Case Report

Life threatening thrombo embolic event following Dengue hemorrhagic fever

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Abstract

Dengue fever (DF) is a highly prevalent infectious disease in Sri Lanka. Even though hemorrhagic manifestations are common in Dengue Hemorrhagic Fever (DHF), thrombo-embolic events are uncommonly reported, despite the wide range of increased procoagulant activity during Dengue fever. Management of a life threatening thromboembolic event during and immediately after DHF is a challenge for treating physician due to high risk of bleeding complications. We report a case of a 25-year-old young male who developed life threatening large vein thrombosis of the internal jugular vein(IJV) complicated by pulmonary thromboembolism (PE) following DHF, which was successfully treated with thrombolysis followed by anticoagulation.
Keywords: Dengue Hemorrhagic Fever, Thromboembolism, Pulmonary Embolism, Thrombolysis, Anticoagulation

Introduction

Dengue fever is a major health concern in Sri Lanka where thousands of cases are diagnosed annually. There were a total of 186,101 reported cases of suspected dengue fever during the year 2017 with over 320 deaths. A total of 47,536 suspected dengue cases were reported up to September 2018 [(1)]. Dengue hemorrhagic fever and dengue shock syndrome are the main concerns which lead to significant mortality. Even though it is uncommonly reported, there is a wide range of increased procoagulant activity during Dengue fever which can lead to thrombo-embolic events [(2, 3)]. Thrombotic events of large veins including ileo-femoral deep vein thrombosis (DVT), PE and rarely mesenteric vein thrombosis have been reported in 5.4% of all dengue inpatients in Brazil [(4)]. Although anticoagulation with or without thrombolysis is the recommended management for PE and DVT, this treatment may be questionable in DF/DHF with high risk of bleeding. The physician who is treating patients with dengue fever should be aware of the range of complications.

Case Presentation

A 25 year old male was treated for Dengue hemorrhagic fever at a local hospital when he was admitted with fever, headache, arthralgia and myalgia for 3 days. The diagnosis was confirmed with a positive dengue NS1 antigen. He had severe thrombocytopenia with lowest platelet count of 26,000/microml and ultra sound scan evidence of leakage with free fluid in the abdomen and pleural effusion.

He was hemodynamically stable throughout the illness. He recovered from DHF and was discharged on day 8 of the illness.

On discharge he had been asymptomatic. However, he developed sudden onset shortness of breath on day 11 without fever or cough and was re-admitted to the same hospital. He was tachycardic (PR – 108/min) with low blood pressure (BP 90/60 mmHg) and his oxygen saturation on air (SPO2) was 88% - 90%. Respiratory examination revealed right lower zone coarse crepitations. Following day he developed fever.

His WBC count was $16.8x10^3$ with neutrophil leukocytosis with normal platelet count and high inflammatory markers (CRP-118mg/dl, ESR – 120mm/1sthr). Chest X- ray revealed a patch of right lower lobe consolidation. He was treated in the intensive care unit with antibiotics (IV. merapenum 1g 8hrly and IV. Levofloxacin 500mg bd) and inotropes with the diagnosis of right lower lobe pneumonia complicated with septic shock. Because of the initial suspicion of pulmonary embolism D-dimer test was performed and which was positive (>3.2 mg/l). Patient was referred to our unit for further evaluation and management.

On admission to our unit patient was febrile (101.2F) and dyspneic at rest with SPO2 88- 92% on air, tachycardic with PR 108/min and low BP of 90/60mmHg.Respiratory system examination revealed right lower zone coarse crepitation and pleural rub. ABG showed low SpO2 of 61mmHg.

Case Report

2D echocardiography showed moderate pulmonary hypertension (TRPG 39 Hg mm), without right atrial (RA) or right ventricular (RV) dilatation with preserved left ventricular function (EF 60%). Main pulmonary artery was not dilated and there were no shunts. Urgent computed tomography pulmonary angiogram (CTPA) was performed, which revealed multiple thromboembolism in both right and left pulmonary arteries with right side lower lobe lung infarction.

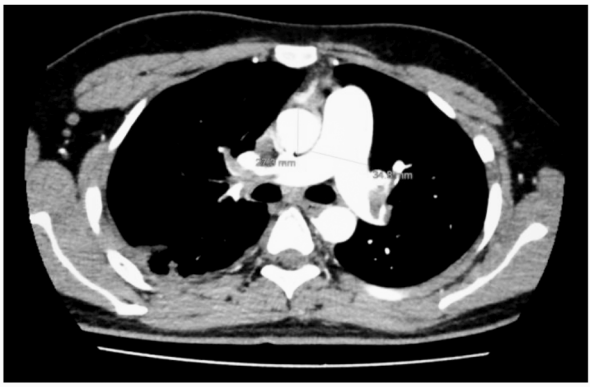

Figure 1- CTPA- Multiple thrombo emboli in right and left pulmonary arteries. A.

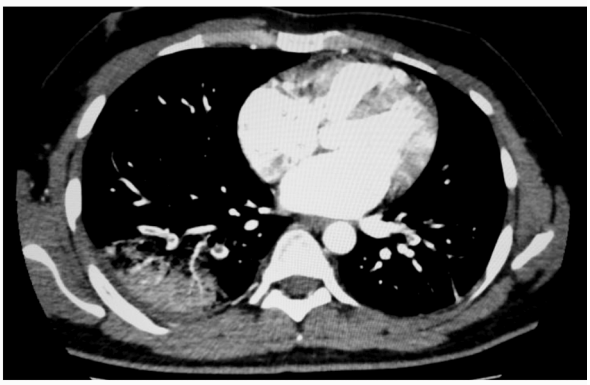

Figure 2- CTPA – Multiple thrombo emboli in segmental pulmonary arteries and right lower lobe infarction.

Patient was further evaluated for primary site of thrombosis. Venous duplex of both legs was negative for deep vein thrombosis. Furthermore we looked for a site of emboli, as it was unusual to manifest bilateral thrombosis in situ. Direct questioning revealed pain in the right side of neck and the Doppler scan of neck veins revealed a hyper-echoic thrombus in the right internal jugular vein with a stenosed area of 98%. Colour flow was seen around the thrombus.

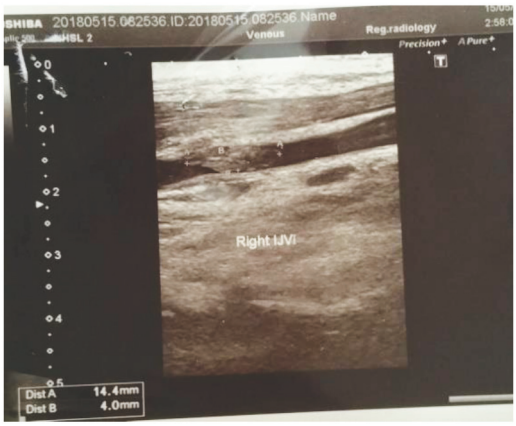

Figure 2 Duplex scan of neck veins – right internal jugular vein thrombosis.

His sputum culture was positive for MRSA and antibiotics were changed according to the sensitivity pattern (intravenous piparacillin tazobactam 4.5g 6hrly, Intravenous vancomycin 1g bd and oral clarythromycin 500mg bd).

Diagnosis of right internal jugular vein thrombosis complicated with pulmonary embolism and pulmonary infarction with super added infection was made.

Patient was successfully thrombolysed with alteplase 100mg over one hour followed by enoxaparin 1mg/kg subcutaneously twice a day with significant improvement of oxygen saturation and blood pressure. He was later converted to wafarin after 5 days and eventually discharged with a diagnosis of DHF complicated with life threatening thrombotic events. Warfarin was continued for 6 months. He had complete recovery with resolution of pulmonary hypertension in follow-up echocardiography and absence of residual thrombus in IJV in venues duplex scan after 6 months.

On further evaluation for a cause of this prothrombotic state apart from dengue fever, revealed negative anti-nuclear antibody (ANA) and negative anti- phospholipid antibody. Hyperfibrinogenaemia, dysfibrinogenaemia and sickle cell disease were excluded. JAK2 V617F mutation analysis was done to exclude occult myeloproliferative neoplasm which was not detected.

Discussion

Several mechanisms have been described in the literature for the association between DF and thrombotic processes. Loss of endothelial non-thrombogenic protective factors has been identified early in the course of severe dengue fever [5, 6]. Dengue virus down regulates thrombomodulin thrombin-protein C complex formation thus reducing activated protein C. Low plasma concentration of protein C, protein S and antithrombin III have been reported in severe dengue fever even it is not associated with Clinical thrombosis [6].

Dengue virus activate endothelial cells and increase the expression of thrombomodulin, and host antibodies formed against non-structural protein in the dengue virus that have cross reactivity with endothelial cells in the host leading to inflammatory responses [2, 3].

Antibodies against phospholipids, cardiolipin and increased lupus anticoagulant have been associated with thrombotic events in peripheral arteries and cerebral vasculature [7] in dengue fever which was negative in our patient. Even though not seen in our patient disseminated intravascular coagulation (DIC) leading to microthrombi formation may contribute to thrombosis in dengue fever [8]. Severe dehydration, a well-known condition associated with thrombotic events is a possibility in dengue hemorrhagic fever. Post dengue fever thrombocytosis is a well-known phenomenon which can be associated with thrombosis following dengue fever [9]. In our patient platelet count was normal when he was admitted with thrombo embolic event.

The majority of reported cases of thrombotic events occurred early in the case of dengue fever which leads to dilemma in the management. Even it was a life threatening thrombotic event treating with thrombolytic and/or with anticoagulant may lead to life threatening bleeding complications in a high risk condition like dengue hemorrhagic fever with severe thrombocytopenia. It was not the case in our patient; he developed DVT complicated PE after full recovery of dengue hemorrhagic fever with normal platelet count. Thrombolysis is indicated in massive pulmonary embolism with hemodynamic instability.

Therefore we thrombolysed the patient with Alteplase followed by anticoagulation with enoxaparin without any bleeding complication. Later anticoagulant was converted to warfarin with maintaining INR between 2-3 and continued for 6 months until he had complete recovery.

There were no other predisposing conditions for thrombosis other than DHF in our patient and other possible thrombotic conditions were excluded with detailed investigation including negative thrombophilic screening.

Conclusion

The present case brings to the limelight one of the rare complications of DF, i.e. thrombotic complication following recovery of DHF. Life threatening thrombo embolic condition such as deep vein thrombosis, pulmonary embolism and mesenteric artery thrombosis can occur during or following recovery of dengue fever. Therefore high degree of suspicion by treating physician, early diagnosis and prompt management is needed to save the life.

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