decreases the synthesis of HbS and HbC from the production of fetal hemoglobin[8, 13], the synthesis of endothelial adhesion molecules (such as ICAM and VCAM)[10] and endogenous nitric oxide, which is a vasodilator, thus preventing vaso-occlusive crises[8, 13], due to a response from the patient's bone marrow to hemolysis, increasing the production and release of erythrocytes and younger red blood cell lineages such as reticulocytes.[17], which could explain the macrocytic anemia that the patient had[14] (**Table 1**), this medication decreases the viscosity of the blood as well and reduces the amount of of leucocytes e reticulocytes[13], besides the other complications of this disease mentioned above[11].

Folic acid prevents hemolysis[4], avoiding complications such as splenic sequestration and hepatobiliary disease[2,5]. In the case, the patient only presented slight skin pallor. There was absence of splenomegaly, musculoskeletal disease and ophthalmological impairment.

Older data from 2010 indicates that the life expectancy of sickle cell diseases, especially sickle cell anemia, is before 40-50 years[12]. In the case of hemoglobinopathy SC, because it is a milder subtype of the sickle cell anemia, it presents lower rates of morbidity and mortality[5] due to its lesser severity and appropriate treatment that prevents the complications which are responsible for reducing the life expectancy of these patients. Just like the example of the patient in the case, who after 7 years since the diagnosis and with the appropriate treatment, is asymptomatic and with the disease under control, ensuring a better prognosis and a higher life expectancy.

The most notable aspects in this case consist of the fact that the patient spent almost five decades of her life without the diagnosis and appropriate treatment for her condition. Nevertheless, despite these adversities, she remained alive and without major complications, especially proliferative retinopathy, which is the most frequent complication. She developed only a vaso-occlusive crisis and macrocytic anemia, which led to the late diagnosis at the age of 45. An intriguing fact of this case is that, despite the hemolytic nature of the disease, the patient does not have signs of jaundice, which is expected as a consequence of hemolysis[14, 15].

Conclusion:

The patient presented belongs to the 30% of individuals with sickle cell disease, in her case, the hemoglobinopathy SC variant, which is a milder subtype of sickle cell disease. The description of the case highlights the need for further epidemiological studies and case studies to obtain more information regarding the incidence/prevalence of the disease, clinical manifestations, diagnosis, treatment, complications, and prognosis, including the life expectancy associated with late diagnosis.

Conflicts of Interest Statement:

The authors have no conflicts of interest to declare.

Funding Statement:

There was no type of funding for this study.

Acknowledgments:

We would like to thank the core of students from the Hematology and Hemotherapy League of the São Leopoldo Mandic Campinas Medical School for their dedication and effort to carry out this work and Clínica Medeiros Campinas for providing us with the patient's data.

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