Severe Sepsis with Kidney and Liver Dysfunction in a Sickle Cell Patient at Brazzaville: About Three Cases

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1. INTRODUCTION

Sickle cell anemia, in its evolution there is an infectious risk both in children and adults. Infectious complications are the main cause of morbidity and mortality in children with sickle cell disease.

Patients and Case Report: We report three cases of severe sepsis with renal and hepatic dysfunction during homozygous sickle cell disease, recorded in the Clinical Haematology Department of the Brazzaville teaching Hospital. The patients were female, aged 10, 17 and 20 years respectively, and were not followed up. The 20 years old patient was 20 weeks and 5 days pregnant. On hydration, blood transfusion and antibiotic therapy, the outcome was favorable in all patients.

Conclusion: regular follow-up, antibiotic prophylaxis and adequate vaccination of sickle cell patients are necessary to prevent sepsis and its complications.

Keywords: homozygous sickle cell disease, severe sepsis, kidney and liver dysfunction, Brazzaville

1. INTRODUCTION

Sickle cell is the most common genetic disease in the world (five percent of the world's population) (1,3). It is a major public health problem in Sub-Saharan Africa (1, 4, 5). It is autosomal recessive and is secondary to a mutation in the sixth codon of the β-globin gene with substitution of adenine by thymine on chromosome 11 (6). It is characterised by the presence of abnormal haemoglobin (Hb), Hb S, which has the property of polymerising in particular under certain conditions such as fever, hypoxia, acidosis or dehydration (7, 8). In Congo, 22% of the population are carriers of the sickle cell trait and 1.25% are affected by homozygous forms (9, 10).

Homozygous sickle-cell anaemia is enamelled in its evolution with a risk of infection, which sets in during the first years of life and persists into adulthood (5,11); a risk linked in part to functional asplenia (3,12).

Infectious complications are the main cause of morbidity and mortality in sickle-cell children, particularly before the age of five. The bacteria involved, in particular the encapsulated germs (5, 11), are the cause of severe infections, which can develop into a multi-organs failure; and are responsible for a significant proportion of morbidity and mortality in patients living with sickle cell disease. We report three cases of severe sepsis with renal and hepatic failure, recorded in the Clinical Haematology Department of the Brazzaville University Teaching Hospital (UTH).

2. PATIENTS AND OBSERVATIONS

Case 1

Patient 1 was a 17-year-old adolescent student living at about 600 km away from Brazzaville. She has been known to have homozygous sickle cell disease since the age of three, not follow up and polytransfused; the last transfusion was a week ago. She was admitted with limbs and abdominal pain, jaundice, and coca cola-coloured urine, in a febrile context having started a week before; accompanied by an anuria that occurred 24 hours before admission.
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Physical examination revealed: normal consciousness, moderate pallor, frank mucocutaneous (MC) jaundice, altered general state (GS), diffuse abdominal tenderness, hepatomegaly (HMG) of 14 cm, right hypochondrium (RH) pain blocking deep breathing; and bones pain.

Urine test strip (UTS) showed: pH 5; nitrite positive.

The haemogram showed moderate normocytic normochromic anaemia (Hb: 9.3 g/dl, MCV: 93 fl, MCH: 32.5 pg, MCHC: 34.8 g/dl, haematocrit (HCT): 26.8%); hyperleukocytosis at 83.6 G/l predominantly neutrophils (70.6 G/l), normal platelet count at 168 G/l.

Biochemistry revealed hypercreatininemia at 532 µmol/l (with clearance at 9.79 ml/min); signs of hepatic cytolysis (ASAT/ALAT: 595.9/613.9 IU/l), hyponatremia at 131 mEq/l; K+: 3.9 mEq/l; Cl-: 95 mEq/l.

Abdominal-renal ultrasound revealed a homogeneous HMG sensitive to the passage of the probe, a muddy, thin-walled gall bladder. Thus, the diagnosis of severe hepatobiliary sepsis with acute renal failure (ARF) was made. A treatment consisting of: hydration, antibiotics (ATB) (Ceftriaxone + Sulbactam), intravenous (IV) metronidazole, antispasmodic, diuretic, potassium supplementation was instituted. The evolution was marked one week later by an improvement of the clinical state (improvement of fever and pain, regression of jaundice, improvement of GS, clarification of urine and normalization of diuresis). At the paraclinical level, there was a correction of hyponatremia, a decrease in the number of white blood cells (WBC) to 18.5 G/l; transaminases (ASAT/ALAT to 184/142 IU/l); creatinine to 256 µmol/l; and subsequently normalisation of renal and hepatic function. The patient was discharged with oral treatment made of Cefixime, Metronidazole, Folic Acid (FA).

Case 2

Patient 2 was a 10 year old girl, a student, living at about 350 km away from Brazzaville. She has been known to have homozygous sickle cell disease since the age of nine months. She is irregularly follow up (lost to follow-up for 18 months). She has been transfused six times since her birth. She has not received recommended vaccines in sickle cell disease (vaccines out of the Expanded Programme on Immunisation (EPI)). She was admitted for abdominal pain and fever, which had occurred three days earlier and for which she received treatment: blood transfusion, anti-malarial, antispasmodic, antibiotic. The evolution was marked by the persistence of the symptoms, the appearance of progressive jaundice, dark red and then dark green urine, and pain in all the four limbs. The clinical examination on arrival showed: temperature (T°): 37.1°c, blood pressure (BP): 100/50 mmHg; heart rate (HR): 120 beats/min; respiratory rate (RR): 44 cycles/min; weight: 25 Kg; SpO2: 84%; a drowsy and prostrate patient, moderate pallor, frank MC jaundice, a less bloated abdomen, epigastric and RH defence, HMG, bones pain.

The haemogram showed a hypochromic microcytic anaemia (Hb: 6.8 g/dl, MCV: 70.1 fl, MCH: 25.1 pg, MCHC: 35.8 g/dl, HCT: 19 %); hyperleukocytosis at 24.45 G/l, predominantly neutrophilic (22 G/l), platelet count at 133 G/l.

Biochemically: hypercreatininemia at 220 µmol/l; hyperbilirubinemia (Total/Direct (T/D): 846.3/579.9 µmol/l); signs of hepatic cytolysis (ASAT/ALAT: 1848/1226.8 IU/l), hypokaliemia at 2.2 mEq/l; hyponatremia at 125 mEq/l; hypochloremia at 91 mEq/l.

Abdominal-renal ultrasound revealed an isolated discrete homogeneous HMG. The diagnosis of severe digestive sepsis with ARF. Therapeutic management consisted of: two pints of packed red blood cell, hydration, ATB (Ceftazidime, Ciprofloxacin), Imidazole, antispasmodic, potassium supplementation, diuretic, vitamin K1 infusion, Lactulose. The evolution was marked on the nine day of hospitalisation by the improvement of the clinical state. On the biological level, we observe the correction of electrolytes disorders (K+: 4.7 mEq/l; Na+: 139 mEq/l; Cl-: 107 mEq/l ), a decrease of the number of WBC to 14.65 G/l; transaminases (ASAT/ALAT: 106/94.4 IU/l); bilirubinemia (T/D : 195.5/34.3 µmol/l); normalization of creatininemia (106 µmol/l, then 57 µmol/l); and subsequently normalization of WBC count (12.6 G/l) and liver function (AST/ALAT: 68.8 IU/l; 68.6 IU/l, T bilirubinemia: 46.8 µmol/l). The patient was discharged with oral treatment; Cefixime, Metronidazole, and subsequently Oracillin.

Case 3

Patient 3 was a 20 years old seamstress living in Brazzaville. She is living with homozygous sickle cell disease discover since the age of six years. She is not follow up. She has been
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transfused three times since her birth. She was admitted for diarrhoea, vomiting and fever, which started three days earlier, at a gestational age (GA) of 21 weeks 5 days' pregnancy. Forty-eight hours later she developed progressive jaundice, dark greenish urine, physical asthenia, dizziness and palpitations.

Her obstetrical history revealed that: she is G3P0. The first pregnancy resulted in a spontaneous miscarriage at 20 weeks; the second resulted in a premature delivery at 29 weeks of age of a newborn who died on the fifth day of life. Physical examination on admission noted: T°: 37.6 °c; HR: 116 b/min; BP: 120/60 mmHg; FR: 29 c/min; SpO2: 88%; a conscious patient, frank pallor, jaundice, altered GS, signs of severe anaemia, epigastic and RH tenderness, painful HMG with regular surface and normal diuresis.

Obstetrical examination revealed: active movements of the fetus were not perceived by the mother, uterine height: 18 cm, abdominal circumference: 83 cm, vagina examination was normal.

At the UTS: pH 6; Bilirubin positive at 3+; haematuria positive at 3+; proteinuria positive at 1+.

The haemogram showed a severe normochromic macrocytic anaemia (Hb: 2.1 g/dl, MCV: 106.9 fl, MCH: 36.2 pg, MCHC: 33.9 g/dl, HCT: 6.2%); hyperleukocytosis at 49.63 G/l with predominantly neutrophils (29.52 G/l); platelet count at 343 G/l; malaria haemoparasite detection: positive.

Biochemistry: hypercreatininemia at 202 µmol/l (clearance at 35.13 ml/min); ASAT/ALAT: 73.8/14 IU/l, hypokalemia at 2.5 mEq/l; hyperchloremia at 113 mEq/l; normal natremia at 143 mEq/l; hypoproteinemina at 56.7 g/l.

Obstetrical ultrasound revealed a single, active fetus with a regular heartbeat, sufficient amniotic fluid and a normal placenta.

The diagnosis of severe digestive sepsis with ARF on pregnancy of 21 weeks 5 days GA was made. The pregnant woman received: transfusion of ten pints of packed RBC, hydration, ATB (Ceftriaxone+ Sulbactam), imidazole, anti-malarial, antispasmodic, potassium supplementation. The evolution was marked nine days later by the improvement of the initial clinical state. Biologically, Hb 7.7 g/dl, correction of hyponatremia, regression of the WBC number to 25.24 G/l; normalisation of renal (creatinine to 93 µmol/l) and hepatic function. The pregnant woman was discharged and transferred to the gynaecology-obstetrics department for further obstetric management.

3. DISCUSSION

As many authors have reported in the literature, people living with sickle cell disease have an increased susceptibility to infections, the most common of which are sepsis, pneumopathy, pyelonephritis and osteomyelitis (12-25).

The risk of infection sets in from the first years of life and persists until adulthood (5); this risk is highest in children under five years of age (15,18,20,26). These infectious complications are extremely serious and can be life-threatening (11,12). They are the main cause of morbidity and mortality in sickle-cell children (12,14,23), particularly before the age of five (11,27). Encapsulated germs (pneumococcus which is the leader, meningococcus, salmonella, Haemophilus influenzae) are the main aetiologies (12,23,27-31). A child with sickle cell disease has a 400 times greater risk of contracting Streptococcus pneumoniae sepsis (27,32). Streptococcus pneumoniae is the leading cause of mortality in sickle-cell children (11,27,33), with an estimated incidence of 100 patient-years and a mortality rate of around 30% in sickle-cell children under three years of age in the United States (34).

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The new pneumococcal conjugate vaccines, combined with preventive antibiotic therapy with penicillin, have been able to reduce the occurrence of these infections in small children by 90% (27,30,32). Several physiopathological mechanisms explain the occurrence of these infections: physiological immaturity of the child's immune system, functional asplenia (due to repeated spleen infarctions), lack of natural immunity (lack of opsonization, lack of complement activation, reduced bactericidal capacity), immunoglobulin abnormalities, leukocyte function and cell-mediated immunity abnormalities (27,29,30,35).

Our study focused on severe sepsis in three patients aged 10, 17 and 20 years respectively. However, these extremely serious infections are rarer in older children and adults with sickle cell disease (3,5,12,19,27,28,36), even if the risk of infection in these patients is persistent and
remains higher than in the general population (5,18). In practice, this is a potentially severe event in this field which justifies systematic vaccination against pneumococcus with a booster shot every five years and against other encapsulated germs (5,12,28,31,37,38), Savadogo et al (15), Douamba et al (20), and Boiro et al (39) also reported cases of sepsis in older children and adolescents with sickle cell disease. These serious infections found in our patients can be explained by: the absence of follow-up or irregular follow-up; the absence of vaccination against encapsulated germs as recommended by the WHO (1); the absence of antibiotic prophylaxis by penicillin V; pregnancy (in patient 3) which is a factor in increasing the risk of infection during sickle cell disease, particularly for severe infectious forms (40).

These explanations have also been reported in many African series.

In our study, all the patients had been vaccinated correctly according to the EPI. It has also been reported in many series in sub-Saharan Africa that satisfactory vaccination coverage of sickle cell disease children according to the EPI has been achieved, with rates varying between 72, 7% and 99% depending on the country (20,39,41).

EPI vaccines are generally well followed because they are free. On the other hand, none of the non-EPI vaccines (Pneumo 23, Typhim Vi, Meningovax; anti Haemophilus influenzae B), recommended for sickle-cell patients by the WHO, the High Authority for Health and other organisations (1,19,27,31,37), was not received by the patients in our study. In fact, these vaccines are not covered in our context, as the social security system is non-existent. These vaccines are expensive and are generally purchased by the parents of the children. Therefore, they seem inaccessible to these patients and to most Congolese patients with sickle cell disease, given that the cost of treating sickle cell crises is much higher than the income of the middle class Congolese, as reported by Ngolet (42,43). This situation was also reported by Boiro in Dakar and Tshilolo in Lumumbashi, who indicated that the socio-economic level in their studies was low; in 46,5% and 70% of cases respectively (39,44); as well as by other African authors (20,41,45).

In our series, no patients were under prophylaxis with oral penicillin V. The same finding was made by Mpemba et al in the paediatric population in Brazzaville (where only 0.4% of children were taking oral penicillin regularly) (24), as well as by Gbadoe in Lomé, Togo (45). Boiro, on the other hand, in his study recorded 74.1% of children who were undergoing penicillin V prophylaxis (39). The financial problem is the reason for the absence of antibiotic prophylaxis (1,24,45). This antibiotic prophylaxis showed a significant reduction in morbidity and mortality associated with pneumococcal infection in children with sickle cell disease (12,27,35,37) with an 84% reduction in pneumococcal sepsis (30-32).

Lack of follow-up or irregular follow-up in our series was also reported by Gbadoe who reported that 66.7% of patients did not keep half of the follow-up appointments (41,45), and by Boiro who recorded 41.7% of children lost to follow-up (39). All these failures were due to a financial problem.

This follow-up problem could also be explained by the distance to reach the hospital, which is in Brazzaville. In our series, patients 1 and 2 lived respectively at 600 and 350 km away from Brazzaville. This problem of distance was also reported by Boiro, who indicated that nearly 35% of the patients in his series resided outside Dakar (39).

There is often a deterioration in kidney function after severe sepsis (28,40).

In our series, the sepsis was severe by both renal (ARF) and hepatic (hepatic cytolysis) failure. Several mechanisms were involved (28,40,46): hypovolemia, hypoxia, damage to endothelial cells of the proximal tube, low liver output, activation of coagulation by bacterial lipopolysaccharides responsible for cell necrosis.

Cultures (haemoculture, cytobacteriological examination of urine) in order to identify the germs responsible for sepsis were not carried out in any of our patients; due to lack of financial means, as reported by Chetcha et al, and Elira (25,47).

Empirical antibiotic therapy, based on the ecology of germs in sickle-cell patients, used a third-generation cephalosporin (Ceftriaxone or Cefazidime) associated or not with Sulbactam or a quinolone; and metronidazole. This was consistent with the data in the literature (20,27,41,46).

Disease outcome was favourable in all patients in our study.
4. CONCLUSION

Severe sepsis is a reality among people living with homozygous sickle cell disease, both children and adults; even more so in the case of irregular follow-up or in the absence of follow-up, in the absence of vaccination or antibiotic prophylaxis. In a country with limited resources, its diagnosis must be suspected in presence of a systemic inflammatory response syndrome and a suspected infectious site, to replace system or site. Hydration, transfusion of red blood packed cells and probabilistic antibiotic therapy guided by the bacterial ecology in sickle cell disease make it possible to obtain a cure ad integrum. Regular follow-up, adequate vaccination, combined with oral penicillin V antibiotic prophylaxis, help to reduce the risk of sepsis.

Therapeutic education of patients and their parents is part of the overall management of these patients.

Social security must be put in place to enable sickle cell disease patients, even the most disadvantaged, to have access to quality care.

REFERENCES


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