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ACUTE RESPIRATORY DISTRESS SYNDROME IN A FOUR-YEAR-OLD BOY WITH DIABETIC KETOACIDOSIS – CASE REPORT

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SUMMARY – Among many disease states as known initiators of acute respiratory distress syndrome (ARDS), diabetic ketoacidosis (DKA) is the rarest one. We present a 4-year-old boy with DKA as the first manifestation of insulin-dependent diabetes mellitus who developed ARDS, required tracheal intubation and mechanical ventilation, and survived without significant sequels. To improve survival of patients with ARDS as a complication of DKA, physicians should be aware of this rare pulmonary complication and its appropriate management.

Key words: *Child; Diabetic ketoacidosis; Diabetes mellitus, type 1; Respiratory distress syndrome, adult*

Introduction

Acute respiratory distress syndrome (ARDS) is an acute diffuse inflammatory lung injury characterized clinically by sudden onset of dyspnea, progressive hypoxemia and decreased lung compliance accompanied by the development of diffuse infiltrates on chest x-ray[1]. The pathogenesis of ARDS involves an inflammatory process at the alveolar-capillary interface leading to the accumulation of protein-rich fluid in the alveolar space[1]. Many causes of acute direct and indirect lung injury have been described as possible initiators of ARDS[2]. According to literature data, ARDS could be a rare complication associated with the acute onset of diabetic ketoacidosis (DKA), occurring usually in adolescents and young adults[3-6].

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Herein we report a case of ARDS in a previously healthy 4-year-old boy admitted to the intensive care unit because of the initial episode of DKA as the first manifestation of type 1 diabetes mellitus (DM).

Case Report

A 4-year-old boy with unremarkable medical and family history presented to the emergency room with a 2-day history of malaise, lethargy, tachypnea, sore throat, abdominal pain, vomiting and dehydration. In retrospect, the history revealed polyuria, polydipsia and a documented 4-kg weight loss in 3 weeks preceding admission. He was afebrile, tachypneic (46 breaths *per* minute) with Kussmaul respirations, his heart rate was 156 beats *per* minute and blood pressure was 90/55 mm Hg. The patient's physical findings included light drowsiness, no jugular distension, with diffuse rhonchi in all lung areas.

Diabetic ketoacidosis was confirmed (plasma glucose level 29.8 mmol/L, pH 6.788, pO_2 5.20 kPa,

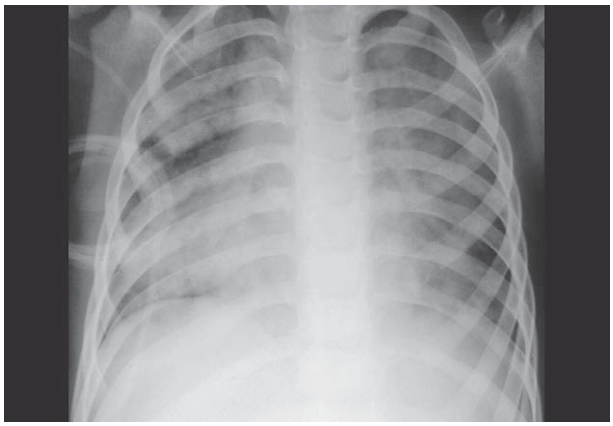

Fig. 1. Chest x-ray demonstrating bilateral severe diffuse infiltrates consistent with acute respiratory distress syndrome.

pCO_2 4.43 kPa, bicarbonate 4.7 mmol/L, sodium 135 mmol/L, potassium 5.1 mmol/L). Urine analysis revealed only glucosuria and ketonuria. Immediate treatment consisted of insulin infusion, intravenous saline, potassium replacement and symptomatic respiratory treatment. Hypotension was controlled with volume expansion, vasopressors and inotropes. In spite of therapy, the patient's status continued to deteriorate and a few hours later he suddenly developed severe dyspnea, increased tachypnea, restlessness and cyanosis. Auscultation of the chest disclosed diffuse crackles and rhonchi in all lung areas. Hypoxemia was confirmed and chest radiograph showed bilateral severe diffuse infiltrates, but no cardiomegaly (Fig. 1). Acute respiratory failure secondary to ARDS was diagnosed. The patient was transferred to the intensive care unit and he was treated initially with oxygen by facemask. However, his condition deteriorated further and a few hours later endotracheal intubation and mechanical ventilation were required. Throat culture was positive for group A beta-hemolytic streptococci, while cultures of urine and blood specimens were negative. Intravenous co-amoxiclav was administered every 8 hours. Due to further clinical deterioration, the patient was transferred to our hospital. On admission to our hospital, he was intubated, mechanically ventilated by transport ventilator (SIMV, FiO_2 56%, arterial oxygen saturation 95%, respiratory rate 25 breaths *per* minute), his heart rate was 136 beats *per* minute and blood pressure was 113/75 mm Hg, afebrile, sedated and diffusely edematous.

Table 1. The main laboratory test results on patient admission to our hospital

	Result	Reference value
Blood glucose level (mmol/L)	13.9	3.9-7.0
Hemoglobin A_{1c} (%)	9.2	<7
C-reactive protein (mg/L)	43.1	<5
Leukocyte (x10^9/L)	18.3	6.0-16.0
Total protein level (g/L)	45	55-80
pH	7.330	7.35-7.45
pCO_2 (kPa)	5.3	4.66-6.60
pO_2 (kPa)	7.4	10.70-12.70
Bicarbonate (mmol/L)	21.2	21-26
Sodium (mmol/L)	135	134-143
Chloride (mmol/L)	102	96-109
Potassium (mmol/L)	4.5	3.5-6.0
Magnesium (mmol/L)	0.75	0.65-1.03
BUN (mmol/L)	5.4	1.8-6.0
Triglycerides (mmol/L)	1.98	<1.7
Cholesterol (mmol/L)	4.8	<4.7
HDL (mmol/L)	1.06	>1
LDL (mmol/L)	2.83	<3

BUN = blood urea nitrogen; HDL = high density lipoprotein; LDL = low density lipoprotein

The main laboratory findings on admission are presented in Table 1. Leukocyte count was 18.3, with differential of 67 neutrophils, 25 lymphocytes, 7 monocytes and 1 eosinophil. Prothrombin time, platelet count, troponin T level, liver function tests and levels of serum and urine amylase were within the normal limits. On urine analysis, only glucosuria was noted. Cultures of tracheal tube, urine and blood specimens were negative. Electrocardiography pattern was normal. Chest high-resolution computed tomography revealed the following: bilateral areas of patchy abnormalities and mixed ground-glass appearance and consolidation, predominantly in the right middle and left upper lobes, but neither cardiomegaly nor mediastinal lymphadenopathy was found (Fig. 2A, B). Treatment with antibiotics was continued for 10 days. In the next 4 days, subcutaneous injections of regular insulin replaced i.v. insulin to maintain euglycemia. During the next three days, his condition improved enough to be weaned from ventilator. He was euglycemic with no ketonuria and continued to receive subcutaneous regular insulin. He made good recovery over the next few

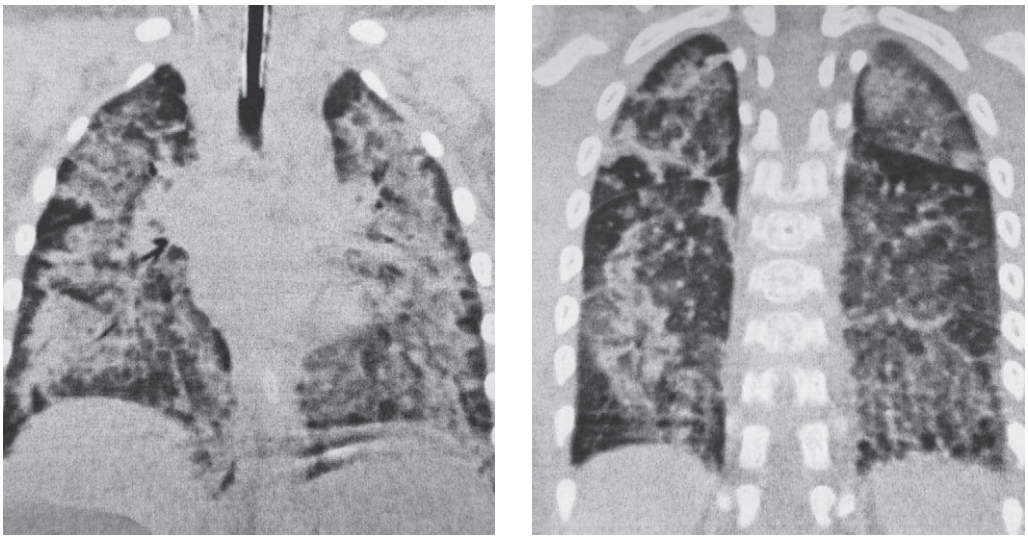

Fig. 2A, B. Chest high-resolution computed tomography demonstrating bilateral areas of patchy abnormalities and mixed ground-glass appearance and consolidation.

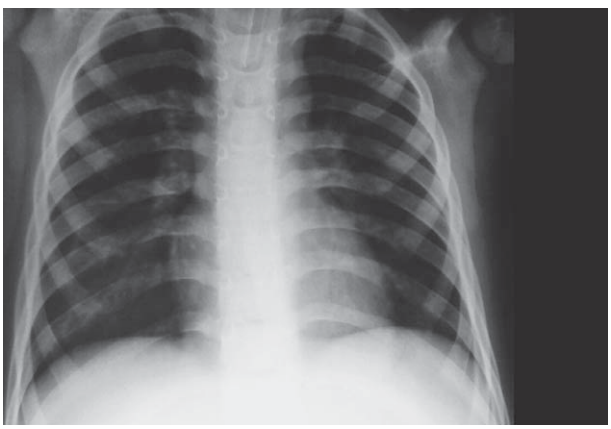

Fig. 3. Chest x-ray demonstrating complete clearance of diffuse infiltrates.

days, his blood gas levels improved steadily, and he was on room air after 7 days of hospital stay. All respiratory symptoms cleared and chest x-ray markedly improved (Fig. 3). Definitive diagnosis was ARDS in association with DKA as the first manifestation of type 1 DM in a 4-year-old boy.

Discussion

The most common causes leading to ARDS are pneumonia, sepsis, aspiration of gastric contents, toxic inhalation, near drowning, and trauma. We report an unusual case of a child with DKA who developed ARDS, required tracheal intubation and mechanical ventilation, and survived without significant sequels. The clinical disorders usually associated with ARDS were systematically excluded on the basis of the complete workup and clinical course, supporting DKA as the probable initiating factor. DKA is a life-threatening condition that is characterized by hyperglycemia, metabolic acidosis, with associated glycosuria, ketonuria and ketonemia as the result of absolute (in previously undiagnosed type 1 DM and when patients on treatment deliberately or inadvertently do not take insulin) or relative insulin deficiency (in cases when the concentrations of counter-regulatory hormones markedly increase in response to stress in conditions such as sepsis or trauma)[7-9]. The mortality rate from DKA in children is 0.15%-0.30% and the major cause that accounts for 60%-90% of all DKA deaths is cerebral edema[8]. Among other causes of mortality and morbidity, ARDS also presents a predictor of high mortality but this entity is rarely encountered in pediatric population[8,10,11]. The true mechanism of ARDS during DKA remains unclear. Previously, it was estimated that DM patients had an increased capillary permeability[12]. It can be speculated that severe acidosis as in our patient with DKA could cause an increase in the permeability of capillary membranes, leading to alteration of the alveolar surfactant metabolism[4]. However, many patients are very acidotic at the onset of DKA but only few of them develop ARDS[11]. This supports the hypothesis of the multifactorial etiology of ARDS as a complication of DKA[13].

The mainstay of treatment of DKA is insulin therapy, rehydration with large quantities of intravenous crystalloid fluids, and replacement of electrolyte deficits[9]. It was shown that overly vigorous hydration raised the risk of ARDS possibly by increasing hydrostatic pressure and decreasing intravascular oncotic pressure[7]. These alterations of the hydrostatic-oncotic forces make the patients with DKA prone to developing pulmonary edema. However, although most patients receive large volumes of fluids, ARDS is an infrequent complication[2].

Hoffman *et al.*[14] showed that metabolic changes in DKA and its treatment had differential effects on cellular activation and cytokine release. A significant decrease in interleukin (IL)-10 as a known anti-inflammatory cytokine and increases in IL-1beta, IL-8 and tumor necrosis factors (TNF)-alfa as proinflammatory cytokines were observed. They also noted that the progression of interstitial pulmonary edema correlated with the time frame of inflammatory cytokine enhancement, supporting their role in diffuse inflammatory lung injury defining ARDS[14].

It is not clear why only a minority of patients with known exposure to risk factors develop ARDS. It seems that genetic predisposition in combination with severe acidosis, alteration in hydrostatic-oncotic forces due to large volumes of crystalloid fluids and proinflammatory cytokine enhancement can lead to ARDS in a patient with DKA. A number of gene polymorphisms associated with the susceptibility to ARDS have been discovered, i.e. angiotensin converting enzyme gene, pulmonary surfactant-associated protein B, IL-6, angiopoietin-2 and coagulation factor V[14-17]. There is hope that these studies may help recognize patients at a greater risk of ARDS early and initiate development of better treatment based on personalized therapy that could improve survival. For now, the mainstay of treatment for ARDS is aggressive management of the underlying cause, mechanical ventilation and high flow oxygen therapy. Survival without sequels is increased with improved management. We therefore suggest that any suspicion of the development of ARDS syndrome, sudden onset of dyspnea, progressive hypoxemia accompanied by development of diffuse infiltrates on chest x-ray in a child with DKA warrants high level of concern and intensive care monitoring.

In conclusion, to improve survival of patients with ARDS as a complication of DKA, physicians should be aware of this rare pulmonary complication and its appropriate management.

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Sažetak

SINDROM AKUTNOG RESPIRACIJSKOG DISTRESA U ČETVOROGODIŠNJEG DJEČAKA S DIJABETIČNOM KETOACIDOZOM – PRIKAZ SLUČAJA

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Među poznatim inicijatorima sindroma akutnog respiracijskog distresa (ARDS) dijabetična ketoacidoza (DKA) je najrjeđi. U ovom radu prikazujemo 4-godišnjeg dječaka s DKA kao prvom manifestacijom o inzulinu ovisne šećerne bolesti u kojega se razvio ARDS te je zahtijevao mehaničku ventilaciju i preživio bez značajnijih posljedica. Kako bi se unaprijedilo preživljenje bolesnika s ARDS kao komplikacijom DKA liječnici trebaju biti upoznati s ovom rijetkom plućnom komplikacijom i njezinim pravilnim liječenjem.

Ključne riječi: *Dijete; Dijabetična ketoacidoza; Dijabetes melitus, tip 1; Sindrom respiracijskog distresa, odrasla osoba*