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Steroid-induced diabetic ketoacidosis in a 9-year-old boy with relapsing steroid-sensitive nephrotic syndrome

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Systemically administered corticosteroids remain the backbone therapy for nephrotic syndrome up to now. Although 80%-90% of children show remission following steroid treatment and are classified as steroid-sensitive nephrotic syndrome, 90% of initial responders will experience relapse at least once, and about 50%-60% may progress to frequent relapsing nephrotic syndrome and hence become steroid dependent. Hyperglycaemia is one of the best-known side effects, although most cases are mild and clinically asymptomatic. Presentation with severe hyperglycaemia is possible but rather uncommon. This paper reports a case of steroid-induced diabetic ketoacidosis in a 9-year-old Asian boy with relapsing steroid-sensitive nephrotic syndrome.

Key words: NEPHROTIC SYNDROME; DIABETIC KETOACIDOSIS; STEROIDS; CHILD

INTRODUCTION

Glucocorticoids are potent anti-inflammatory drugs frequently prescribed for various diseases, some of which may require high doses and prolonged use (1). In paediatric population, nephrotic syndrome is one of them. Systemically administered corticosteroids remain the backbone therapy for nephrotic syndrome up to now (2,3). Although 80%-90% of children show remission following steroid treatment and are classified as steroid-sensitive nephrotic syndrome (SSNS), 90% of initial responders will experience relapse at least once (3) and about 50%-60% may progress to frequent relapsing nephrotic syndrome (FRNS) and hence become steroid dependent (3-6). This relapsing group will require higher and prolonged steroid administration, eventually with an increasing rate of side effects (2).

Development of hyperglycaemia is one of the best-known side effects, although most cases are mild and clinically asymptomatic (7). Presentation with severe hyperglycaemia is possible but rather uncommon (7,8). This paper reports a case of steroid-induced diabetic ketoacidosis (DKA) in a 9-year-old boy with relapsing SSNS.

CASE REPORT

A 9-year-old Asian boy (body weight 25 kg, body height 128 cm, standard deviation score (SDS) -0.91; body mass index (BMI) 15.3 kg/m^2, SDS -0.53; body surface area (BSA) 0.94 m^2) was brought to the emergency department with chief complaint of profuse vomiting for two days prior to admission. In the past three weeks, the patient showed excessive micturition and polydipsia. He did not have bloody vomitus, diarrhoea, fever, or cough. On examination, the patient was lethargic, showing Kussmaul breathing pattern, smelled ketone, and was severely hypovolemic. Venous blood glucose was 800 mg/dL (44.8 mmol/L) and HbA1c was 5.1%. Arterial blood gases showed pH 7.080, HCO_3 3.0 mmol/L, and pCO_2 6.0 mm Hg. Urinary ketone was +3 and urinary protein +2 with no leukocyturia. The patient was assessed as DKA. He received fluid resuscitation using normal saline and syringe-pumped insulin at 0.05 IU/kg/h.

In-depth history taking revealed that the patient had been diagnosed with nephrotic syndrome four years before. At that time, the patient was brought to the hospital because of generalized body swelling and oliguria. He had no haematuria or hyperglycaemia, and there was no family history of kidney disease. Laboratory testing showed hypoalbu-

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minemia, hypercholesterolemia, and severe proteinuria. Renal biopsy was not done due to insurance limitation. The patient was referred to a paediatric nephrologist and treated with oral prednisone 40 mg/day. After four weeks, urinary protein was negative and symptoms gradually disappeared. The patient showed complete remission and was classified as SSNS. Treatment was tapered off and stopped after eight weeks. At the age of seven years, his symptoms relapsed and the patient was treated with similar regimen. Two weeks prior to admission to our emergency department, his symptoms relapsed again. Urinary protein was +3, without glycosuria. The patient was treated with oral prednisone 40 mg/day for 2 weeks. Urinary protein was planned to be checked after four weeks, unfortunately, the patient was brought to our emergency department before the scheduled time.

Upon admission to our hospital, steroid therapy was discontinued. The patient was treated with insulin and blood glucose gradually normalized. However, on day 7, oedema began to re-appear. Urinary protein was +3, without glycosuria. The patient was transferred to paediatric nephrologist for further assessment.

DISCUSSION

Nephrotic syndrome is a tetrad of oedema, nephrotic-range proteinuria, hypoalbuminemia, and hyperlipidaemia (2). Despite its high response rate to steroids, many of its initial responders eventually experience relapse or become steroid dependent (5). It is currently recognized that relapses are frequently triggered by acute respiratory tract infections, urinary tract infections, diarrhoea, allergic episodes, and vaccination (6). In this case, the parents did not monitor the presence of infections, while in fact during the period of infection, initiation of steroid therapy and zinc supplementation should be considered because they are reported effective in reducing relapse rates (4). Relapses expose patients to a higher and prolonged use of corticosteroids.

Steroids, which have a profound effect on glucose production, glucose uptake, and insulin production, may precipitate new-onset diabetes mellitus (DM) in a previously normal individual, or exacerbate pre-existing controlled DM (1,7,9). While it is expected that a normal person could produce extra insulin to counteract the hyperglycaemic effect, some vulnerable individuals might need extra monitoring (1, 8). Nearly 50% of patients consuming steroids for >2 weeks will develop hyperglycaemia (1, 8). It is thus logical that the patient in this case eventually developed hyperglycaemia after a repeated course of high-dose prednisone.

However, steroid-induced hyperglycaemia is often mild and clinically asymptomatic (7). Although possible, presentation with DKA is rather uncommon (7,8). DKA is usually related to patients with type 1 DM with coexisting stressors, medications, or sudden discontinuation of insulin, or very rare to patients with type 2 DM in adolescence (10). In our case, the absence of hyperglycaemia prior to steroid therapy indicated that the patient had not been previously diabetic.

Although steroid-induced diabetes is usually transient and easily treated, hyperglycaemia may persist in about half of the cases (8). Nephrotic symptoms can also re-appear when steroid is discontinued, as in our case.

Hence, early detection of steroid-induced DM in patients administered higher and prolonged dose of corticosteroids should not be overlooked. Although mostly mild and asymptomatic, in some cases, it may become potentially harmful when severe hyperglycaemia develops. Hyperglycaemia may also persist and hence increase hospital admissions, patient burden, and reduce their quality of life. In this case, the patient tolerated the high dose of steroid initially, yet eventually developed DKA after his third relapse. Relapses of SSNS should be avoided by preventing prolonged use of high-dose steroids.

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SAŽETAK

Dijabetička ketoacidoza izazvana steroidima u 9-godišnjeg dječaka s recidivirajućim nefrotskim sindromom osjetljivim na steroide

Eunike Vania Christabel

Sistemski primijenjeni kortikosteroidi do danas ostaju osnovna terapija za nefrotski sindrom. Iako 80-90% djece pokazuju remisiju nakon terapije steroidima i klasificiraju se kao nefrotski sindrom osjetljiv na steroide, 90% onih koji odgovore na prvu primjenu dožive barem jedan recidiv, dok njih 50-60% može progredirati prema nefrotskom sindromu s čestim recidivima i time postati ovisni o steroidima. Jedna od najbolje poznatih nuspojava je hiperglikemija, iako je većina slučajeva blaža i klinički asimptomatska. Pojava teške hiperglikemije je moguća, ali prilično rijetka. Opisuje se slučaj dijabetičke ketoacidoze izazvane steroidima u 9-godišnjeg azijskog dječaka s recidivirajućim nefrotskim sindromom osjetljivim na steroide.

Ključne riječi: NEFROTSKI SINDROM; DIJABETIČKA KETOACIDOZA; STEROIDI; DIJETE