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Case Report

Thrombosis At Unusual Sites in Reproductive Age Group-A Case Series

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ABSTRACT

Thrombosis is one of the causes of morbidity and mortality in women of reproductive age group. Thrombosis at unusual sites may pose diagnostic and management dilemma for health care personnel. Teamwork and good communication provide the best modalities for maximum benefits to patients. Here with, we presented case a series of thrombosis at unusual sites seen and managed in our clinic. A 35 year-old Malay lady presented with left hemiparesis while she was on oestrogen based combined contraception pills (C-OCP). Imaging studies showed extensive venous thrombosis with bilateral acute cortical infarct. Thrombophilia screening of antiphospholipid syndrome were negative. She was put on anticoagulant and stopped 2 years after the incident. A 40 year-old Malay lady presented with abdominal discomfort, lethargy and massive splenomegaly. Bone marrow and trephine examination revealed primary myelofibrosis with positive JAK2617F. Imaging study showed chronic portal vein thrombosis with portal vein hypertension, complicated by gastro-oesophageal varices. She was put on hydroxyurea and later started on ruxolitinib with banding done over her gastro-oesophageal varices. A 26 year-old Malay lady presented with serositis, mouth ulcer and anaemia symptoms. Laboratory studies were positive for systemic lupus erythematosus and negative for antiphospholipid study. Imaging study showed long segment thrombosis of right internal jugular vein with surrounding subcutaneous oedema. She is currently stable on anticoagulants and steroid. Teamwork and holistic approach is practiced in the investigation and management to provide maximum benefits for patients.

Keywords: Thrombosis, Unusual sites, Reproductive age group, Teamwork

INTRODUCTION

Venous thromboembolism (VTE) is a multifactorial disease defined by multiple interactions between genetic and acquired risk factors. Thrombosis is one of the causes of morbidity and mortality in women of reproductive age group. Women are subject to specific hormonal changes (either naturally occurring or induced by common hormone treatments) which influence factors relevant to thrombosis and put them at a temporary increased risk of VTE. During the reproductive years, contraceptive use, pregnancy and profertility ovarian stimulation may alter the levels of pro- and anticoagulants as well the fibrinolytic system.

Thus, for periods of a woman's life, the risk of VTE is significantly increased above baseline (1). While VTE is a major cause of morbidity & mortality and one of the leading causes of maternal mortality, thrombosis at unusual sites may poses diagnostic and management dilemma for health care personnels.

Teamwork and good communication provide the best modalities for maximum benefits to patients.

CASE REPORT

We retrospectively reviewed our reproductive age group patients who were seen at our haematology clinic in Hospital Serdang from February 2014 to February 2015 and found 3 cases of thrombosis occurring at unusual sites.

Case 1: A 35-year-old lady on combined oral contraceptives (C-OCP) presented with status epilepticus in November 2012. CT scan and MRI showed extensive venous sinus thrombosis with bilateral acute cortical infarcts.

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A hypercoagulable work-up did not reveal any additional thrombophilia. She was initially managed with systemic anticoagulation using intravenous heparin (80IU/kg bolus,then 18IU/kg/hr) and subsequently was put on warfarin (3mg once daily). She was switched to SC Enoxaparin (40 mg twice daily) & T Aspirin (100 mg once daily) during her pregnancy in 2013. Following childbirth in April 2014, she underwent bilateral tubal ligation in November 2014. A repeat magnetic resonance venography (MRV) in 2014 (Figure 1.) revealed residual venous sinus thrombosis in right sigmoid and right transverse sinus with partial recanalization of the superior sagittal sinus thrombosis with bi-parietal chronic cortical venous infarcts. She recovered well without any neurological deficit. Since her work-up for thrombophilia ie anti phospholipid syndrome (APLS), factor V Leiden (FVL) mutation and activated protein C resistance (APCR) were negative, she was counselled and opted to stop warfarin.

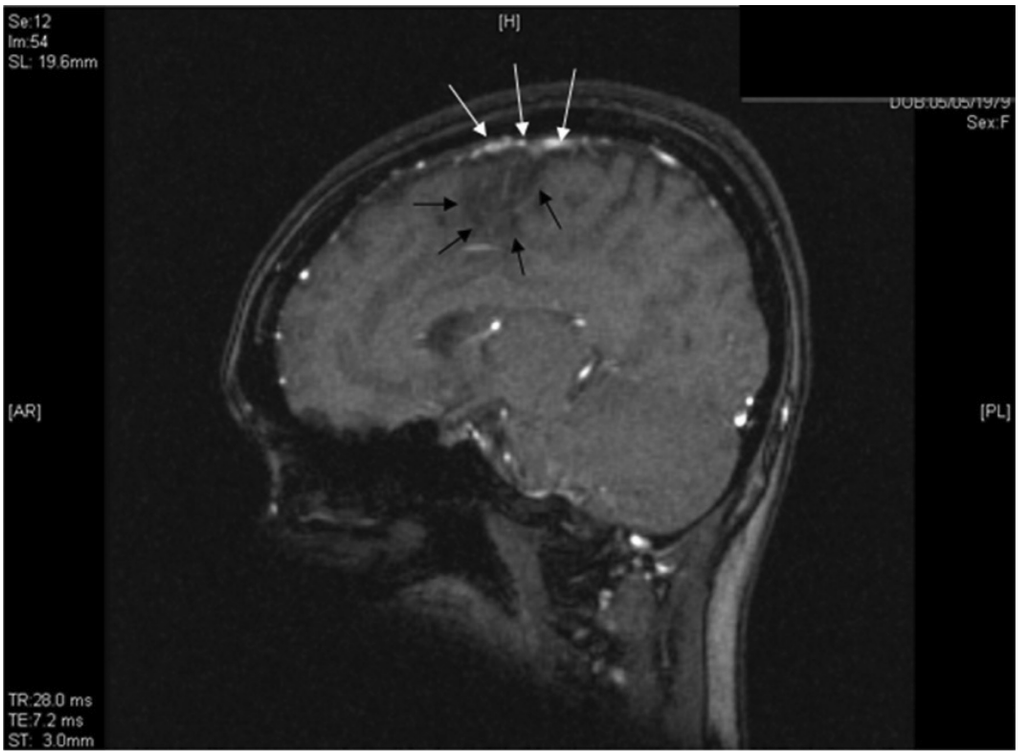

Figure 1. A sagittal Magnetic Resonance Venography (MRV) showing hypointensity at the right parietal region showing old infarcted area (black arrows) and areas of hyperintensity signals within superior sagittal sinus suggesting residual thrombus (white arrows).

Case 2- A 41-year-old Malay lady was diagnosed with primary myelofibrosis in July 2014 when she presented earlier with massive splenomegaly and acute abdomen. She was admitted previously for bleeding oesophageal varices in December 2012 whereby CT scan revealed chronic portal vein thrombosis (PVT) with portal hypertension and established splenorenal portosystemic shunt together with sclerosing mesenteritis (Figure 2.). Apart from the above, she had euthyroid colloid goitre and past history of tubulovillous sigmoid polyp. Her gastrointestinal symptoms were well controlled with esomeprazole (20 mg once daily) and propanolol (40 mg twice daily) together with variceal banding. Her primary myelofibrosis (MF) was initially treated with hydroxyurea (500 mg twice daily) and had been managed with ruxolitinib (5 mg once daily) since December 2014. Her latest laboratory analyses were notable for normal coagulation panel, haemoglobin of 9g/dL and platelet of 76 X 10^9/L. Analysis of DNA extracted from her blood revealed the presence of the V617F mutation within the JAK2 gene.

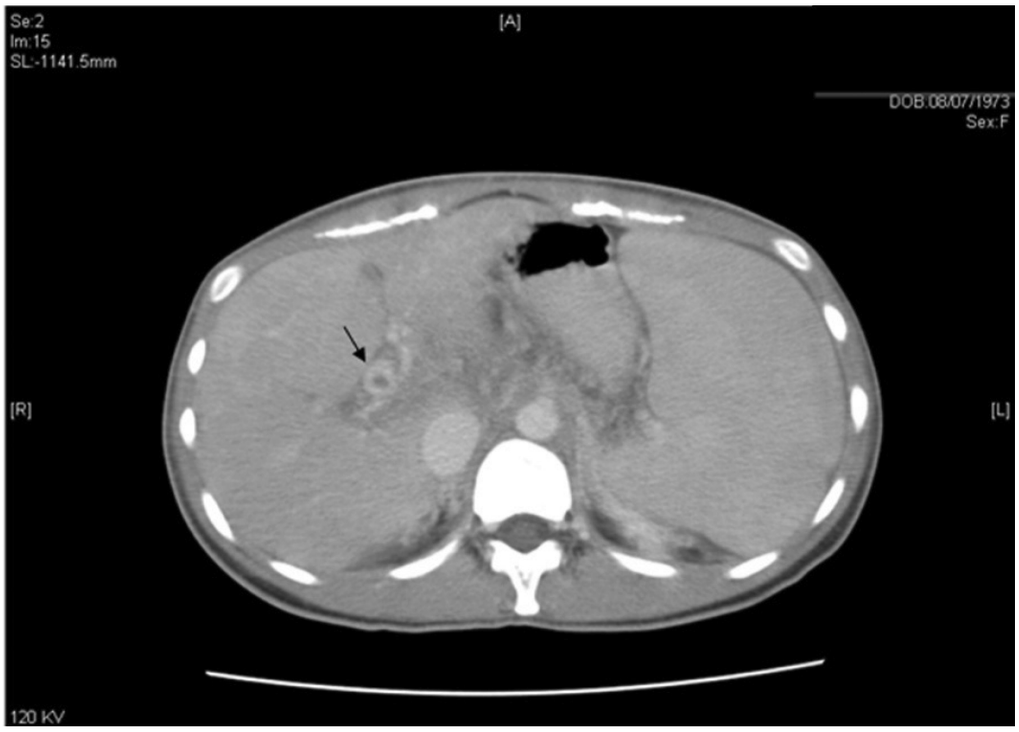

Figure 2. An axial Contrast Enhanced Computed Tomography shows rounded vascular structure with central hypodensity seen at porta hepatis region which represent thrombosed portal vein (black arrow). There are evidence of collaterals with the spleen and liver hugely enlarged.

Case 3- A 26 year-old Malay lady presented in December 2012 with serositis (ascites, pleural effusion and pericardial effusion), mouth ulcers and anaemia symptoms. Her laboratory investigation revealed positive anti nuclear antigen (ANA), low complements, positive rheumatoid factor and anti ribonucleoprotein (RNP) thus was diagnosed with systemic lupus erythematosus (SLE). She was treated with prednisolone (7.5mg daily). She is co-jointly managed in National Heart Institute (IJN) due to her chronic thromboembolic pulmonary hypertension (CTEPH) and history of left atrial clot. She is treated with sildenafil (50 mg thrice daily) and diuretics (frusemide 40 mg daily and spironolactone 12.5mg daily). She had unprovoked long segment right internal jugular vein thrombosis in January 2013 and was put on warfarin (2.5 mg daily).

DISCUSSION

As illustrated in the case series, a diverse clinical manifestations and outcome arose from these thromboses at unusual sites.

C-OCP is identified as the provoking factor in the first case and the neurological deficits were resolved 2 years post event. Risk of thrombosis increased when using combined hormonal contraception (CHC) or hormone replacement therapy (HRT). While the increased risk is related to the dose of estrogen, it is also influenced by the type of progestogen, with the second generation progestogens [levonorgestrel (LNG) and norethisterone] regarded as being safer than the newer progestogens (1). Recurrence is low for CVST due to C-OCP. Duration for anticoagulation is advised for a minimum of 3 months. Period to be extremely cautious is during the acute event where cerebral herniation can be fatal. Coma, thrombosis of deep cerebral vein, CNS infection, malignancy and intracerebral haemorrhage are regarded as poor prognosis (2).

The diagnosis of myeloproliferative neoplasm (MPN) in the second case was embarked after 2 years of having portal vein thrombosis leading to portal hypertension and its complication. Manifestation (symptoms & laboratory indices) of MPN and portal hypertension were similar which leads to a delay in diagnosis of MPN. A lesson learnt here is testing for the JAK2 mutation is strongly indicated for patients with splanchnic vein thrombosis (3). MPNs account for up to a quarter of cases and PVT is a common presenting manifestation of MPN (2). Therefore, it is recommended

that PVT patients should be assessed for JAK2 V617F mutation. Long term anticoagulation is recommended for patients presented with abdominal vein thrombosis with underlying paroxysmal nocturnal haemoglobinuria (PNH) or MPN (2).

As for the third case, the provoking factors are her autoimmune condition and this has made her to have thrombophilia trait manifested by atrial clot and thrombosis at internal jugular vein. Jugular vein thrombosis is most commonly seen in association with local sepsis, inflammation or trauma. Low dose vitamin K antagonist and anticoagulation for a period of 3 to 6 months is recommended (2).

Acquired risk factors are more common than inherited risk factors, (4) thus searching for acquired factors is much more warranted than focusing on inherited thrombophilia which are rare and incur huge financial implication and do not provide much information as for management of patients per se (4). Teamwork and holistic approach is practiced in the investigation and management to provide maximum benefits for patients.

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