

Case Report

Wide Spread Arterial and Venous Thrombosis in a Case of Hyperglycemic Hyperosmolar State (HHS)

Ganaw A¹, Shaikh N¹, Marcus AE¹ and Soekarman D²

¹Department of Anesthesia, ICU and Perioperative Medicine, Hamad Medical Corporation, Weil Cornell Medical College, Doha, Qatar

²Department of Internal Medicine, Hamad Medical Corporation, Weil Cornell Medical College, Doha, Qatar

Abstract

A case is presented with a patient in a Hyperglycemic Crisis (HC), complicated by widespread thrombo ischemia including the left upper and lower limb, and the aortic arch. Extreme hyperglycemia and dehydration added to the pro-thrombotic state of diabetes and resulted in lower limb ischemia with ultimate limb loss. Current guidelines provide for thrombo-prophylaxis against Deep Venous Thrombosis (DVT) in HHS. Further development of the guidelines is needed to cover the risk of an arterial thrombosis as well.

Introduction

Diabetes mellitus is regarded as a pro-thrombotic state [1]. Extreme hyperglycemia and dehydration in the Hyperglycemic Hyperosmolar State (HHS), a subtype of Hyperglycemic Crisis (HC), add to the risk for thrombo-ischemic events [2]. Lower limb ischemia and occlusion of the femoral arteries in HHS is a distinct

***Corresponding author:** Ganaw A, Department of Anesthesia, ICU and perioperative medicine, Hamad Medical Corporation, Doha, Qatar, Tel: + 97433605110; E-mail: AGanaw@hamad.qa

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association, but its development may be hard to recognize due to its infrequent occurrence in daily practice [3,4]. Prompt recognition is important, since the window of opportunity to prevent irreversible damage is narrow. For teaching purposes, the following case is reported.

Case Presentation

A 50 years old female was admitted to the intensive care unit with polyuria and polydipsia, epigastric abdominal pain, vomiting and dizziness since 1 day. She had been successfully treated for carcinoma of the uterus, 1 year prior to the current episode. She reported no other medical conditions except for high blood pressure. Clinical examination showed a fully conscious female who was severely dehydrated. Clinical and laboratory parameters on admission are represented in table 1. Based on a glucose level >30 mmol/L and an osmolarity >320, a Hyperglycemic Hyperosmolar State (HHS) was diagnosed. Other investigations (septic work up, chest X ray, and ECG) were normal.

Characteristics	Clinical Parameters	Normal Range
Age	50 years	
Gender	female	
BMI	31.1 Kg/m ²	
Heart rate	126 beats/min.	
Blood pressure	93/40 mm Hg.	
Temperature	38°C	
Resp. rate	28 breaths/min.	normal range
Blood sugar	84.4 mmol/L	3.3-5.5 mmol/L
Calculated osmolarity	348.4 mOsm/Kg	275-295mOsm/Kg
Sodium	132 mmol/L	135-145 mmol/L
Potassium	6.1 mmol/L	3.5-5.5mmol/L
Urea	18 mmol/L	2.5-7.1 mmol/L
Creatinine	312 µmol/L	50-98 µmol/L
Leucocytes	23X10 ⁹ /L	4-10X10 ⁹ /L
Platelets	425 x10 ³	150-400x10 ³
Serum Lipase	1400 IU/L	13-60 IU/L

Table 1: Characteristics of the patient.

The patient was admitted into the ICU and received a total of 9 liters of 0.9% saline I.V. with insulin/potassium and Esmoprazole 20 mg twice daily. Dalteparin was given subcutaneously (5000 IU daily). On the 2nd day of admission signs of an acute ischemia were noticed in her left upper and left lower limbs. An ultrasound doppler and CT angiography confirmed the occlusion of the left subclavian and left femoral artery (Figures 1-4). Echocardiography showed a thrombus in the aortic arch. An emergency thrombectomy of the brachial and femoral arteries and a left arm fasciotomy took place and the patient was admitted into the Surgical Intensive Care Unit (SICU) for further management, Antithrombotic medication was started, unfractionated heparin infusion to keep APTT 45-70 seconds.

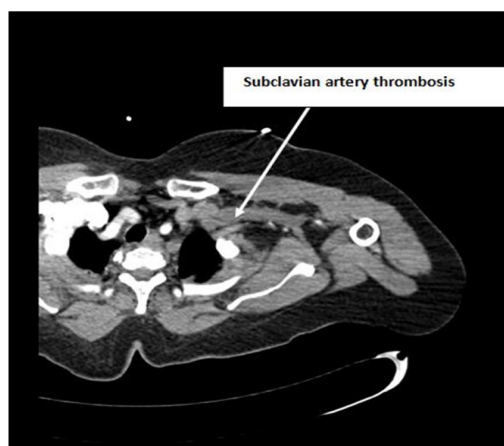


Figure 1: CT angiogram is showing subclavian artery thrombosis.

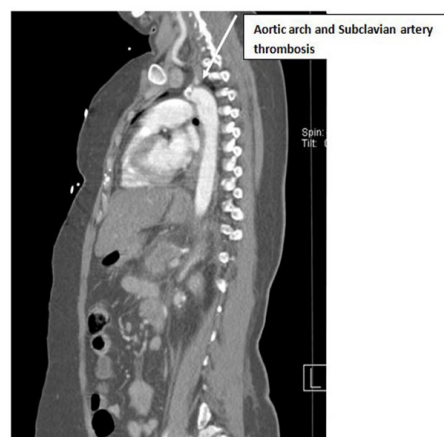


Figure 4: CT angiogram is showing Aortic arch and Subclavian artery thrombosis.



Figure 2: CT angiogram is showing Aortic arch thrombosis.



Figure 3: CT angiogram is showing Aortic arch thrombosis.

A thrombophilia work up testing for Antiphospholipid syndrome, Heparin Induced Thrombocytopenia (HIT test), Complement 3 (C3), Complement 5 (C5), Antinuclear Antibody (ANCA), lupus screen, Homocysteine, Antithrombin, Factor V Leiden, Anticardiolipin, anti B2 glycoprotein, protein S, C activity was normal. The patient and the family denied a personal or family history of thrombo-embolic events.

On the 5th day post intensive care admission, the patient had spikes of fever (39°C), hypotension, increased WBC (13×10^9 /L), and procalcitonin was 32ng/ml. The patient was diagnosed with a septic shock and multi-organ failure. She required high doses of Noradrenaline (4 µg/kg/hr) and Vasopressin (0.04 IU/hour). Parameters of her coagulation profile in the first week are given in table 2. Hemodialysis was performed and Piperacillin/Tazobactam was given i.v. On the 7th day the patient improved and she was weaned successfully from inotropic medication. Enteral feeding was started. Intravenous N-acetyl-cysteine (300mg over 24 hours) was given and her liver functions improved.

On the 9th day the patient developed dry gangrene in the left foot, which required a below the knee amputation. On the 11th day the patient was extubated, and a neurological assessment was showing right sided hemiparesis. The MRI was showing multiple micro cerebral hemorrhages, an infarction in the left paramedian pons and a cerebellar infarction, confirmed by CT (Figures 5 and 6). On the 14th day the patient developed abdominal distension, epigastric tenderness, and food intolerance. The CT showed partial mesenteric vein thrombosis (Figure 7). An ultrasound of the right internal jugular vein, where the catheter was located, showed a big thrombus, despite the patient being on a therapeutic of heparin (Figure 8). Blood sugar levels were maintained between 6-10 mmol/l by titrated insulin infusion.

On the 17th day the patient had a tracheostomy, and was discharged from the ICU for rehabilitation on a therapeutic dose of subcutaneous Dalteparin 5000 IU daily, which was continued for 3 months. On the 25th day she was discharged home from the hospital on Warfarin,

Amlodipine, Lisinopril, Rosuvastatin, Insulin, Propranolol and Escitalopram. The patient stayed in follow up with a visit at 3 months in the outpatient clinic. Her coagulation profile had normalized after 6 weeks (including the protein C activity) and her mobility kept improving. Eventually she left the country and was lost to our follow up.



Figure 5: MRI is showing cerebellar infarction.

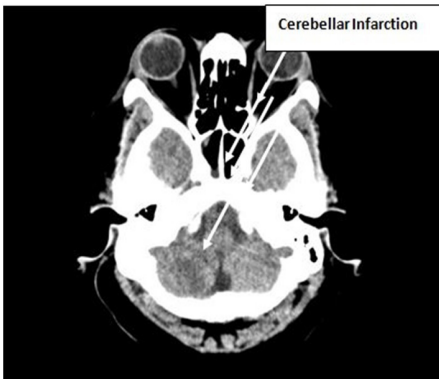


Figure 6: CT scan is showing cerebellar infarction.

Discussion

The age of onset and mode of presentation in this patient, is suggestive for an underlying type 2 diabetes [5]. Ketosis-onset diabetes, showing more similarities to type 2 than type 1 diabetes, has been associated with lower limb atherosclerotic lesions [6]. Changes of the vascular wall start at an earlier age in case of diabetes and might predispose to the formation of an arterial thrombus at certain predilection places in the arterial system [7]. In our patient thrombosis presented

with upper and lower limb-ischemia on the left side. Further imaging identified a thrombus in the aortic arch as well. The number of case reports with a limb- ischemia combined with a proximal aortic thrombus is growing, supposedly due to the development of novel imaging techniques [8,9]. This high-risk phenotype might not be as rare as previously thought.

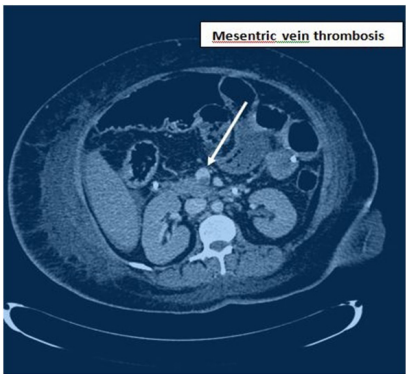


Figure 7: CT angiogram is showing mesenteric vein thrombosis.

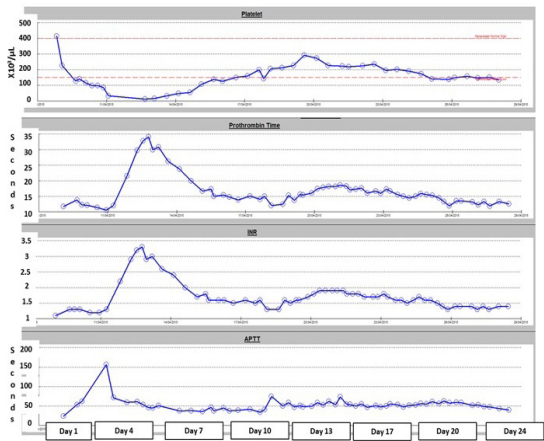


Figure 8: Coagulation during stay in intensive care unit.

Current guidelines provide for thrombo-prophylaxis in HHS, i.e., LMW Heparin during admission if no major contra-indications exist [10]. This covers the risk for a deep venous thrombosis, but might be insufficient in case of an imminent arterial thrombosis, especially in case of a long existing diabetes [11]. Alternative compounds, targeting crucial factors in the coagulation pathway leading to an arterial thrombus, should be searched for [12]. The development of an algorithm for thrombo-prophylaxis in a hyperglycemic crisis needs our ongoing attention to be able to improve the outcome of this high risk condition.

Item (normal range)	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8
Platelets (150-400x10.3/ μ L)	415	226	99	32	19	17	48	106
INR (1-1.1)		1.1	1.2	1.3	2.9	3	2.4	1.7
D-Dimer (less than 0.46 mg/L)			4.48		23.26			35.2
Fibrinogen (1.8-3.5 g/L)			2.6		2.3			2.2

Table 2: Coagulation profile of the patient in week 1.

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