Hypoglycemia in bacterial septicemia

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ABSTRACT

In the emergency department (ED), the typical manifestation of impaired glucose homeostasis seen in patients with severe bacterial infections is hyperglycemia. Severe hypoglycemia is generally not a presenting feature of sepsis in children in the emergency setting, and thus may lead to delayed diagnosis and management. We present a case of a 14-year-old boy who attended the ED with constitutional symptoms and severe hypoglycemia as the initial presentation of overwhelming meningococcal sepsis and discuss the impairment of glucose homeostasis in patients with sepsis.

Key words: hypoglycemia; septicemia; meningococcal sepsis; acute presentations; emergency medicine

RÉSUMÉ

Au département d'urgence, la manifestation typique d'une altération de l'homéostase glucidique chez des patients atteints d'une infection bactérienne grave est l'hyperglycémie. L'hypoglycémie sévère n'est généralement pas un signe révélateur de la septicémie chez les enfants dans le cadre de l'urgence et peut par conséquent mener à des délais de diagnostic et de prise en charge. Nous présentons le cas d'un garçon de 14 ans reçu à l'urgence chez qui les premiers signes d'une septicémie méningococcique irrépressible étaient des symptômes généraux et une hypoglycémie sévère et nous discutons de l'altération de l'homéostase glucidique chez les patients septicémiques.

Introduction

Profound hypoglycemia is typically a late phenomenon in patients with severe bacterial septicemia, and is thought to be a manifestation of increased tissue uptake of glucose and impaired gluconeogenesis.[1] Severe hypoglycemia is generally not a presenting feature of sepsis in older children presenting to the emergency department (ED), and thus may lead to delayed diagnosis and management. We present a case of a 14-year-old boy who attended the ED with constitutional symptoms and severe hypoglycemia as the initial presentation of overwhelming meningococcal sepsis.

Case report

A 14-year-old boy, weighing approximately 60 kg, arrived by ambulance to the ED at 0900 h with chills, weakness and abdominal pain. He had an 18-month history of systemic lupus erythematosus (SLE), treated with prednisone and hydrochloroquine, but had been doing well until the evening before. At 0200 h on the day of presentation, he

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began feeling vaguely unwell, and his symptoms worsened overnight.

On initial assessment by emergency medical services personnel, he was found to have a capillary blood glucose (CBG) level of 1.1 mmol/L. He was given one ampoule (5 g) of D50W intravenously (IV) while on route to hospital, and a repeat CBG level was found to be 1.6 mmol/L. In the ED, he was afebrile, alert and oriented (Glasgow Coma Scale score, 15), but in obvious discomfort. His vital signs were as follows: blood pressure (BP) 59/43 mm Hg by cuff, pulse rate 153 beats/min, respiratory rate 20 breaths/min, oxygen saturation 100% on oxygen at 2 litres/min via nasal cannula. There were no obvious skin lesions, no nuchal rigidity, and no focal neurological findings. His chief complaint continued to be generalized abdominal pain.

The patient was aggressively resuscitated with repeated 10 cc/kg boluses of 0.9% saline solution through large bore peripheral IV catheters. Initial boluses of IV D50W, totalling 25 g, were given along with oral glucose solution with only modest improvement in CBG levels. His neurological status rapidly deteriorated and he was intubated. Empirical treatment with antibiotics was initiated using a third generation cephalosporin. Volume expansion led to an improvement in blood pressure, and the hypoglycemia normalized with parenteral dextrose infusion. He was referred to the pediatric intensive care service for ongoing management.

Laboratory results were: hemoglobin 111 g/L; leukocytes 3.8×10^9/L (neutrophils 0.5×10^9/L; platelet count 107×10^9/L; sodium 141 mmol/L; potassium 2.9 mmol/L; chloride 104 mmol/L; bicarbonate 19 mmol/L; creatinine 206 µmol/L; urea 3.4 mmol/L; glucose 17.3 mmol/L; calcium 1.71 mmol/L; magnesium 0.59 mmol/L, and INR 1.4. Venous blood gases analysis revealed a pH of 7.25, P_{CO_2} 44 mm Hg, P_{O_2} 37 mm Hg, bicarbonate 19 mmol/L and a base deficit of 7.8 mol/L. Liver function tests were within normal limits. A Gram stain of peripheral blood demonstrated gram-negative diplococci, later identified as *Neisseria meningitidis*. Cerebrospinal fluid was not obtained, as resuscitative efforts were ongoing.

In the pediatric intensive care unit, the patient required inotropic support with large doses of dopamine and epinephrine, as well as further IV fluid boluses and hydrocortisone, 600 mg. The patient rapidly developed severe pulmonary edema with ventilatory compromise and suffered a pulseless electrical activity cardiac arrest. Despite aggressive resuscitative efforts, he developed an irreversible agonal cardiac rhythm and was pronounced dead at 1242h, approximately 3½ hours after presenting to the ED.

Discussion

Meningococcal sepsis in children is a rapidly progressive illness that produces a systemic inflammatory response, with fever and constitutional symptoms giving way to purpura and shock. Presenting symptoms range from non-specific fever, rash or flu-like illness to meningismus and florid septicemia.[2–4] Its incidence in children is bimodal, with peaks occurring around age 2 and again among teenagers. The mortality rate ranges from 20% to 50%, and is higher in younger children than in teenagers.[5,6]

A disproportionate incidence of meningococcal sepsis, up to 100 times higher than the general population, has been observed in patients with acquired complement disorders such as SLE. This may result from inefficient opsonization of the pathogen, or terminal membrane attack complex defects.[7,8]

Impaired glucose homeostasis has been well documented in patients with sepsis.[9,10] Hyperglycemia is the most common blood glucose abnormality seen early in the course of bacterial sepsis. Hyperglycemia occurs because of a blunted hepatic response to insulin, and because of high levels of circulating catecholamines, glucagon and cortisol, which enhance glycogenolysis and gluconeogenesis. In pre-terminal sepsis, profound hypoglycemia may occur because of increased tissue uptake of glucose and the failure of hepatic glucose production.[1,11,12] Romijn and colleagues reported a case of fatal meningococcal sepsis in which sequential measurements of plasma concentrations of glucoregulatory hormones were obtained.[13] They postulated that sepsis-related hypoglycemia is a manifestation of high levels of cytokines, including tumour necrosis factor and interleukin-6. Elevation of these cytokine levels has been well described in patients with meningococcemia and, given the absence of increased levels of insulin or other catabolic hormones in their patient, the traditional model of glucose autoregulation does not explain this hypoglycemia phenomenon.[13–15]

Hypoglycemia with cardiovascular collapse is also seen in patients with adrenal insufficiency. Because of long-standing prednisone use, our patient was at risk of adrenal crisis; however, he was treated appropriately with hydrocortisone and his blood cultures confirmed *Neisseria meningitides* bacteremia, a disease to which he was also predisposed because of his SLE.

Summary

Impaired glucose homeostasis is often seen in patients with severe bacterial infection, and hypoglycemia is often a pre-

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terminal finding in sepsis. Our patient developed profound hypoglycemia within hours of the onset of illness, demonstrating the rapid progression of sepsis associated with meningococcemia. In acutely septic patients presenting to the ED with hemodynamic compromise, physicians should recognize and address derangements in glucose metabolism, especially early in the course of the illness and during active resuscitation.

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