

Case Report

Disseminated Intravascular Coagulation in Diabetic Ketoacidosis - Rare but Dangerous

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Abstract

Diabetes Mellitus and Diabetic Ketoacidosis are known prothrombotic disorders. As a result, there is a potential risk of developing Disseminated Intravascular Coagulation. In this case study, we present an 84-year-old male with a history of uncontrolled insulin dependent diabetes that progresses to Diabetic Ketoacidosis and subsequent Disseminated Intravascular Coagulation. Physical examination, laboratory studies and imaging could not elucidate another possible cause for the patient's Disseminated Intravascular Coagulation. As of the time of this writing, there are few studies that have been performed to analyze the link between Diabetes/Diabetic Ketoacidosis and the development of Disseminated Intravascular Coagulation. We believe that further study into this possible connection should be performed in the future.

Keywords: Diabetes Mellitus; Diabetic Ketoacidosis; Disseminated Intravascular Coagulation; Internal Medicine; Hematology

Introduction

Diabetes Mellitus (DM) and its many sequelae, including Diabetic Ketoacidosis (DKA), are an established risk factor of atherothrombotic disorders. These affect the coronary, cerebral and peripheral arteries. Patients with diabetes are more prone to thrombotic events due to platelet hyper-reactivity. They also have increased activation of prothrombotic coagulation factors coupled with decreased fibrinolysis [1,2]. These clinical features of diabetes have the potential to promote Disseminated Intravascular Coagulation (DIC). Furthermore, diabetic patients are more likely to develop other diseases that may trigger DIC, such as severe infection and some cancers [3].

Case Report

Patient Description

84-year-old male, with a history of Type Two Diabetes and treated with Jardiance Duo and rapid acting insulin, has a hemoglobin A1C of 8.3%. He also suffers from hypertension, iron deficiency anemia and ischemic heart disease. Previous heart mapping showed mild ischemia and a small infarct in the circumflex artery. He receives only conservative treatment in relation to his infarct. In addition, he is known to have orthopedic problems in his spine. He had received an epidural injection of Diprospan/Depomedrol + Lidocaine 1% into his spine two days before admission.

He was admitted to the Emergency Room (ER) due to hyperglycemia of 400 mg/dl at home. He had no fever, weakness, respiratory or gastrointestinal complaints or recent weight loss. In the ER, he was fully conscious and lucid. Blood pressure was 183/108 mmHg, temperature 36.3°C, pulse 84 bpm and saturation 96% in room air. An Electrocardiogram (ECG) was performed and showed regular sinus rhythm without signs of acute ischemia.

A series of blood tests were taken. Blood gas showed combination of metabolic acidosis with high anion gap and positive non-anion gap metabolic acidosis by (delta anion gap / delta Bicarbonate Ratio). Complete blood count returned with leukocytes 12.8 K/uL, hemoglobin 12 g/dL, platelets 40K/uL. Hemoglobin 12.7 g/dL, Reticulocytes 81 (INDEX 1.1). A complete blood count from three months prior was normal.

Chemistry - sodium 134 mmol/L, potassium 5.8mmol/L, creatinine 1 mg/dL. Bilirubin 1.3 mg/dL, mostly direct. Urine ketones were elevated. Alkaline phosphate 1120 IU/L, lactate dehydrogenase 7700 IU/L, Aspartate Aminotransferase 190 IU/L, Alanine Aminotransferase 30 IU/L, Gamma Glutamyl Transferase 35 IU/L and C-Reactive Protein 21mg/L. Coagulation test INR 2.5, PT 60 Seconds, Serum haptoglobin 75 mg/dL and Di Dimer 54 mg/L.

As part of a DIC investigation, a total body Computed Topography (CT) scan was performed to rule out malignancy and inflammatory diseases. There was no evidence of axillary or mediastinal lymphadenopathy. Large vessel vasculature was unremarkable. There were no pathological findings of the lungs or heart. Abdominal organs were also without acute pathological findings. Lastly, there was no evidence of retroperitoneal, iliac or inguinal lymphadenopathy.

DKA protocol treatment with fluids and insulin was started. DIC protocol treatment was started with cryoprecipitate and fresh frozen plasma. Over the course of his treatment, the patient recovered and was discharged.

In the absence of any definitive causes of DIC in relation to malignancies, infectious processes or signs of hemorrhaging; it was decided that the DIC was triggered by the patient's diabetes and ketoacidosis.

Ethical Statement

This case report did not require the approval of the hospital ethics committee. All information about the patient was retrieved with the approval of the patient.

Discussion

Disseminated Intravascular Coagulation (DIC) is a serious illness characterized by the widespread and persistent activation of coagulation factors. Activation of the coagulation system, such as hemostatic factors like platelets and coagulant factors, are depleted in DIC. This can result in the development of microthrombi which in turn can cause organ failure through ischemia. The degree of coagulation and subsequent fibrinolysis can vary depending on the pathogenesis of the specific disease. This may in turn lead to consumption coagulopathy with bleeding from various sites. The three most common clinical conditions associated with DIC are sepsis, acute leukemia and solid tumors [4].

Diabetic Ketoacidosis (DKA) is characterized by uncontrolled hyperglycemia, metabolic acidosis and increased body ketone concentrations. This is a life-threatening complication of diabetes. This disease is worsened by hyperglycemia, dehydration and acidosis. In most cases, the trigger is an infection, new-onset diabetes or lack of compliance with treatment. As a result of these complications, the association of diabetes with coagulation, thrombosis and fibrinolysis has been studied and is well documented in the literature. However, we were able to find only a dozen case reports on DIC in diabetic patients and no observational research examining the association between DKA and DIC. Most of these studies have examined the association between DIC and the administration of antithrombin or thrombomodulin, but they do not consider the association between DIC and diabetes.

In the case of our patient, we hypothesized that he may have been undertreated for his diabetes and had heightened glucose levels as a result of the steroid injection (Diprosan/ Depomedrol + Lidocaine 1%) he received prior to his admission to our institution. One use of steroids is for treating severe pain. However, steroid use is accompanied by various side effects such as fever, facial flushing, nausea and fatigue. Steroid use has also been shown to inhibit the function of the Hypothalamic-Pituitary-Adrenal (HPA) axis, thus rendering patients vulnerable to adrenal insufficiency. It can also lower the function of glucose metabolism and stimulate gluconeogenesis, thereby increasing blood glucose levels and resistance to insulin. It is well documented that blood glucose level elevates after steroid injection. The duration of blood glucose level elevation and whether that increase is higher in patients with poor blood glucose control remain controversial [5].

Atherothrombotic complications are the main cause of mortality in patients with diabetes. Premature atherosclerosis, increased

platelet reactivity and activation of coagulation factors with associated hypo-fibrinolysis all contribute to increased cardiovascular risk in diabetic patients [1,2]. Increased plasma levels and/or activity of hemostatic factors, including tissue factor 6, Factor VII (FVII), thrombin, fibrinogen and Plasminogen Activator Inhibitor-1 (PAI-1), have all been reported in diabetic patients [6,8]. The pathogenesis of DIC is similar, in terms of persistent widespread activation of coagulation in the presence of underlying disease.

There are three types of DIC. The first type is with suppressed fibrinolysis that can be seen in sepsis. In this case, coagulation activation is severe but fibrinolytic activation is mild. This is because Plasminogen Activator Inhibitor (PAI) is overexpressed in the vascular endothelium as a result of the action of lipopolysaccharide and cytokines. In this form of DIC, microthrombi remain in circulation and can thereby lead to the progression of multi-organ failure [3,9].

The second type of DIC is a state of enhanced fibrinolysis in Acute Promyelocytic Leukemia (APL). In APL, coagulation and fibrinolytic activation are both severe and fibrinolysis is strongly activated in response to the slightest elevation in PAI. As a result, thrombi can be more readily dissolved and thereby trigger the onset of severe bleeding. The third type of DIC with balanced fibrinolysis is usually seen in solid tumors, with an intermediate pathogenesis between the first two types.

In our case, a higher risk of DIC was observed in a Type Two Diabetes Mellitus (T2DM) patient with DKA and non-septic severe infection or solid cancer. A potential cause of this higher risk is the suppressed fibrinolysis by increased PAI due to T2DM, which may promote organ failure.

In T2DM patients, platelets are thought to adhere to the vascular endothelium and aggregate more readily when compared to the general population at large, which may increase the risk of DIC. The higher fatality rate in T2DM group may be due to augmented organ failure caused by increased coagulation and/or suppressed fibrinolysis in T2DM.

Conclusion

There is limited data regarding the extent to which diabetes increases the risk of Disseminated Intravascular Coagulation (DIC). We hypothesize that acute illness in Type Two Diabetes Mellitus and especially Diabetic Ketoacidosis, is associated with a higher risk of developing DIC and further study into this possible correlation should be investigated.

Conflict of Interests

The authors certify that there is no conflict of interest for this manuscript.

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Authors Contribution

The authors confirm contribution to the paper as follows:

Study Conception: Mohammad Haydar.

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Data Availability

The information about the patient of this case report is held within his private medical record. This record is kept within a secure server of Laniado Hospital. Sharing of this information will be done under the discretion of Laniado Hospital Privacy Policy and Israeli Medical Privacy Law.

Consent for Publication

The subject of this case report gave their informed consent for inclusion of their medical information to be shared for this study.

There was no dissemination of private information within this case report and the patient was anonymized.

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