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Original Research Article

Morbidity associated with sickle cell trait carriers

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ABSTRACT

Background: Sickle cell trait carriers has long considered asymptomatic. This affirmation is now challenged because many patients complain of osteoarticular pain and several organic degenerative complications in particular; renal, eye and sudden death have been described. The objective of this study was to evaluate the morbidity of sickle cell trait and identify risk factors associated.
Methods: This is a prospective study with duration of 16 months including 50 patients with sickle cell trait received regular visits (every 6 months) for painful events. Biological assessment was carried out systematically to eliminate rheumatic disease (CRP, ASLO, latex Waler Rose) or metabolic disorders (serum calcium, serum magnesium, and serum uric acid). A correlation between clinical and laboratory data was performed to study the relationship between morbidity observed and biological abnormalities.
Results: Mean age of patients was 32 years (12-59) and mean age at diagnosis was 24 years (12-55 years). Sex ratio M/F was 0.16. Clinical symptoms were osteoarticular pain (88%), headache (86%), abdominal pain (76%), muscle cramps (70%), dizziness (56%), biliary lithiasis (6%), femoral head osteonecrosis (2%) and gross haematuria (2%). Seventeen patients (34%) had abnormal metabolic or rheumatic analysis. No risk factor associated with morbidity of patients was identified.
Conclusions: This work has allowed us to find that the symptoms presented by sickle cell trait patients are dominated by painful events. This morbidity associated with porting sickle cell trait was not secondary to inflammatory or metabolic disorders or physical activity.

Keywords: Abdominal pain, Headache, Muscle cramps, Osteoarticular pain, Sickle cell trait

INTRODUCTION

Sickle cell trait (SCT) is genetically characterized by the presence of the S gene on one allele and in electrophoresis by the presence of hemoglobin A (55 to 70%) and hemoglobin S (35 to 45%).[1] In Africa, 10 to 40% of the population is heterozygous for sickle cell anemia. In Senegal, the prevalence of hemoglobin S is 8 to 10%, but major forms represent only 0.4%.[2,3] According morbidity, only major sickle cell syndromes are considered symptomatic and are characterized by acute complications (vaso-occlusive crises) and chronic (degenerative organ damage).[4] SCT carriers has long considered asymptomatic and without acute or chronic complications. This affirmation is now challenged because many patients with SCT complain of osteoarticular pain and several organic degenerative complications in particular, renal, eye and sudden death have been described.[5-8]

Most studies of SCT evaluated biological parameters such as blood viscosity and effects of hydration during physical effort.[9] Similarly, in Senegal, SCT studies evaluated hemorheological parameters, erythrocyte deformability and effects of hydration.[10,11] Thus, an evaluation of SCT morbidity is necessary to identify the

risk factors associated with the occurrence of clinical symptoms in these patients.

METHODS

This study included 50 patients with SCT followed at the clinical hematology service (CHS) in Dakar either regularly (every 6 months) or irregularly (when they had pain symptoms).

The patients were diagnosed by alkaline pH hemoglobin electrophoresis method. All patients had chronically clinical events such as osteoarticular pain, abdominal pain, headache, muscle cramps and/or acute or chronic degenerative complications described in sickle cell anemia (stroke, biliary lithiasis, osteonecrosis, retinopathy, renal failure). SCT patients affected any other type of haemoglobinopathies or rheumatic or metabolic diseases were excluded.

We realized a prospective study during 16 months performed at the CHS in Dakar. After obtaining informed consent from the patient, two tubes of 5 ml were collected, an EDTA tube for control of hemoglobin electrophoresis and blood count, and a dry tube to perform rheumatic analyzes (CRP, ASO, latex Waler Rose) and metabolic disorders (serum calcium, serum magnesium, serum uric acid). Such examinations were carried out to remove inflammatory or metabolic diseases that can coexist with SCT.

Radiological exams (pelvis, abdominal, Heart) were performed if clinical signs of organ damage in order to seek osteonecrosis, biliary lithiasis or cardiac disease, and proteinuria to detect renal failure. S

ocio-demographic variables were studied: age, sex, education level, occupation of patients, lifestyle (sports activity by the frequency per week, smoking or alcohol). Clinical data were: age at diagnosis, age of onset of first clinical manifestations, discovery circumstances, functional signs (osteoarticular pain, headache, muscle cramps, abdominal pain, dizziness and asthenia).

Biological data were: anemia (hemoglobin level <12 g / dL in adults), ASO (<200 IU / L), CRP (<6 mg/l), Latex Waler Rose (<30 IU/mL) serum calcium (86-104 mg/l), magnesium levels (17-24 g/l), uric acid (35-70 mg/l). A correlation between clinical and laboratory data was performed to investigate the relationship between SCT morbidity and biological abnormalities.

Statistic study was conducted in Sphinx software version 5.1.0.2. Descriptive study is conducted by calculating the frequencies for categorical variables and determining the averages for quantitative data with a 95% confidence interval. Chi 2 test was used for the correlation of quantitative variables and Student's test for the correlation between qualitative and quantitative variables. The tests were considered significant for P <0.05.

RESULTS

General characteristics of SCP patients

Mean age of patients was 32 years (12-59 years) and mean age of SCT diagnosis was 24 years (12-55 years). The diagnosis has been determined for 10 years older in 2 cases (4%), between 10 and 30 years older in 35 cases (70%) and after 30 years in 13 cases (26%). The sex ratio M/F was 0.16. Over 80% of patients were enrolled in school, 30% had attained the upper level and had professional activity. Only 28% of SCT patients made physical activity (Table 1).

Table 1: General characteristics of the patients with sickle cell trait.

Parameters	Number (n=50)	Frequency
Under 20 years	6	12%
Between 21 and 40 years	27	54%
Above 40 years	17	34%
Female	43	86%
Male	7	14%
No schooling patients	7	14%
Schooled patients	43	86%
Professional activity	40	80%
Without activity	10	20%
Regular sports activity	14	28%
Tobacco	2	4%
Alcohol	8	16%

SCT patient's clinical features

The first symptoms had appeared before 10 years older in 11 cases (22%), between 10 and 20 years older in 12 cases (24%) and after 20 years older in 27 cases (54%).

Table 2: SCT patient's clinical symptoms.

Parameters	Number (n=50)	Frequency
Functional symptoms		
Osteoarticular pain	44	88%
Headaches	43	86%
Abdominal pain	38	76%
Muscle cramps	35	70%
Dizziness	28	56%
Asthenia	23	46%
Complications (n=5)		
Biliary lithiasis	3	6%
Femoral head osteonecrosis	1	2%
Gross hematuria	1	2%

The circumstances of discovery were dominated by osteoarticular pain (64%) whose frequency was 3 episodes per year (2-5), fortuitous discovery was found in

13 patients (26%) during a health check or screening and complications discovery for 5 patients (10%). Functional symptoms that motivated medical consultations are described in Table 2 as well as chronic complications.

SCT patient's metabolic and inflammatory disorders

Seventeen patients (34%) had abnormal laboratory tests. Anemia and elevation of CRP levels were more frequent respectively reaching 7 patients each (14%) (Table 3).

Risk factors associated with SCT patient's morbidity

We noted no statistically significant difference in morbidity between patients who had laboratory abnormalities (group A) and those who had normal laboratory tests (group B) (Table 4). Similarly, there was no influence of physical activity on the incidence of osteoarticular pain (p = 0.37).

Table 3: SCT patient's metabolic or inflammatory disorders.

Parameters	Number (n=50)	Frequency
Positive CRP level	7	14%
Positive ASO level	4	8%
Positive latex waler rose test	1	2%
Hypercalcemia	3	6%
Hypocalcemia	1	2%
Hypermagnesemia	1	2%
Hypomagnesemia	4	8%
Hyperuricemia	2	4%

Table 4: Risk factors associated with SCT patient's morbidity.

Variables	Group A (n=17)	Group B (n=33)	P
Age (mean, SD)	29.8 (13.4)	33.55 (12.4)	0.7
Sex	17	33	0.2
Age of diagnosis (mean. SD)	23.2 (10.8)	24.4 (9.8)	0.6
Osteoarticular pain (n=44)	16	28	0.32
Complications (n=5)	2	3	0.55

DISCUSSION

This study included 50 SCT patients who presented painful symptoms dominated by osteoarticular pain, abdominal pain, headache and muscle cramps. These clinical manifestations were rarely reported in the literature that SCT was still considered an asymptomatic.[12] Most studies in SCT evaluated their performance over physical activities and not related morbidity in SCT patients.[9,11]

In Senegal, no studies have evaluated clinical manifestations or complications of SCT patients. However several SCT patients have functional symptoms constituting their reasons for medical consultations. All studies that evaluated morbidity and mortality in sickle cell disease have focused on major sickle cell syndromes.[13,14]

Women are predominant in this study with an average age of 32 years. This predominance of adults allows us to say that clinical manifestations in SCT arise belatedly in life. Two hypotheses can be cited for this, firstly this period of life is the active phase of the individual and the other, it also corresponds to the emergence of co-morbidity may be responsible for painful symptoms such as rheumatic or metabolic diseases. The fact that the majority of patients (80%) had a professional activity is an additional argument of this first assumption. In addition, 28% of these patients practiced regular physical activity with more than one session per week when we know that physical exercise is a trigger pain in sickle cell disease.

Present patients were diagnosed late with a mean age at diagnosis of 24 years, which explains the tolerance of SCT compared to SCD of which the first clinical manifestations arise around the age of 6 months. These clinical manifestations appeared after 20 years older for half of the patients. Depending on the time between diagnosis and the onset of clinical symptoms, more than half of the patients had presented their first clinical manifestations before SCT diagnosis. This allows us to point out that this is not the screening that could diagnose these patients but their painful symptoms.

SCT discovery was also made to complications such as femoral head osteonecrosis, biliary lithiasis and gross hematuria.[15] The most frequently reported complications in SCT patients are kidney or eye failure.[5-7,16,17] Renal disease is dominated by papillary necrosis manifested clinically by hematuria.[5,6,12,16]

Symptoms were dominated by osteoarticular pain. Joint pain were more common than bone pain and interested in order of frequency decay wrists, knees, ankles, shoulders and hips. These main localizations coupled with an etiological research, allowed to eliminate a rheumatic

disease (rheumatoid arthritis, rheumatic fever, osteoarthritis, gout).[18] Etiological research allows eliminating other diseases such as hypocalcemia, hypercalcemia, hypomagnesemia or hypermagnesemia. The results showed no correlation between clinical symptoms and laboratory abnormalities observed in these patients.[18] This allowed us to conclude that these laboratory abnormalities were not in themselves explain the occurrence of osteoarticular pain and other symptoms in SCT patients. This confirms that osteoarticular pain and ischemic complications or anemia were attributable to SCT.[19]

Radiological exploration headache is necessary to avoid exposure to the risk of stroke, which is not negligible in SCD[20] all the more so cases of death sudden have been described. An evaluation of the interest of transcranial doppler could be performed in SCT patient with chronic headache and those especially as the current literature data show a plausible association between the occurrence of stroke and SCT.[21]

We have also studied the influence of physical activity on the painful events. In fact, physical activity causes hypoxia which can trigger painful phenomena in sickle cell patients. Present results showed no statistically significant relationship between the practice of regular physical activity and SCT morbidity. This study confirms that the sport activity is not a factor that triggers painful symptoms in SCT[11] contrary to the homozygous form.[22]

So it is clear that painful manifestations could well appear in SCT. It remains to determine whether the symptoms are linked to SCT or a co-morbidity. Studies on larger series are needed to better understand the reasons for the occurrence of clinical symptoms and/or complications in some SCT patients and not in others. Moreover, a fundamental study is needed to assess the status of blood viscosity in these patients.

CONCLUSION

This work has allowed us to find that the symptoms presented by SCT patients are dominated by painful events. This morbidity associated with porting SCT was not secondary to inflammatory or metabolic disorders or physical activity.

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