

Case Report

Early onset type 1 diabetes mellitus in an infant during COVID-19 pandemic: case report

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ABSTRACT

Type 1 diabetes mellitus (T1DM) is an endocrine disorder, marked by elevated blood glucose level caused by autoimmune process destroying the β -cells of the pancreas which mostly affects children. It is an often-overlooked condition, with low awareness among clinicians and parents alike which led to late diagnosis and patients often presenting with acute complications. Often triggered by a viral infection, here we presented an interesting case of early onset T1DM presenting with Diabetic ketoacidosis (DKA) during a COVID-19 pandemic. A female infant, aged 1 years and 2 days old, presented with dyspnea and fever. Physical examination was otherwise normal, without any rhonchi or wheezing found during pulmonary auscultation. Nasopharyngeal swab and SARS-CoV-2 antigen test was found negative. Laboratory workup found random blood glucose level of 577 mg/dl accompanied by acidosis and ketonuria. The patient also had elevated white blood cells and platelet counts. She was admitted for treatment in the Pediatric intensive care unit (PICU) with therapeutic regimens consisting of slow intravenous insulin infusion, potassium chloride intravenous fluid, antibiotics, and antipyretics. Close monitoring of blood glucose ensues and the patient was treated for 5 days followed by outpatient therapy with mixed insulin treatment twice per day. This case was interesting as T1DM usually manifested in older children with median age of diagnosis ranging from 8 to 13 years old, depending on population. T1DM diagnosed in children younger than 6 years old are classified early onset and it is especially rare to found in infants. Although the patient tested negative for SARS-CoV-2 antigen, the onset of the case coincides with a recent surge of cases locally. It meant that we cannot rule out possibility of prior unknown exposure or infection which may precipitate the condition.

Keywords: Type 1 diabetes mellitus, Early onset, Infant, COVID-19, Indonesia

INTRODUCTION

Type 1 diabetes mellitus (T1DM) is often an overlooked condition affecting children and infants. Recent data showed incidence of T1DM reached 15 new cases per 100,000 people annually and its prevalence reached 9.5%. In Asia, the incidence was similar, at 15 new cases per 100,000 people, although it was accompanied by lower incidence at 6.9%.¹ This indicates either there are some undiagnosed T1DM cases in Asia or T1DM cases have much lower life expectancy, skewing the prevalence rate.

The incidences figure are especially important as there has been evidence of increasing incidence over the years.^{2,3}

Despite this, awareness of this condition remains low among clinicians and parents alike. Low awareness led to late diagnosis cases, often when the child with T1DM already suffered acute complications such as Diabetic ketoacidosis (DKA). In fact, prevalence of DKA among T1DM patients at diagnosis has been used as indicators of awareness and timely diagnosis of T1DM. A systematic review found that prevalence of DKA at time of T1DM

diagnosis correlates with awareness and Asian countries was found with much higher prevalence of DKA compared to American and European countries.⁴ In Indonesia, the figure stand at 79%, at the upper end of the 12.8% to 80% range between various countries in the world.^{3,4}

Early onset T1DM is also more concerning compared to other cases. Median age of T1DM diagnosis ranged from 8 to 13 years in different countries.¹ Cases diagnosed in patients younger than 6 years old can be classified as early onset.⁵ Early onset T1DM is especially concerning as it affects future development of the child as well as quality of life and life expectancy.^{6,7}

The awareness of T1DM should be especially heightened during this time of COVID-19 pandemic. Perinatal or neonatal viral infections has been identified as a risk factor for T1DM. Enterovirus infection has been especially studied for this association.⁸ Viral infection in susceptible children led to the formation of autoantibodies that led to β -cell destruction in the pancreas, precipitating T1DM.⁹ It is concerning that similar mechanism has been postulated for SARS-CoV-2, the etiological virus of COVID-19.¹⁰

In light of this information, we presented a case of an infant presenting with dyspnea which later was found to be caused by DKA and T1DM. Although the patient was tested negative for SARS-CoV-2 antigen, the case was presented during the height of a local COVID-19 surge. As we were not able to rule out prior COVID-19 infection or exposure, this case is an interesting case study of how T1DM cases might present itself in a limited resource setting during COVID-19 pandemic.

CASE REPORT

A female infant, aged 1 year and 2 days old, was presented by her parents to the emergency room with dyspnea for 1 day which progressively got worse accompanied by a recent onset of somnolence. The parents reported that she had fever 2 days before presentation to the emergency room also it has subsided. The patient also reported to have vomited once, producing yellow-colored liquid. She was reported to drink and urinate more in the last few days. In the same period, her appetite was reportedly decreased. Defecation was reportedly normal. The patient had no prior history of illness. She was never admitted for inpatient care. She had no prior complaints and had no history of being diagnosed with diabetes mellitus, asthma, or allergy. There also no family history for diabetes mellitus, hypertension, thyroid disorders, heart disorders, pulmonary disorders, or allergy.

The patient was delivered by caesarean section with birth weight of 4,500 g. She cried instantly and there was no history of cyanosis or icterus. Since then, the patient reportedly fulfilled normal development milestones. She was able to hold her head up by 3 months, sit up by 6 months, crawl by 8 months, and stand by 11 months. She was exclusively breastfed for 6 months and currently

receive breastmilk with complementary soft food. She received complete immunization for her age.

Physical examination found an infant with signs of severe illness. Her body weight was 9 kg and her body length was 85 cm. She was somnolent, with heartbeat of 132 times per minutes and respiratory rate of 30 times per minute. Body temperature was 38.4°C and oxygen saturation was 93%. General physical examination found no signs of abnormalities. Labial mucosa was moist and her skin was supple. Pulmonary auscultation found vesicular sounds on all fields, with no wheezing or rhonchi present.

Further investigation was conducted. Due to fever at presentation, the patient was screened for COVID-19 with rapid antigen test and found negative. Other laboratory investigations conducted included complete blood count, random blood sugar level, blood chemistry workup, urine test, and blood gas analysis (Table 1). On the first day, blood count found elevated white blood and platelet counts. Random blood sugar was found severely elevated at 577 mg/dl accompanied by metabolic acidosis. Meanwhile, urinalysis found acidic pH as well as traces of glucose and ketone bodies.

Based on examination and laboratory workup, the patient was diagnosed with DKA. Initial treatment in the emergency room included oxygen flow of 8 l per minute by non-rebreather mask, intravenous fluid consisting of normal saline and potassium chloride 4.5 mcq solution, and insulin treatment consisting of 1 IU rapid acting insulin per milliliter of normal saline, dripped at a rate of 0.08 ml/kg/hour. The patient was also given antibiotic course consisting of 250 mg ceftriaxone, twice per day.

Following stabilization, the patient was admitted to the Pediatric intensive care unit (PICU) where she was treated for 6 days. During treatment in the PICU, she underwent blood glucose tests 4-5 times per day. Intravenous fluid was given according to the most recent blood glucose results. Normal saline and potassium chloride 4.5 mcq solution was given if blood glucose result was over 300 mg/dl. For blood glucose in the range of 200-300 mg/dl, intravenous fluid solution would consist of 5% dextrose with potassium chloride 4.5 mcq solution. Meanwhile, for blood glucose lower than 200 mg/dl, intravenous solution given would be 10% dextrose with potassium chloride 4.5 mcq solution.

The patient also received insulin treatment, adjusted to the development of her condition. In the first to fourth day in PICU she received a continuation insulin solution in the emergency room with a rate of 0.08 mL/kg/hour. In the fifth day, her insulin regiment was changed to a mix of 30% insulin aspart and 70% insulin aspart protamine with a dose of 5 IU in the morning and 3 IU at night. She also continued her antibiotic course through PICU treatment. In addition, she received antipyretic 100 mg acetaminophen intravenously every 4 hours from first to fourth day in PICU. Following three consecutive normal blood glucose

results in the fifth day, the patient was discharged for outpatient care with maintenance treatment including

mixed insulin regiment, 4 IU at morning and 3 IU at night, and 800 IU vitamin D3 supplement daily.

Table 1: Laboratory results in the course of the patient's treatment.

Parameters	Day 1	Day 2	Day 3	Day 4	Day 5	Reference range
Blood count						
White blood cells ($10^9/l$)	21.2*					4.5-13.5
Red blood cells ($10^{12}/l$)	3.97*					4-12
Hemoglobin (g/dl)	10.1*					10.8-15.6
Hematocrit (%)	29*					33-45
MCV (fl)	72.9					69-93
MCH (pg)	25.4					22-34
MCHC (g/dl)	34.9					32.1-36.1
Platelet ($10^9/l$)	769*					184-488
Blood chemistry						
Sodium (mmol/l)	136	149*				135-148
Potassium (mmol/l)	4.73	3.1*				3.5-5.3
Chloride (mmol/l)	104.5	114*				95-110
Blood sugar (mg/dl)	06.00: 577* 19.00: 58* 21.25: 150	01.00: 408* 05.00: 429* 09.00: 322* 13.00: 326* 17.00: 31* 21.00: 342*	05.00: 35* 09.00: 91 13.00: 281* 17.00: 97 21.00: 102	12.00: 153 14.00: 147		60-100
HbA1c (%)						4.4-5.4
Urea (mg/dl)	31					10-50
Creatinine (mg/dl)	0.9					0.3-1.2
C-peptide (ng/ml)					0, 29*	0.78-5.19
Vit. D 25-OH (ng/ml)					16, 6*	20-100
Blood gas analysis						
pH	7.08*	7.23*		7.35		7.35-7.45
pCO ₂ (mmHg)	14*	17*		33*		35-45
pO ₂ (mmHg)	177	170		118		80-100
cHCO ₃ (mmol/l)	4*	7*		18*		23-33
ABE (mmol/l)	-26*	-20*		-8*		(-2) - (+2)
SBE (mmol/l)	<5*	8*		19*		22-26
sO ₂ (%)	99	99		99		95-99
Urine analysis						
Color						Yellow
Clarity						Clear
Density	1.025					1.000-1.030
pH	5.5					4.5-8.0
Protein	+2*					Negative
Glucose	+1*					Negative
Ketone	+4*					Negative
Blood	+1*					Negative
Bacteria	+*					Negative

Note: *Abnormal values.

DISCUSSION

We described the presentation, diagnosis, and initial treatment of an infant suffering from DKA caused by an early onset T1DM. A unique finding in our case is how early DKA manifested in the patient. Our patient is only 1 year and 2 days old. A large study comprising of 59 thousand children with T1DM found that median age of

diagnosis for T1DM was 9 years old with interquartile range between 5.5 to 11.7 years old.² A more recent study in Germany found similar findings, with median age of diagnosis of 9.9 years old.¹¹ Our case fulfill the criteria for early onset T1DM, being diagnosed at an age younger than 6 years old.⁵

Similarly early-onset T1DM is on the rise in various countries with 0-4 years old age bracket observed with

highest increased incidence of T1DM compared to other age groups.^{12,13} One factor implicated in this trend is the impact of perinatal factors in the onset of T1DM pathophysiology. Viral infections have been identified as one risk factor of an infant developing early onset T1DM with enterovirus being the most cited pathogen. Another perinatal risk factors included high birth weight and caesarean delivery.^{8,14}

With viral infections being a risk factor, we should bear attention to the COVID-19 pandemic. There has been a case report of an 8 months old infant presenting with T1DM and DKA, similar to our patient, with concurrent COVID-19 infection.¹⁵ A literature review has also postulated a potential pathogenesis pathway from SARS-CoV-2 infection to development of T1DM.¹⁰ Our patient presented with fever although COVID-19 antigen screening was found negative. However, we cannot rule out possibility of undiagnosed past COVID-19 infection or exposure which may precipitate the current event.

Meanwhile, DKA is a common first presentation of T1DM. Analysis of records from 2006 to 2016 showed that 29.9% of children with T1DM presented with DKA at diagnosis.² As T1DM is not congenital in nature with unpredictable onset, many parents were unaware that their children already develop the T1DM until the blood sugar is uncontrollably high and presenting as DKA. The rate of DKA in T1DM at diagnosis at varied between countries, largely associated with the level of T1DM awareness among its populace. In countries with low awareness about T1DM, DKA prevalence was higher among children with T1DM at presentation. A 2012 systematic review found this prevalence reached as high as 80% in some countries.⁴

The laboratory workup and treatment of this patient closely follow the recommendation for treatment of DKA in infant and children.¹⁶ Fluid rehydration was given with supplemental potassium chloride indicated by patient's history of passing urine. Initial insulin treatment was given by slow intravenous infusion. Blood glucose levels was tested periodically. Meanwhile, insulin treatment and intravenous glucose supplementation was given with periodic adjustments based on blood glucose level.

Our patient also suffered from unspecified systemic infection, indicated by elevated white blood and platelet counts, as well as vitamin D deficiency. This infection seems to be bacterial in nature, evidenced by it responding to antibiotic course she received during treatment. Bacterial infection is a known potential complication of uncontrolled diabetes, given that it compromised the patient's immune system. However, it usually responded well to aggressive antibiotic therapy.¹⁷ Vitamin D deficiency has also been frequently observed among T1DM patients. It has been associated with DM pathogenesis in general and vitamin D supplementation was recommended to help control glycemic level for T1DM patients.^{18,19}

Following her discharge, the patient should be followed closely, especially regarding her physical and cognitive development. T1DM was associated with changes to the nervous system, including to the cerebral structure.⁶ Thus, it affects the cognitive development of the child and potentially translate to the academic skills later in life.²⁰ Further, early onset T1DM was also associated with poorer glycemic control and contributed to higher risk of cardiovascular events which led to lower life expectancy, even compared to later onset T1DM cases.⁷ Continuous engagement with healthcare provider as well as close adherence to treatment regimens would be necessary to offset these risks and provide the patient with full recovery potential.

CONCLUSION

We presented a case of early onset type 1 diabetes mellitus, complicated by diabetic ketoacidosis. This case was presented under the backdrop of increasing T1DM incidence worldwide as well as ongoing COVID-19 pandemic. While the association in our patient is unclear, it should be noted that exposure to SARS-CoV-2 virus has been associated with T1DM incidence among children and infant.

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