

Treating Triple Thrombus-Pulmonary, Cardiac, and Cerebral: A Case Management with Calculated Conscience

Dear Sir,

A 23-year-old lady, presented to us with right-sided weakness and global aphasia of 190 minutes duration. She had a history of cough, breathlessness, and orthopnea of one-month duration. One day prior, she was diagnosed to have an extensive pulmonary artery and vein thrombus extending into the left atrium [Figure 1] by the cardiologist, yet to start any treatment. She also had polycystic ovarian syndrome and was on combined hormonal oral contraceptive agents (OCP) with Ethenyl Estradiol 0.03 mg and Levonorgestrel 0.15 mg for the last two months.

On examination, she was found to have tachycardia, normal blood pressure, normal cardiac examination. Neurologically, she had global aphasia, normal blood pressure, right hemianopia, right UMN facial palsy, and right hemiplegia. Her National Institute of Health Stroke Scale (NIHSS) was 17. Computed tomography [Figure 2] showed Alberta Stroke Programme Early CT Score (ASPECTS score) of seven and CT angiography revealed left proximal MCA (M1) occlusion with good collaterals (Miteff- 3).

She was treated with injection Tenecteplase 0.20 mg/kg (17 mg) intravenous bolus after explaining the

risk of systemic thromboembolism to parents and shifted to the Cath lab for angiography immediately. Digital Subtraction Angiography (DSA) showed left M1 occlusion. Hence, thrombus aspiration was done using penumbra ACE 68 catheter, achieving thrombolysis in cerebral infarction (TICI) score 2b recanalization in 70 minutes.

Detailed blood investigations revealed macrocytic anemia (hemoglobin-8.2 g/dl), normal prothrombin time, normal lipid profile, normal electrocardiogram (ECG), low Vitamin B12 (86.72 umol/L) (normal: 197-771 umol/L), elevated serum homocysteine (54.2 umol/L) (normal <15), normal folate (9.72 umol/L). Serology for autoimmune, HIV, syphilis, vasculitis, and procoagulant disorders were negative. Trans-esophageal echocardiography and cardiac MRI [Figure 1] done one day before, showed pulmonary thromboembolism (pulmonary artery and vein) extending till left atrium and pulmonary artery hypertension (PAH).

Twenty-four hours after the procedure, she was started on subcutaneous heparin (5000 international units, once in 6 hours), overlapped with acenocoumarol 1 mg per day, with a target prothrombin time-international normalized

ratio (PT-INR) of 2-3. She improved over the next two days, from NIHSS 17 to 2, with persistent mild facial weakness and dysarthria. During her last visit at 3 months of her ictus modified Rankin Score (mRS) was 0.

DISCUSSION

Our patient presented with right hemiplegia and global aphasia on a background of thrombosis in the pulmonary artery and vein extending till the left atrium. Since she was in the window period of AIS, the option of IVT followed by EVT with calculated risk was attempted after consenting from the relatives. Probably OC pills, macrocytic anemia, vitamin B12 deficiency, and hyperhomocystenemia were the triggers for triple thrombus as the other procoagulant workup was negative. To our knowledge, this is the first case in literature with pulmonary vasculature and left atrial thrombus with M1 occlusion who underwent IVT followed by EVT and improved completely without any complications. At presentation, we had the option of directly going for EVT. But we decided to go ahead with IVT (Tenecteplase) followed by EVT for the following reasons: 1. As per the guidelines, IVT is recommended first before EVT if the patient is eligible for the former, 2. Technical difficulties in EVT may cause recanalization difficult and the time window for IVT may be over by that time, 3. Complications due to anesthesia during EVT may occur since she has cardiac and pulmonary vascular thrombi.^[1] In our patient, tenecteplase was chosen over alteplase since: it is less expensive, more fibrin specific, can be given stat without causing delay in EVT.^[1]

It is estimated that around 3.6% of patients with ischemic stroke have cardiac thrombus, and transesophageal echocardiography (TEE) may increase the yield of visible cardiac thrombus.^[2] The role of IVT in acute ischemic stroke for patients with LA thrombus is not defined clearly. Prior case reports showed varied results. Few reports are there which conclude that IVT is safe in the cardiac thrombus. In a case series studied during 2001, five patients of acute ischemic stroke with known cardiac thrombus were given IVT. Two patients improved completely within three months, two had a moderate outcome, one had a late recurrent cerebral embolism and died. None of them had early ischemic or hemorrhagic complications.^[2]

We had apprehensions about giving IVT for the following reasons. The tPA (tissue plasminogen activator) can cause hemorrhagic (more common 6.4%) as well as thrombotic complications (Early Recurrent Ischemic Stroke). It can activate coagulation cascade by stimulating plasminogen activator inhibitor (PAI) and increasing thrombin.^[3] It takes 20 minutes for the IVT dose to reduce to 6.25% in circulation. But it takes 24 hours for fibrinogen levels to reach 80% of its normal range. Hence early recurrent ischemic stroke can occur within the first few hours of infusion, and hemorrhagic complications can occur as late

as 24 hours after infusion.^[3] The IVT done for pulmonary thrombosis can lead to cerebral embolization.^[4] It can cause hypercoagulability and lead to new thrombus in the left ventricle.^[3] The patient may develop right MCA occlusion after treating with tPA for left MCA occlusion.^[5] The close differential for LA clot is LA myxoma in which literature is sparse and guidelines are unclear. Few reports claim that it is safe.^[6,7] In LA myxoma causing embolic infarct, thrombolysis may lead to hemorrhagic infarction.^[8] After a stroke, pulmonary embolism can occur rarely, which is usually a complication of deep venous thrombosis (DVT) of legs. The frequency of pulmonary embolism till 30 days of stroke is 0.78%. However, the co-occurrence of pulmonary thrombosis and cerebral thrombosis at same time is rare.^[9] Prior history of deep venous thrombosis, cancer, pulmonary embolism are the chief risk factors. If a patient has pulmonary thrombosis and ischemic stroke at the same time, anti-coagulants can be started according to the size of infarct and severity of stroke within 4-14 days.^[10] In acute pulmonary thrombosis, management depends on the hemodynamic condition of the patient and catheter/surgical embolectomy, or IVT is advised. In a patient with In stable patients and in sub-acute thrombosis, anticoagulants are the treatment of choice. She was continued on the oral anticoagulants for her condition.

A thorough search for the cause of the procoagulant state was done. Hormonal contraceptive agents are known to increase pro-coagulant factors (fibrinogen, factor VII and VIII), reduce anti-thrombin III levels, and cause acquired APC resistance leading to extensive arterial and venous thrombosis.^[11] Hyperhomocysteinemia is also associated with increased

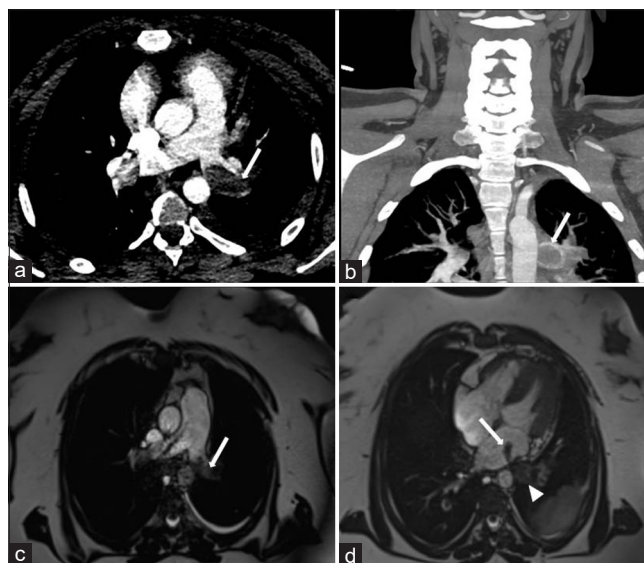


Figure 1: (a and b) Computed Tomography Angiography (CTA) axial and coronal sections reveal left pulmonary artery thrombus (white arrow). (c) Magnetic resonance imaging (MRI) heart, T2 sequence shows left pulmonary artery thrombosis. (d) MRI heart, T2 shows left atrial thrombus (arrow) and pulmonary vein thrombus (arrow head)

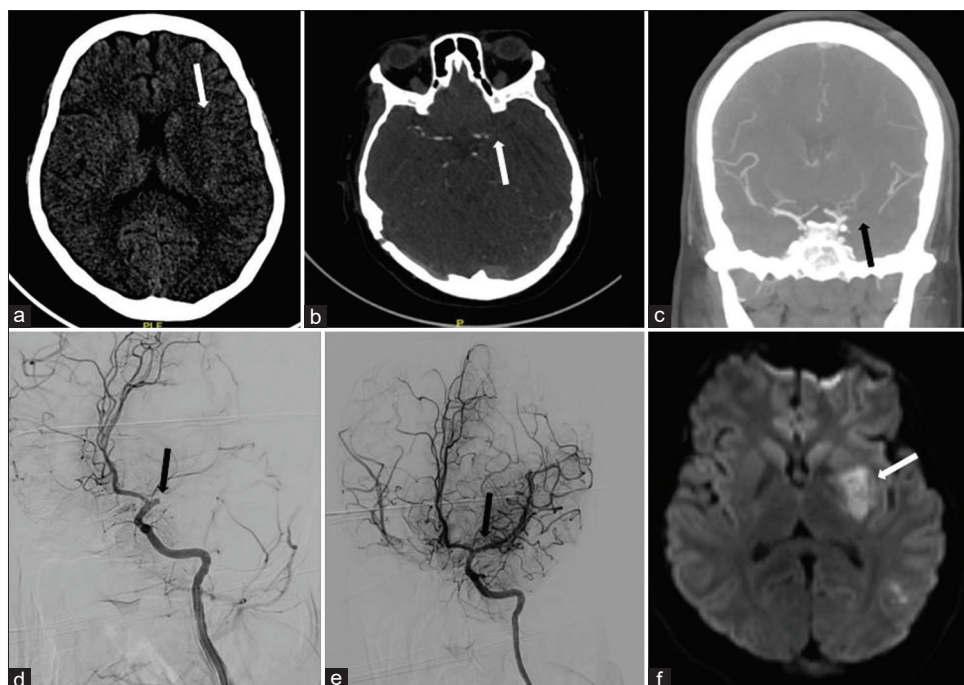


Figure 2: (a) Non contrast Computed Tomography shows hypodensity in left insular area (arrow) and lentiform nucleus. CT Angiography (b & c) shows left M1 occlusion with good collaterals. Digital subtraction Angiography, antero-posterior view shows left M1 cut off (arrow) before procedure (d) and normal flow after aspiration thrombectomy (e). (f) MRI after procedure shows diffusion restriction in left posterior putamen area (arrow)

risk of both arterial and venous thrombosis. Probably OC pills, B12 deficiency anemia, and Hyperhomocysteinemia have triggered the procoagulant state in our patient. The treatment recommended is anticoagulation and vitamin B12, folate, and pyridoxine replacement. To our knowledge, this is the first case reported in the literature with triple thrombus and managed successfully with IVT, EVT followed by anti-coagulants. In our patient we consciously thought and discussed with relatives and treated her with IVT, EVT followed by anticoagulation. We need to balance available resources with current knowledge and manage such cases with a calculated conscience.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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Submitted: 24-Jul-2020 **Revised:** 01-Sep-2020 **Accepted:** 23-Sep-2020

Published: 05-Apr-2021

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DOI: 10.4103/aian.AIAN_771_20