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Sepsis in Latent Autoimmune Diabetes in Adults with Diabetic Ketoacidosis: A Case Report

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Abbreviations: ANOVA: Analysis of variance; BRS: brain relaxation scale; CVP: central venous pressure; MAP: mean arterial pressure; GDT: goal-directed fluid therapy; PPV: pulse pressure variation; SPSS: Statistical package for social science;

Abstract

BACKGROUND: This case report intends to highlight the challenge in diagnosing type 1 diabetes on an adult patient. Latent Autoimmune Diabetes in Adult (LADA) types I diabetes Mellitus, which found in adulthood and characterised by progressive damage to pancreatic β cells that happened slowly. Incidence of LADA is around 2-12% of the total diabetes population. Sepsis in LADA patients will trigger diabetic ketoacidosis (DKA).

CASE REPORT: We report a case of a 33-year-old woman patient presents with decreased consciousness accompanied by rapid and deep breathlessness for 1 day. Before, the patient complains of fever and cough. Physical examination found soporous, blood pressure 120/80 mmHg, pulse 110 x/minute, temperature 38.8°C, breathing 32 x/minute Kussmaul. Bronchovesicular breath crackles in both lower lung fields. leukocytes were 22,100/mm^3, random blood glucose 638 mg/dL, urine ketone +++, HbA1C 17.2%, HOMA IR less than 2 units. C-peptide 0.3 ng/mL and GADAs 16.9 U/mL. Chest Xray indicated bronchopneumonia. Patients were diagnosed with diabetic ketoacidosis, LADA, and sepsis caused by bronchopneumonia. Patient treated with DKA management and sepsis. On the second day, the treatment of DKA was resolved and continued with the administration of short-acting insulin and regular long-acting.

CONCLUSION: Sepsis in LADA with DKA requires fast and appropriate management. Further search is needed to diagnose LADA.

Introduction

Latent Autoimmune Diabetes in Adult (LADA) types I diabetes mellitus found in adulthood which is characterised by progressive damage to β cells that lasts slowly [1]. Indonesia population was about 237.6 people in 2010, and make it become the world's fourth most populated country. Indonesia has the seventh-largest number of diabetic patients (7.6 million) [2], [3]. LADA occurs in about 2 - 12% among diabetic patients in the entire diabetes population. Symptoms of LADA are similar to Type 1 diabetes but are found in adulthood. The slow progression of pancreatic β cell damage in LADA is initially almost always diagnosed as type 2 diabetes mellitus [4], [5].

The Diagnosis of LADA is made from the clinical complaints of diabetes symptoms accompanied by high fasting plasma glucose, low *C-peptide*, without insulin resistance characterised by low HOMA IR [6]. Due to the slow progression of pancreatic β cell damage usually, in the first 6 months, LADA patients still respond with oral anti-diabetic therapy, but when plasma glucose levels can no longer be overcome with oral anti-diabetes drugs and lifestyle changes, daily insulin injections are needed [7].

It is estimated that more than 50% of patients diagnosed with type 2 diabetes without obesity are LADA, but not all LADA patients are underweight; some are overweight [6]. Glutamic Acid decarboxylase autoantibody (GADA), islet cell autoantibody (ICA), insulinoma-associated (IA-2) and zinc transporter autoantibodies (ZnT8) were found in

patients with LADA type DM [6], [7]. LADA patients usually have low C-peptide levels, although sometimes in moderate amounts according to the progression of the disease. While patients with insulin resistant or type 2 diabetes mellitus, usually have high C-peptide levels [8], [9].

Case Report

A 33-year-old woman comes with a major complaint is suddenly unconsciousness accompanied by shortness of breath that is fast and deep for 1 day. Before declining consciousness, the patient complains of fever, cough, and vomiting.

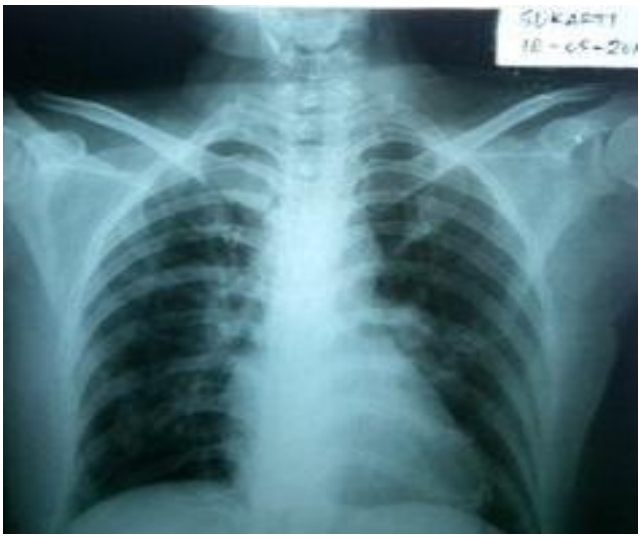

Figure 1: Chest Xray

On physical examination found soporous awareness, blood pressure 120/80 mmHg, pulse 110 x/minute, temperature 38.8°C, breathing 32 x/minute Kussmaul, BMI: 16.8 kg/m2. Bronchovesicular breath, fine wet cracks in both lower lung fields. On laboratory examination, leukocytes were obtained 22,100/mm3, blood sugar levels when 638 mg/dL, urine ketone +++, HbA1C 17.2%, HOMA IR was less than 2 units. C-peptide 0.3 ng/mL and GADAs 16.8 U/mL. Chest Xray indicated bronchopneumonia and plain radiograph of the pancreas, and no pancreatic calcification was found (Figure 1 and Figure 2).

Patients were diagnosed with diabetic ketoacidosis, LADA, and sepsis caused by bronchopneumonia. The management of DKA in these patients is given fluid resuscitation, intensive plasma glucose control with DKA, intravenous insulin protocol, and trigger factor control, namely infection with broad-spectrum cephalosporin class 3 antibiotics. On the second day, the DKA treatment is resolved, and insulin therapy is given for hyperglycemia. Short-acting and long-acting regularly.

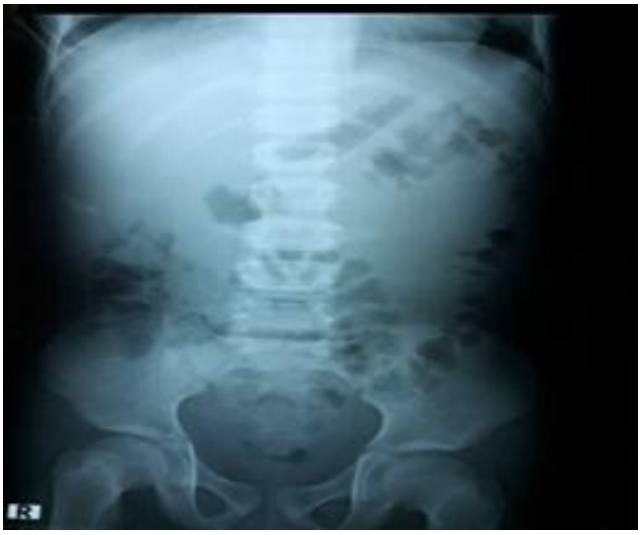

Figure 2: Pancreatic Xray

Discussion

Infections are still the main cause of morbidity and mortality in diabetics patient. Diabetes could increase the risk of developing infections and sepsis to the patient [10]. The main reason for diabetes predisposes to infection appears to host response abnormalities, particularly in neutrophil chemotaxis, adhesion and intracellular killing, defects that have been attributed to the effect of hyperglycaemia [11]. There is also evidence for defects in humoral immunity, and this may play a larger role than previously. Diabetes is associated with elevations in C-reactive protein (CRP), tumour necrosis factor-alpha (TNF-α), interleukin (IL)-6 and IL-8, but no differences are seen in circulating cell surface markers or coagulation markers between patients with and without diabetes in the context of sepsis [11], [12].

Organ systems where bacterial infections predominate as well as fungal diseases were associated with substantial increases in magnitude among patients with both T1DM and T2DM, but risks were consistently higher for T1DM. Patients with T1DM are at approximately double the risk of patients with T2DM for infection-related to death. Bacterial eradication is needed to treat the infection. Antibiotic regiments are not different in a patient with or without diabetes [11].

Lung infections suffered by these patients trigger sepsis which then increases the risk of diabetic ketoacidosis. In stress situations, the body is thought to activate the central nervous system and neuroendocrine axes which release hormones such as catecholamines, glucagon and cortisol which are known to stimulate hepatic glucose production and lead to hyperglycemia [13], [14].

Ketoacidosis is a metabolic state associated with pathologically high serum and urine concentrations of ketone bodies, namely acetone, acetoacetate and beta-hydroxybutyrate. DKA can occur in patients with diabetes mellitus. This may be caused by precipitating physiologic stress or in some cases, maybe the initial clinical presentation in patients with previously undiagnosed diabetes [14], [15]. Some of the more common risk factors that can precipitate the development of extreme hyperglycemia and subsequent ketoacidosis are infection, non-adherence to insulin therapy, acute major illnesses like myocardial infarction, sepsis, pancreatitis, stress, trauma, and the use of certain medications DKA management must be carried out quickly and precisely given the high mortality rate [16].

DKA management protocols are replacement of lost fluids and salts, administration of insulin and management of infection. Considering that severe acidosis can interfere with the balance of homeostasis, it is reasonable to treat patients with pH < 7.0 using sodium bicarbonate. DKA in these patients can be resolved well because of the provision of therapy following the protocol, which are fluid resuscitation, blood sugar control and infection management with the administration of broad-spectrum antibiotics, which is the third generation of cephalosporin [11], [17].

A 33-year-old woman with a diagnosis of diabetic ketoacidosis, LADA, and sepsis caused by bronchopneumonia was treated. The problem with this patient is whether this patient is type 2 DM or another type of DM, given that clinically type 2 DM and other types of DM can be found in young adults [3], [4].

According to the literature where the percentage is 10%-20%. Usually, 85% are overweight or obese; urinary ketones are found in 33% of cases while 5%-25% with ketoacidosis [17]. DKA triggers in these patients are septic bronchopneumonia (Masharani, 2010). This is consistent with the literature that the most common trigger factor of DKA is an infection, and is thought to trigger more than 50% of DKA cases [15]. In infection, there will be an increase in cortisol and glucagon secretion so that there is a significant increase in blood sugar levels [12].

At the beginning of admission, this patient is diagnosed with type 2 DM, so to ensure diagnostic tests are carried out several tests including HOMA IR, C-peptide and GADAs. In these patients, there was a low HOMA IR; this was not my type 2 DM. Then examination was performed C-Peptide to prove whether this patient was pure type 1 DM or another type of DM. In these patients, C-Peptide is low, which is 0.3 ng/mL. The results of the examination C-peptide describe endogenous insulin secretion. Insulin and C-peptide are secreted equimolarly and released into the circulation through the portal vein. Low C-peptide indicates that endogenous insulin production in these patients is low and that high levels of GADAs are obtained, which is 16.9 U/mL, which indicates these patients have clear antibodies. In low HOMA IR conditions, low C-peptide and autoantibody abnormalities indicate that this patient does not type 2 DM but LADA type DM [18], [19], [20].

Diabetes is a much heterogeneous disease than the present subdivision into type 1, and 2 assumes. Both type 1 and type 2 diabetes seem to result from a collision between genes and environment [18]. Type 1 diabetes is believed to be an autoimmune disease characterised by genetic, immunological and metabolic features. The incidence is highest in children, but adults also get the disease. Data reported in LADA show that this is the most frequent form of adult-onset autoimmune diabetes and may account for 2% to 12% of all cases of diabetes in the adult population. Moreover, multicenter studies carried out in Europe, Asia and North America, reported that 4% to 14% of patients diagnosed with T2DM are positive for T1DM associated autoantibodies which are diagnostic for LADA [17]. In LADA, metabolic changes at diagnosis reflect a broad phenotype ranging from diabetic ketoacidosis to mild non-insulin-requiring diabetes [20].

Adult-onset autoimmune diabetes and childhood-onset type 1 diabetes are barely distinguishable immunologically. In LADA, the dominant autoantibody is GADA and lower C-peptide levels. At diagnosis, the clinical phenotype in patients with autoimmune diabetes is remarkably broad, ranging from diabetic ketoacidosis to diabetes that can be controlled with diet alone. Patient with LADA tend to have a lower age at diabetes onset, lower BMI and waist-to-hip ratio, but a more pronounced loss of C-peptide and an increased likelihood of insulin treatment [9].

To diagnose LADA, the Immunology of Diabetes Society has established three main criteria including (1) adult age of onset (> 30 years); (2) presence of any islet cell autoantibody; and (3) absence of insulin requirement for at least 6 months after diagnosis. However, the definition of LADA remains controversial, and open debate regarding these diagnostic criteria still exist [8].

A correct therapeutic strategy for LADA patients should aim to the preservation of residual β-cell function as well as improvement of neurometabolic control, to reduce the risk of long-term complications. Maintenance of β-cell function, as demonstrated by the Diabetes Control and Complication Trial, is indeed associated with a reduction of long teen diabetic complications [6].

In conclusion, sepsis in LADA with DKA requires fast and appropriate management. Further search is needed to diagnose LADA. LADA type DM is initially almost always diagnosed with type 2 DM or other types of DM because pancreatic β cell damage occurs progressively slowly (ADA, 2004). Diagnosis of

LADA patients are found clinically in diabetes, increased plasma glucose, HOMA IR less than 2 units, low C-peptide and the presence of autoantibodies.

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