



Acute paraplegia as a manifestation of COVID-19

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Abstract

Background: One of the many complications of COVID-19 infection is the risk of arterial and venous thromboembolism owing to cytokine storm and hypercoagulability. Here we report one such patient who presented with paraplegia and limb ischemia due to an aortic thrombus.

Case Information: 56-year old obese diabetic lady presented with sudden onset complete paraplegia with absent lower limb pulsations. CT angiogram showed aortic thrombus extending from level of renal artery origin till bilateral common iliac artery bifurcation, while CT chest showed CO-RADS 4, moderate COVID pneumonia, with a negative RTPCR on nasopharyngeal swab. While less common, several cases of aortic thrombosis as a result of COVID-19 infection have been described, attributed to the "thromboinflammatory" state seen in severe cases.

Conclusion: This report is to highlight the various differential diagnoses of acute aortic occlusion, with key reference to COVID -19 and associated hypercoagulability.

Keywords: SARS-CoV-2, arterial thrombosis, COVID-19 complication, acute paraplegia, aortic thrombosis.

Introduction

The current COVID-19 pandemic is the fifth major documented pandemic in history, caused by SARS-CoV-2 virus. While majority of the patients are asymptomatic or have only mild symptoms, various complications have also been described, which include inflammatory and thromboembolic phenomena. This case report describes a patient with complications due to COVID-19 infection who presented to our casualty in a tertiary care hospital in south India.

History and Presentation

56-year old obese diabetic lady presented to our casualty with sudden onset severe weakness and complete loss of sensation of both lower limbs, associated with persistent aching pain over lower

back and thighs. She presented after 4hrs of onset of symptoms. There was also loss of bowel bladder control. She was apparently completely normal before the symptoms set in and reported having done no strenuous activity prior to onset, and had no history of falls, fever, vomiting or diarrhoea in the past month.

Examination and Course in Hospital

Patient was conscious, restless, diaphoretic but responding well to questions. She was mildly dyspneic with blood pressure of 140/80 equally measured on both upper limbs, pulse rate of 96/min, regular, normal volume, felt equally on both radial arteries, SpO₂ of 94% on room air, respiratory rate of 22 breaths per minute and capillary blood glucose of 246mg/dL. She was afebrile, obese with a BMI

of 34.17 kg/m² and fairly hydrated. She had mild pallor, no icterus, clubbing or any edema. Cyanosis was not evident on any limb at time of presentation although lower extremities were significantly cooler than upper extremities.

CNS examination revealed a power of 0/5 in both lower limbs, with all sensations absent, absent deep tendon reflexes and non-responsive plantars. Upper limb power was 5/5 with intact sensations and reflexes. No spinal tenderness elicited.

Pulses were absent in both femorals, popliteal, dorsalis pedis and posterior tibial arteries. Blood pressures not heard by sphygmomanometer in lower limbs. Ankle brachial index was hence 0; ABI of <0.30 suggests severe ischemia and vascular compromise. Pulse oximetry on toes showed saturation of 46% and 50% on left and right toes respectively.

A clinical diagnosis was made of a probable aortic obstruction, blocking blood flow to spinal cord as well as impeding circulation to lower limbs. An urgent arterial Doppler showed a large thrombus extending from suprarenal aorta till its bifurcation and extending into left femoral till popliteal artery. Patient was immediately referred to a vascular surgeon for further intervention and management.

Routine investigations showed elevated total white counts with neutrophilic predominance, mild anemia and elevated serum creatinine of 1.4mg/dL followed by 2.5 mg/dl on day2. Borderline hyperkalemia was present. Liver enzymes and bilirubin were within normal limits. ECG showed

no significant changes. PT INR, aPTT were within normal range.

After the patient was shifted to intensive care under vascular surgeon, CT angiogram was taken which showed near complete occlusion of abdominal aorta from renal artery origin level extending distally till bilateral common iliac artery bifurcation. Complete filling defect noted in left renal artery right from its origin causing multiple left renal infarcts. Bilateral internal and external iliac arteries appear to be normally opacified with contrast. (Fig.1)

Patient's general condition deteriorated the next day and oxygenation dropped to 85% on room air, with a respiratory rate of 28 breaths per minute. She was started on CPAP ventilation, and Covid-19 pneumonia suspected. RTPCR swab was taken which came negative. Plain CT chest showed score of CO-RADS 4, with severity score of 15/25. Serum ferritin was elevated, in the range of 1400ng/mL, D-dimer of 2540 FEU/ml. Other routine blood investigations stayed same except for elevation in renal parameters, with serum creatinine of 2.5, urea 42mg/dl and hyperkalemia.

A diagnosis of CT positive Moderate Covid Pneumonia was made, with patient in severe cytokine storm and hypercoagulable state. Patient was started on IV steroids, heparin infusion and antibiotics. Surgical intervention was deferred owing to poor general condition. She went into severe respiratory distress and was intubated on Day3. Patient expired by the end of the day.

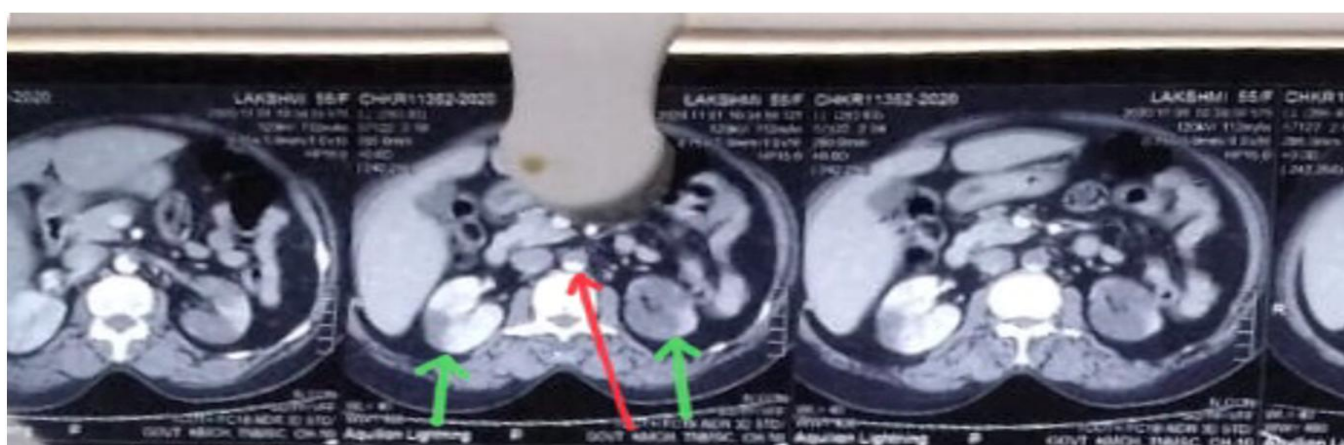


Fig.1: CT angiogram of our patient. Red arrow shows occluded aorta with filling defect. Green arrows show kidneys with multiple infarcts.

Discussion

Acute aortic occlusion (AAO) is a rare entity, with an incidence of 1.5 per 10,000 population.^[1] Causes of occlusion in a native aorta include aortic thrombosis, as a result of severe atherosclerosis, aneurysm thrombosis, aortic dissection, low flow state or thrombophilias, and emboli to aorta originating from a cardiac source, arterial source or paradoxical embolus. Thrombosis also occur following intervention such as grafts, stents or angioplasty. The patient we report has had no previous cardiac illness and has never had any surgical intervention done. Here we aim to explore the differential diagnoses in a patient with acute aortic obstruction in a native vessel, in the context of current COVID pandemic.

Atherosclerosis: Atherosclerotic plaque leads to stenosis of vessels and eventually complete obstruction due to low flow, stasis and thrombosis. It may occur progressively over months to years with development of good collateral circulation, leading to a less dramatic presentation of chronic or acute on chronic limb ischemia. Occlusion in an atherosclerotic vessel may also occur by intraplaque haemorrhage and local hypercoagulability. Diseased iliac arteries may get thrombosed with retrograde propagation usually till level of renal arteries. Associated organ ischemia could include renal, gastrointestinal, or spinal cord ischemia, which presents with sudden paralysis as in our patient.^[2] Diabetes, hypertension, obesity and age are known risk factors.

Aneurysm: Profound and acute distal limb ischemia occurs in thrombosis of aneurysm, most commonly reported in popliteal arteries.

Dissection: Lower limb ischemia as result of acute aortic dissection suggests extensive dissection and has very poor prognosis.

Hypercoagulability: This is a very important cause affecting both diseased native vessels and vessels with grafts or stents. Even normal native vessels may be affected like in arteritides or other low flow

states. Hypercoagulable state may occur as a result of various aetiologies:

(i) Malignancy: Thrombosis in malignancy is very well known and mostly results in venous thromboembolism. Various factors contributory include tissue factor, cancer procoagulant (a calcium dependent cysteine protease found in malignant and fetal tissue), and host cell procoagulant activity mediated by activators such as P-selectin cell adhesion molecule. Platelets become increasingly reactive as a result of interaction with tumour cells. Endothelial cells become procoagulant under effect of TNF and IL-1, TNF is also said to downregulate thrombomodulin expression diminishing activity of protein C.

(ii) Chronic disseminated intravascular coagulation (DIC): Chronic DIC especially as a result of malignancy presents mostly as thrombotic complications rather than bleeding since procoagulant factor production keeps pace with ongoing thrombi generation. It may present as venous thromboembolism such as VTE and DVT, arterial thrombosis with limb or organ ischemia, non-bacterial thrombotic endocarditis, and superficial migratory thrombophlebitis.

(iii) Antiphospholipid syndrome: Both venous and arterial thrombosis is seen, and is higher in patients with positive lupus anticoagulant and high levels of anticardiolipin antibodies.^{[3][4]} Arterial thrombosis mostly present as stroke or transient ischemic attack. Retinal, coronary, renal and mesenteric occlusions also occur.

(iv) Hyperhomocysteinemia: Pathologic hallmarks include intimal thickening, elastic laminate disruption, smooth muscle hypertrophy, platelet accumulation and formation of platelet rich thrombi. High risk of cardiovascular and cerebrovascular disease is found, although reduction of homocysteine levels does not change this risk.^[5]

(v) **COVID-19:** Many mechanisms have been hypothesised for the various described complications of COVID-19. Concerning thromboembolic events, underlying hypercoagulable state and cytokine storm are said to be the culprits, but even then the pathogenesis of the same are still incompletely understood. Severe COVID-19 infection is now found to have all the contributing factors for clot formation as per Virchow's triad:

(a) **Endothelial injury:** The SARS-CoV-2 virus is said to damage the protective endothelial system in various ways. It has been recently found to directly invade the endothelial cells and cause injury. Also, some studies have postulated that COVID-19 is ultimately an endothelial disease (7) with endothelial injury, micro vascular inflammation, endothelial exocytosis and endothelialitis playing the central role in pathogenesis of ARDS and organ failure, wherein cytokines are said to shift the endothelial functions from the homeostatic into the defensive mode. [6][8] Mediators of acute systemic inflammatory response such as cytokines like IL-6, and other acute phase reactants are also implicated in endothelial damage.

(b) **Stasis:** Immobilization in hospital whether or not patient is COVID-19 infected is a cause for stasis of blood flow.

(c) **Hypercoagulable state:** Elevated factor VIII, fibrinogen, hyperviscosity, circulating prothrombotic microparticles and NETs have all been recently postulated to be contributory. [9] D-dimer levels have been correlated with disease severity, but not specific to Covid-19 infection. "Covid-19 Associated Coagulopathy (CAC)" or thromboinflammation is a newly coined term for this state, and it is distinct from DIC (Disseminated intravascular coagulation). Some studies have also reported a transient antiphospholipid antibody positivity.

Clinically, a myriad of manifestations has been reported as a result of thromboembolic phenomena in CoVID-19. Venous thromboembolism, deep vein thrombosis, and pulmonary embolism have been commonly reported in ICU setups inspite of patient being on prophylactic anticoagulant therapy. Risk factors include older age, male gender, higher BMI, coronary artery disease, prior myocardial infarction, diabetes mellitus, hypertension and elevated D-dimer on admission to hospital.

Arterial thrombosis is relatively less common, most of which manifest as ischemic large vessel strokes, and coronary artery occlusions leading to myocardial infarction, and most of these events happened in young individuals below age of 50years. There have been various reports of limb ischemia in older individuals who benefitted from surgical revascularisation. Few case reports have been published with evidence of occlusion of a major vessel such as aorta due to hypercoagulable state in COVID-19.

Embolism: Most common source of embolism is the heart, following atrial fibrillation, left ventricular dysfunction, endocarditis or myocardial infarction. Femoral artery is a common location of lodging of the embolus, as well as bifurcations of common iliac and popliteal arteries. 20% of peripheral emboli are said to be originating from aneurysms and atherosclerotic lesions, constituting arterial-to-arterial embolization.

Spinal cord ischemia: A knowledge of vascular supply of spinal cord at the thoracic and lumbar level is important to explain this patient's presentation. The intrinsic vasculature of spinal cord is supplied by the greater radicular artery (GRA) also called the Artery of Adamkiewicz, which arises on the left side of aorta at the level of seventh through twelfth thoracic vertebra in 85% of population.[10] Remaining population have a lower origin from level of L3-L5, with the balance provided by the anastomotic arterial ansa of the conus at L1-5 levels supplied by pelvic vasculature.

Our patient presented with signs of acute limb and spinal cord ischemia, and is a middle-aged obese diabetic with poorly controlled glycemic status. In absence of any previous investigations or vascular imaging, we definitely need to consider thrombosis of an atherosclerotic aorta or iliac arteries as an important differential. CT angiogram rules out presence of aneurysms and dissection of aorta. A normal echocardiogram rules out cardiac sources of embolism as well a paradoxical embolism, although arterial-to-arterial embolization from another atherosclerotic plaque is still possible.

Her nasopharyngeal swab gave a negative RTPCR report, but non contrast CT chest had features of COVID-19 pneumonia with moderate severity. She also deteriorated and succumbed to the same within 48 hours of presentation. Hence the possibility of a thrombus in aorta as a result of hypercoagulability in COVID-19 cannot be ruled out, in fact is highly likely taking into consideration the elevated d-dimer and ferritin levels.

Other investigations which could have been done if not for her very short stay include total cholesterol and complete lipid profile, anticardiolipin antibody, anti-beta-2-microglobulin antibody, lupus anticoagulant, protein C and S, factor 5 Leiden, antithrombin, homocysteine, serum complement levels, and imaging and tumour markers to rule out malignancies such as cancers of colon, breast, lung, and kidney. A normal PT INR and aPTT could possibly rule out chronic DIC.

Conclusion

A complete systemic examination narrowed down cause to a vascular issue. Although palpation of peripheral pulses alone has been shown to be a poor indicator of extremity perfusion, calculation of ankle brachial index (ABI) has been noted to be of significance in acute vascular pathology. Since there was a significantly large thrombus found in our patient, occluding entire diameter of aorta at renal artery level (L2-L3), it would explain both the paraplegia due to GRA occlusion as well as reduced blood flow to lower limbs leading to limb ischemia. The thrombus itself could be a result of the cytokine

storm and hyper coagulable state due to COVID-19 infection. Hence prophylactic anticoagulant therapy assumes extreme importance in severe cases of COVID-19 at the optimum dosage and duration. Since in our patient further investigations could not be carried out, causes such as atherosclerosis, plaque rupture, hypercoagulability due to malignancy, antiphospholipid antibodies and thrombophilias still constitute the main differential diagnoses along with COVID-19 infection.

Conflict of Interest: None

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