Sickle Cell Disease and its complications in our clinical practice

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Abstract

Aim: Although the frequency of the painful sickle cell crisis, which is an important marker of sickle cell disease related complication, is considered a parameter of this disease's severity, most patients do not frequently experience such crisis that can require always medical assistance.
Methods: We studied 64 patients with sickle cell disease from December 2011 to December 2012 at the University Hospital Center, Tirana, Albania. About 63% of the patients were female. Pain rate was assessed by calculating the cumulative number of admissions for painful crisis (like articular, muscular, abdominal pain). The patients were categorized into three groups: 0, 1, or ≥1 crises per year. Painful crises that did not require medical assistance were excluded.
Results: Sixteen patients did not have crisis, and 15 patients had more than one crisis per year. Avascular necrosis, acute chest syndrome, cholelithiasis and iron overload were significantly related to pain rate. Cholelithiasis was the prominent clinical manifestation amongst this group of patients. There was no significant change in laboratory findings. Pain was evaluated as an important marker and was present (one or more per year) in 15 patients with Sickle Cell Disease and Thalassaemia Sickle Cell Disease.
Conclusion: The association between iron overload and the pain rate is probably the result of many blood transfusions used for treating painful crisis. Our data shows that several major diseases which are complications of sickle cell disease are not strictly related to pain rate and occur in a very significant number of patients that seem clinically well. Hence, we have to evaluate systematically these complications, even in patients which represent a mild-to-moderate clinical panorama of disease in order to prevent the severe complications.

Keywords: acute chest syndrome, avascular osteonecrosis, hydroxyurea, organ damage, pain rate, sickle cell disease.

Introduction

Sickle Cell Disease is a chronic pathology, very heterogeneous in its presentation, which can cause multiple organ damages with different severity at patients affected with this disease. Homozygous Sickle Cell Disease may vary in its clinical presentation from continuously admitted for the management of acute complications to a rare follow up. Clinical view is dominated by vaso-occlusive episodes manifested with episodic articular and muscular pain, cerebral stroke, frequent infections (especially respiratory ones), leg ulcers, avascular osteonecrosis, icterus, cholelithiasis, renal and hepatic damages, priapism, ocular damages (retinopathy), chronic anemia etc. Vaso-occlusion and chronic hemolysis are major determinants of Sickle cell disease-related organ damage. The early detection of these complications is the key of success in their management. One of the most important interventions in such cases is transfusion of red blood cells. Blood transfusion for a patient suffering from sickle cell disease can:

- Treat a sudden or short-term event related to sickle cell disease.
- Treat the complications of sickle cell disease.
- Prevent the complications of sickle cell disease.
- Minimize the risk of cerebral stroke at the youngest and oldest children.

Blood transfusion in sickle cell disease minimize amount of hemoglobin S present in human cells (1). If those sickle red cells can be reduced in blood stream, the possibility to cause the obstruction of blood vessels is low. Through blood transfusion, there are more normal erythrocytes in circulation, bringing the oxygen in the tissue.

The "bad concern" is that patient having transfusions will start slowly to accumulate iron in his body, iron-overload, which can be fatal if untreated. The second step, in patients' follow-up is to start iron chelation therapy to remove excess iron from the body (2).

Some sudden acute circumstances of Sickle Cell Disease can cause a fulminant drastic hemoglobin decrease, sometimes life-threatening. Need for pure red blood cells is crucial in circumstances of acute thoracic syndrome, aplastic crisis, splenic sequestration (3).

Blood transfusions are essential before an intervention, or before general anesthesia, in order to prevent the sickling. On the other hand transfusions can treat the cutaneous ulcers in inferior extremities (4). Frequent transfusions can help in prevention of cerebral insult, for the young patients who have undergone a stroke or are at a higher risk of having such a pathologic situation.

Although the frequency of the painful sickle cell crisis, which is the marker of sickle cell disease related complication, is considered a parameter of this disease's severity, most patients do not frequently experience such crisis that can require always medical assistance. But, above all, patients born and suffering from sickle cell, seem to have a reduced life expectancy, not a qualitative life, full of crisis, and a lot of hospitalizations.

Considering pain an important tool of sickle cell severity, we have analyzed a sample of patients, and have tried to understand if the prevalence of Sickle cell disease is related to the frequency of painful crisis.

Methods

Sixty-four patients (sickle cell and thalassaemia sickle cell) are being followed-up at the University Hospital Center "Mother Teresa" in Tirana, Albania. We studied these patients from December 2011 to December 2012.

The study was approved by the Albanian Committee of Medical Ethics.

Manifestations related to Sickle Cell Disease

- Iron overload: When the subject has received more than 20 transfusions and the iron overload is above 1000 ng/ml in three consecutive occasions.
- Cholelithiasis: presence of gallstones in ultrasound examination or cholecystectomy because of gallstones (5).
- Retinopathy: presence of at least mild non proliferative retinopathy.
- Symptomatic avascular osteonecrosis: local pain and reduced function with documented osteonecrosis of the femoral or humeral head (hip or shoulder X ray) (6).
- Acute Chest Syndrome: Hospitalizations due to febrile episodes with respiratory disorders (7).

- Leg ulcers: chronic ulcers of the ankle not always explained.
- Stroke: history of stroke confirmed by magnetic resonance imaging or computerized tomography (8).
- Priapism: spontaneous painful erection requiring hospital care (9).
- Pain: It varies amongst patients, but is present in almost more than 90% of patients at least once in two years (10).
- Pain rate: It is assessed by calculating the cumulative number of admissions for painful crisis (like articular, muscular, abdominal pain) from December 2009 until December 2012. The patients were categorized into three groups: 0, 1, or ≥ 1 crises per year. Painful crises that did not require medical assistance were excluded.

Statistical analysis

Continuous data were presented as medians with their interquartile range. Categorical data were presented as percentages. P-values below 0.05 were considered statistically significant.

Table 1. Characteristics of the patients

Diagnosis	**HbSS/S-Thal**
Number	64
Female %	63%
Laboratory findings	
Hemoglobin (g/dl)	9 (8.1-9.8)
Reticulocytes (%)	8.2 (5.9-10.9)
Leucocytes (x10^6/L)	9.0 (7.2-11.7)
Creatinine (μmol/ L)	51(42-57)
Organ damage and clinical manifestations (%)	
Cholelithiasis	34
Iron overload	17
Leg ulcers	14
Acute Chest Syndrome	32
Avascular osteonecrosis	16
Stroke	11
Number of crises/year	
None	16
Less than one	33

Table 2. Prevalence of sickle cell disease related complications

N of crises/year	**0**	**0-1**	**≥ 1**	**P**
N	16	33	15	
Sex (% male)	34	43	36	0.851
Hydroxyurea use (%)	13	11	36	0.014
Organ damage (%)				
Iron overload	6	6	24	0.041
Cholelithiasis	32	48	75	0.002
Leg ulcers	13	6	8	0.512
Stroke	9	2	12	0.803
Avascular necrosis	3	13	24	0.019
ACS	0	0	40	<0.001

Results and Discussion

Sixty-four patients were studied. These patients were admitted in our service every two months for a general check up.

Acute Chest Syndrome and Cholelithiasis were the common causes of hospitalizations. Stroke was found in 11 patients. Iron overload is evaluated with ferritin level above 1000 ng/ml in three consecutive measurements. Patients with sickle cell disease not very often were treated with blood transfusions. However, the iron overload was still present, not only because of iron intake by transfusions, but form chronic haemolysis too. Pain was present in almost more than 90% of the patients, at least once in two years.

Although more patients with frequent crisis used hydroxyurea (in a significant way), there was no difference in sickle cell disease related complications between patients treated or non treated with hydroxyurea. So, the use of hydroxyurea still remains not clear in our practice.

Avascular necrosis, acute chest syndrome, cholelithiasis and iron overload were significantly related to pain rate (7). The association between iron overload and the pain rate is probably the result of many blood transfusions used for treating painful crisis. In such crisis we often use pure blood transfusions or exchange transfusion in order to minimize sickling and hemolysis. The data above show that several major diseases which are complications of sickle cell disease, are not strictly related to pain rate and occur in a very significant number of patients that seem clinically well (10). This finding suggests us to systematically screen these complications, even in patients which represent a mild-to-moderate clinical panorama (8). Hence, our attention is to treat carefully and monitor closely these patients, giving them at the same time the right advices in order to prevent the sudden events of this pathology.

This study presents some shortcomings. The history of acute painful crisis was really limited to one year period and we have studied and evaluated only painful crises for which patients were admitted. Therefore, the conclusions may not be extrapolated for the number of painful crises happening at home or before the period of evaluation. Secondly, this kind of retrospective study may suffer from selection bias. On the other hand, our study is conducted in a tertiary center, which does not permit generalization to the overall Albanian population. Nevertheless, our study sample seems to be representative compared to the other studies. In conclusion, systematic screening for evaluation of organ damage in all sickle cell patients is very important and allows us to intervene at a proper time. The protocol is well-defined and we respect it meticulously in our clinical practice.

Conflicts of interest: None declared.

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