

Generalized venous thrombosis in diabetic ketoacidosis: A case report and review

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Abstract

Diabetic ketoacidosis (DKA) is a medical emergency with multi-organ complications. Venous thromboembolism (VTE) is a rare complication of DKA. We are presenting a 58 year old male patient with poorly controlled type 2 diabetes mellitus who was hospitalized with DKA secondary to noncompliance. His clinical picture was complicated by generalized thrombosis involving multiple venous locations including bilateral femoral and common iliac veins. Because of his increasing shortness of breath, he was also diagnosed with large saddle pulmonary emboli. The patient had no family history or personal history of any coagulation disorders. Hypercoagulability evaluation remained negative. He was subsequently anticoagulated with heparin and discharged home on warfarin. In reviewing the medical literature and to the best of our knowledge, this is one of the few reported cases of multiple venous thromboses occurring as a DKA complication, with no other risk factors for venous thrombosis. This case highlight the fact that venous thrombosis (VTE), although rare, should always be considered as a potential complication of DKA.

Keywords

diabetic ketoacidosis (DKA); venous thromboembolism (VTE); hypercoagulability; virchow's triad

Abbreviations

DKA: diabetic ketoacidosis, VTE: venous thromboembolism

Introduction

Venous thromboembolism (VTE) complicating DKA is rarely reported in medical literature. Most of the cases described have been either in association with central venous lines or in the cerebral veins by location. Our case described a 58 year old male patient admitted for diabetic ketoacidosis (DKA) presenting with acute venous thrombosis at multiple sites including large saddle emboli. We also reviewed the current medical literature describing the acute hypercoagulable state induced by the DKA process.

Case Presentation

A 58 year old male with history of hypertension and chronic obstructive lung disease and type 2 diabetes mellitus presented to the local emergency room for 3 day history of shortness of breath and 2 week history of polyuria and polydipsia and fatigue and generalized malaise. He denied any fevers or chills or chest pains or coughing or dysuria. He had been very noncompliant with his diabetic medications

of metformin and glipizide for several weeks now. Patient's physical exam at the time of admission was unremarkable except for tachycardia at 110 and tachypnea at 25 and mild bilateral leg swelling. His chest x-ray showed no pneumonia or pulmonary edema. His EKG just revealed sinus tachycardia. The patient was found to be in DKA with serum glucose of 490, anion gap of 18, 2+ serum ketones, and hyperkalemia at 5.5, and pH of 7.27. Patient had negative cardiac enzymes. The patient was admitted to ICU for insulin drip and intravenous fluids and electrolyte replacement. His DKA resolved within 24 hours and the insulin drip was bridged to Lantus basal insulin and aspart insulin with meals.

Patient continued to have dyspnea despite resolution of his DKA and acidemia during hospital day 2. His oxygen saturation was 95% on 3 liters supplemental oxygen. His alveolar-arterial oxygen gradient was 40. He remained tachycardic despite generous volume resuscitation. Beside cardiac echo done by cardiology showed right ventricular free wall hypokinesis consistent with "McConnell sign", highly suspicious for pulmonary emboli. Venous duplex scan of his legs showed acute extensive venous thrombosis involving bilateral common femoral and popliteal veins. Chest CT angiogram showed saddle embolus in main pulmonary artery with extensive emboli to all branches of the lobes bilaterally. Because of his stable hemodynamics, patient was not treated with thrombolysis or surgery for his saddle emboli. He was instead started on heparin drip and oral warfarin therapy.

The patient had no known personal or family clotting disorder. He has no documented declining thrombocytopenia since admission, thus excluding the possibility of heparin-induced thrombocytopenia and secondary thrombosis.

Hypercoagulability work up was initiated. Factor V Leiden mutation and prothrombin mutation were undetectable. Protein C and S and anti-thrombin levels were normal prior to warfarin administration. Anti-cardiolipin antibodies and antinuclear antibodies were negative. Malignancy work-up including CT of abdomen and pelvis and serum cancer markers were negative. With no evidence of any underlying hypercoagulable state and no clinical cancers found, the generalized venous thrombosis was attributed to DKA. Patient's respiratory status and clinical condition improved over the next few days in the hospital and was discharged home on warfarin therapy.

Discussion

This case highlights the concern that diabetic ketoacidosis should be considered as a risk factor for venous thromboembolism. Review of the current medical literature showed more documented reports of arterial thrombosis in DKA state rather than venous. Most cases described have been in pediatric patients. They have been either in association with central venous lines or have been in the cerebral veins by location [1,2]. DKA as a risk factor for venous thrombosis was supported by the 2007 study by Keenan et al showing a 1.7% overall incidence of VTE among patients with diabetic hyperosmolarity. This was higher than the incidence of VTE among patients hospitalized with sepsis and decompensated heart failure, risk factors generally considered for VTE. The same study showed that hip arthroplasty patients had the highest risks for VTE at 3.7%. Thus, patients with DKA had higher incidence of VTE compared to hospitalized patients with other acute medical issues, but only modestly lower than the orthopedic patients with joint replacements who are considered the highest risks for VTE [3].

The metabolic conditions of DKA interfere with the basal hemostatic mechanisms and induce a

prothrombotic state. With poorly controlled diabetes, it is well documented that the levels of protein C and protein S are decreased, especially in an acidosis condition. In his study on hemostatic markers in DKA, Carl et al showed low levels of these proteins before treatment for DKA [2,3].

The same study also showed persistently increased levels of von Willebrand factor which increases platelet adhesion. The increased level of vWF is also a marker for endothelial activation. The hypertonicity seen in DKA also caused endothelial injury and increased red cell rigidity and increased serum viscosity. The expected intravascular volume depletion and dehydration in DKA also leads to vascular stasis [3]. These conditions form the Virchow's triad for increased risk of thrombosis: venous stasis, endothelial injury, and hypercoagulability.

There are more documented reports of arterial thrombosis in DKA than venous. The cause for this difference is unknown. Furthermore, a few studies have reported increased incidence of VTE in pediatric patients with DKA and central venous catheters [1]. However, venous thrombosis complicating DKA in the adult population has been rarely described. A case series by Biegelman on fatalities in DKA patients showed pulmonary embolism as the cause of one death. Quigley et al in 1994 described a case of massive pulmonary thromboembolism caused by DKA [4]. Another case report by Gill et al. in 2006 described a DKA case complicated by axillary vein thrombosis [5] In general, establishing DKA as the cause of thrombosis required the clinician to exclude other causes of prothrombotic states as in our patient who had no known hypercoagulable conditions or precipitating triggers for the generalized thrombosis. VTE prevention is part of the standard treatment protocol for hospitalized medical patients, as in our patient. The issue of therapeutic anticoagulation as part of DKA management remains open to debate, though our case would support therapeutic anticoagulation from the beginning of hospitalization [6].

Figures



Figure 1: Arrow shows saddle pulmonary embolus on chest CT angiogram

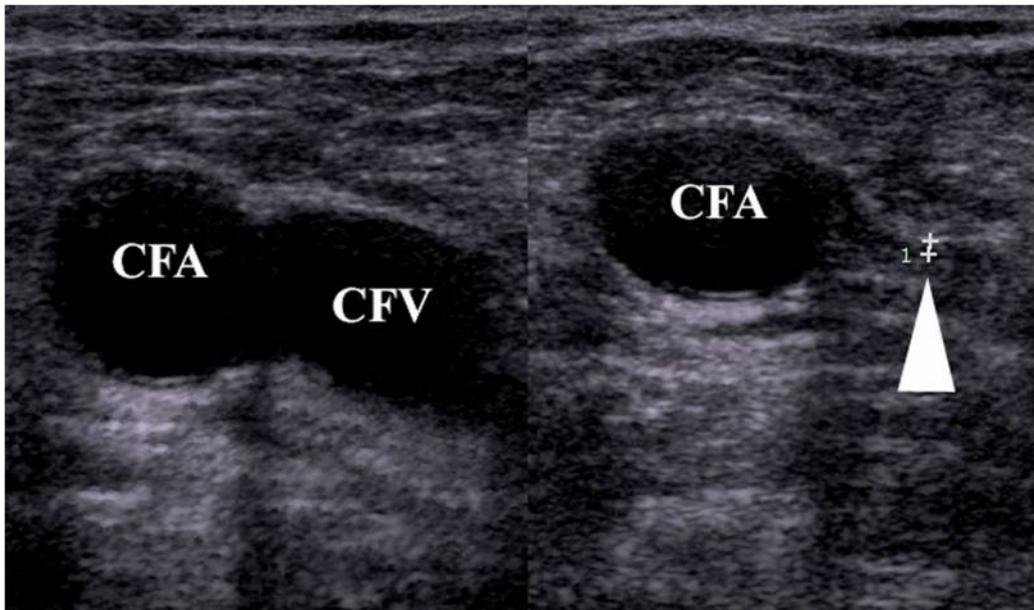


Figure 2: Left ultrasound image shows non compressible image of common femoral veins, indicative of acute DVT Right ultrasound image shows normal compression of common femoral vein, which is normal (shown by large arrow)

Conclusion

Our case highlighted extensive venous thrombosis as a rare complication of DKA. This is one of the very few cases described in medical literature showing generalized thromboses in an adult patient occurring in a setting of DKA alone despite prophylactic anticoagulation. The case emphasized the need for DVT prophylaxis therapy in these patients. It also opened up the debate for the role of therapeutic anticoagulation in management of diabetic ketoacidosis, due to the potential deadly complications from such thromboses.

More importantly, this case emphasized the need for having a very high degree of clinical suspicion for thromboses in every patient with DKA.

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