Case study

Diabetes keto-acidosis in children: a report of two cases and literature review

ABSTRACT

Aims: To present features of two clinical cases of Diabetes keto-acidosis observed in the Nouveau Village de Pédiatrie, Democratic Republic of Congo, between June 2014 and June 2018.

Cases presentation:

The first case was a male patient, 13 years-old, who arrived at hospital with fever, vomiting, polyuria, unconsciousness, respiratory distress and coma. His fasting plasma glucose was 570 mg/dl. Urea nitrogen 56,4 mg/dl; Creatinine 2,1 mg/dl. C reactive protein was 27 mg/l. The treatment of Diabetes ketoacidosis was based on insulin. He received also antibiotics. Despite the normalization of his plasmatic glucose, he died with sepsis. The second case was a female child of 6 years, received with fever, intense thirst, polydipsia, asthenia, polyuria, a familial history of diabetes mellitus. Random plasma glucose was 500 mg/dl. C reactive protein was 10 mg/l. She was treated with insulin and antibiotics but her clinical prognosis worsened by a pyelonephritis and pulmonary tuberculosis. She also died despite plasma glucose normalization.

Conclusion: Diabetes mellitus type 1 in children, complicated with DKA and sepsis, have worse prognosis. More children death would be avoidable by correct *global* treatment including insulin and hydro-electrolytic balance. Underweight children and those with tuberculosis should realize routine screening for diabetes mellitus and inversely.

Keywords: children, diabetes keto-acidosis, tuberculosis, mortality

1. INTRODUCTION

Diabetes is one of the most common chronic medical disorder in children. Its management remains a substantial burden on children with diabetes and their families, despite improvements in treatment. The African literature situates its prevalence between 7 and 10 for 100000 inhabitants per year among children. Most children with diabetes have type 1. In low-income countries the diabetes of type 1 is insufficiently diagnosed and its mortality is high due to insufficient access to healthcare. Diabetic ketoacidosis (DKA) is the most frequent discovery syndrome. It has significant morbidity and mortality [1-4]. The diabetes burden is growing in all countries including Sub-Saharan Africa (SSA). Due to economic, demographic (population expansion, urban migration), epidemiological and nutrition transitions in SSA, the growing prevalence of diabetes appears to be related to obesogenic lifestyles, the declining physical activity, and dietary factors. The organization of diabetes care is poorly coordinated, especially at the primary and secondary tiers of the public health care system, with consequent poor outcomes. Both overnutrition and undernutrition have been associated with the development of diabetes [5-7].

This study describes clinical and biological features of two children hospitalized for diabetes mellitus in the Nouveau Village de Pédiatrie between June 2014 and December 2016. The main purpose is to make physicians of this part of the Democratic Republic of Congo (DRC) aware of this disease, and the challenging management of its complications.

2. PRESENTATION OF THE CASES

The first case was a male patient, 13 years-old, who arrived at hospital with fever, vomiting, polyuria and unconsciousness. The axillary temperature was 39°C. He had Kusmaul's respiration type. Neurologic exam showed no focal sign. Glasgow's coma scale was 6. He had a BMI of 14,8 (2nd

percentile in the WHO BMI chart for age and sex). The fasting plasma glucose (Contour®, Bayer) was 570 mg/dl. Urea nitrogen 56,4 mg/dl; Creatinine 2,1 mg/dl. Both thick blood smear and rapid diagnostic test for malaria (Pan/Pf Standard Diagnostic Bioline®) were negative. Hemoglobin (Hemocue® 301) was 13 g/dl. C reactive protein (QuickReadGo® CRP, Orion Diagnostica) at admission was 27 mg/l.

The diagnosis of sepsis and DKA was decided. Treatment was based on infusion of lactate ringer and saline isotonic given alternatively. Quantity was estimated on the basis of daily water requirements and gradient between all water intake (polydipsia) and loss via polyuria. Hydro-electrolytic assessment was not available, rapid insulin at a dose of 1,5 IU/kg/day given intravenously after each hour. He received also cefotaxime (Claforan®), associated to gentamycine. On day 2, C reactive protein was 26 mg/l: antibiotherapy was then reviewed by replacing gentamycin by amikacin. Dietetic care was based on local food with low glycemic index in mush given via nasogastric tube thrice a day

There was light clinical improvement. The same day the coma improved from grade 3 to grade 1 and glucose blood level dropped to 295 mg/dl. When plasmatic glucose reached 139mg/dl on day 2, the insulin therapy shifted to a three doses of rapid insulin associated with 2 bolus of long acting insulin. The blood glucose lowered to 93mg/dl but the sepsis did not improve. C reactive protein raised up to 67 mg/dl on day 3. Despite negative malarial exams, he received intravenously artesunate (Artesun®, Guilin Pharmaceutical Co. Ltd. China) at 2,4mg/kg at hours zero, 12 and 24, then once daily. On day 4, blood glucose raised again (260mg/dl) and the boy had abdominal distension. He died on day 5. Body temperature ranged from 37,1° to 39°C.

The second case was a female child of 6 years, with fever, intense thirst, polydipsia, asthenia, headache and polyuria. She had 17 kg for 115,5 cm of height (BMI 12,7; 2,5 th percentile of BMI for age and sex). There was a familial history of diabetes mellitus. The respiration was acidotic. She was agitated and comatose (Grade 1 on days 1 and 2). The axillary temperature was 37°C. Random plasma glucose was 500 mg/dl. The thick blood smear and the rapid diagnostic test for malaria were negative. The white blood count was 6400/mm3. The C reactive protein was 10, 76 and 36 mg/dl respectively on days 1, 3 and 6. The diagnosis of sepsis and DKA was decided. The insulin treatment started with a dose of 1,5 IU/kg/day (Actrapid®) divided in equal doses given intravenously after every hour. She also received lactate ringer and saline infusions. Hypertonic glucose infusions (10%) were used only in the cases of hypoglycemia. Food of low glycemic index were given in mush via nasogastric tube. The first antibiotherapy associated cefotaxime (Claforan®) and gentamycine. After the second CRP dosage, the antibiotherapy shifted to the association Vancomycin (Sandoz) and amikacin (Mylan). The axillary temperature improved till 36°C on day 8.

Blood glucose raised during the first two days up to 600 mg/dl but improved after antibiotics revision until it reached 149 mg/dl. The insulin treatment was then revised. Two thirds of the dose were the rapid insulin given every 8 hours. And the rest was the long acting insulin given subcutaneously at the same time as the first and third rapid insulin bolus. Note that the blood glucose lowered difficultly and irregularly. The clinical state worsened with dyspnea, crackles and respiratory distress. Chest X-ray, normal on day 3, showed, on day 7, bilateral and sparse opacities. HbAc level was 10,4%. Blood pH was 7. Urine dipstick revealed proteinuria, ketonuria, leucocyturia and hematuria. The diagnosis was revised as pulmonary tuberculosis and pyelonephritis. Antituberculosis treatment started immediately but the girl died two days later. The last dosage of blood glucose showed 122mg/dl.

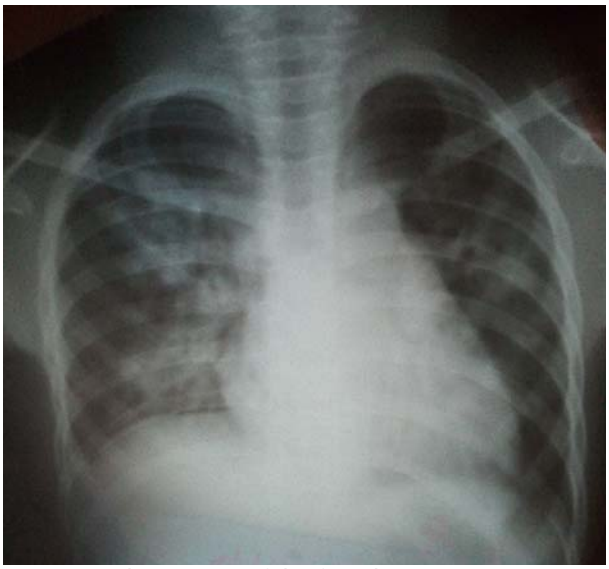

Image 1. Chest-X ray of the female case

3. DISCUSSION

These two cases of diabetes mellitus were diagnosed in school-level children, who were underweight. Both had type 1 diabetes mellitus and DKA was the principal clinical manifestations. Cases definitions matched those of American Diabetes Association [8].

Both had serious sepsis co-morbidity that made blood glucose control difficult. Despite glycemia improvement with insulin treatment, the main cause of their death might be cerebral edema for the first case and pulmonary edema for the second. Ophthalmoscopy was not realized but clinical features looked like what many authors found. Cerebral edema is the most common cause of death and a high index of suspicion is always required. Cerebral edema may be exacerbated by factors related to both DKA presentation and therapy. Intravenous fluid boluses should be given cautiously. [9-10] Other authors found that cerebral edema, pulmonary edema and septic shock were predictors of mortality [10-12]. Both children had bacterial infection: sepsis in the former, pneumonia and urine tract infection in the second.

Patients came from high socio-economic level families. Richer patients and those living in urban area were reported by some studies [10, 14]. One child had acute kidney injury (AKI). AKI is reported to increase morbidity and mortality of children with type 1 DKA [13]. Death from diabetes in children and adolescents is potentially preventable through increased awareness of diabetes symptoms (including symptoms of low blood sugar), genetically exposed children (with positive familial history), good nutrition practices (breastfeeding, avoidance of sugar beverages for example), earlier treatment and education related to diabetes, and management of diabetes ketoacidosis [10, 13, 15, 16].

Both children died despite availability of good quality insulin, antibiotics, fluids and nutritional assistance. This high mortality rate has been reported by many authors [3, 7, 9, 10, 11]. Despite appropriate use of insulin and fluids, and continuous clinical observation, the mortality rate has not improved, and has remained the same as that reported in the 1970s. Worldwide, infection is the most common precipitating cause for DKA, occurring in 30-50% of cases. Urinary tract infection and pneumonia account for the majority of infections [17]. Diabetes mellitus is also reported as a risk factor of tuberculosis [18-19].

This study had many limits. There was almost no biological data about electrolyte and acid-base balance at admission and during treatment because neither in The Nouveau Village de pédiatrie nor in local private laboratory such exams were available. So we could not precisely say the children died because of the confirmed sepsis, kidney injury, metabolic disorders due to DKA or insufficient hydro-electrolytic therapy. These limitations in the diagnostic work-up, treatment and outcome of the cases, compared to the international guidelines must help physicians, public and private laboratories, to address this issue. As one author said, in a lot of " countries in development", the burden of the infectious and parasitic pathology in pediatric environment made of the obesity and other non-infectious diseases a marginal preoccupation [20].

4. CONCLUSION

Diabetes mellitus type 1 in children, complicated with DKA and sepsis, have worse prognosis. More children death would be avoidable by correct *global* treatment including insulin and hydro-electrolytic balance. Underweight children and those with tuberculosis should realize routine screening for diabetes mellitus and inversely.

ETHICAL APPROVAL

This study had the agreement of research Authorities of the faculty of medicine and Pharmacy of the University of Kisangani.

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