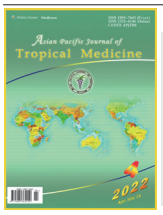

Case Report

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Diffuse alveolar hemorrhage complicating dengue haemorrhagic fever in a 15−year−old boy: A case report

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ABSTRACT

Rationale: Dengue fever is a viral infection that is spread through the bites of infected female *Aedes* mosquitos. It can cause life threatening complications, including dengue haemorrhagic fever (DHF) and dengue shock syndrome.

Patient concerns: A 15-year-old male presented with fever and petechiae and later developed hemoptysis.

Diagnosis: Dengue fever with DHF with diffuse alveolar hemorrhage.

Interventions: Invasive ventilation with high positive end expiratory pressure, multiple transfusions of packed red blood cells, fresh frozen plasma, single donor platelets and inotropic support

Outcomes: The patient was stabilized and discharged on minimal supplemental oxygen.

Lessons: Diffuse alveolar hemorrhage, although very rare, should be considered in a patient with dengue who presents with hemoptysis. The treatment is directed at providing respiratory and circulatory support, and preventing the progression of microcirculation damage.

KEYWORDS: Diffuse alveolar hemorrhage; Dengue haemorrhagic fever; Dengue virus; Pulmonary hemorrhage; Acute respiratory distress syndrome

1. Introduction

Dengue fever is an arthropod-borne viral disease spread to humans through the bites of infected female *Aedes* mosquitos. Dengue virus is a positive-sense single stranded RNA virus that belongs to the *Flavivirus* genus (family Flaviviridae). Any of the four antigenically distinct serotypes (DEN-V 1-4) can cause infection[1]. It presents with non-specific symptoms such as fever, headache, and myalgia, making clinical diagnosis more difficult. To diagnose dengue infection, a combination of clinical and laboratory parameters (positive tourniquet test, relative bradycardia, leukopenia, and specific aspartate aminotransferase elevation with prolonged activated partial thromboplastin time) could be used as bedside markers[2]. Dengue virus can cause serious disease in humans, including dengue haemorrhagic fever (DHF) and dengue shock syndrome[3]. Minor to major bleeding, thrombocytopenia, and plasma leakage are signs of DHF. Epistaxis, gum bleeding, gastrointestinal bleeding, hypermenorrhoea, and haematuria are common hemorrhagic manifestations[4].

Lung involvement in dengue remains a contentious issue. In experimental infections and autopsies, viral antigens were detected in lung tissue, and the virus appears to be capable of infecting macrophages as well as lung endothelial and epithelial cells. Pleural effusion, pneumonitis, non-cardiogenic pulmonary edema, acute respiratory distress syndrome (ARDS), and hemorrhage/hemoptysis are possible pulmonary complications[1].

Diffuse alveolar hemorrhage (DAH) is a syndrome with several manifestations that can complicate various clinical conditions and can be life-threatening, necessitating urgent treatment. DAH symptoms include acute or subacute cough, hemoptysis, diffuse

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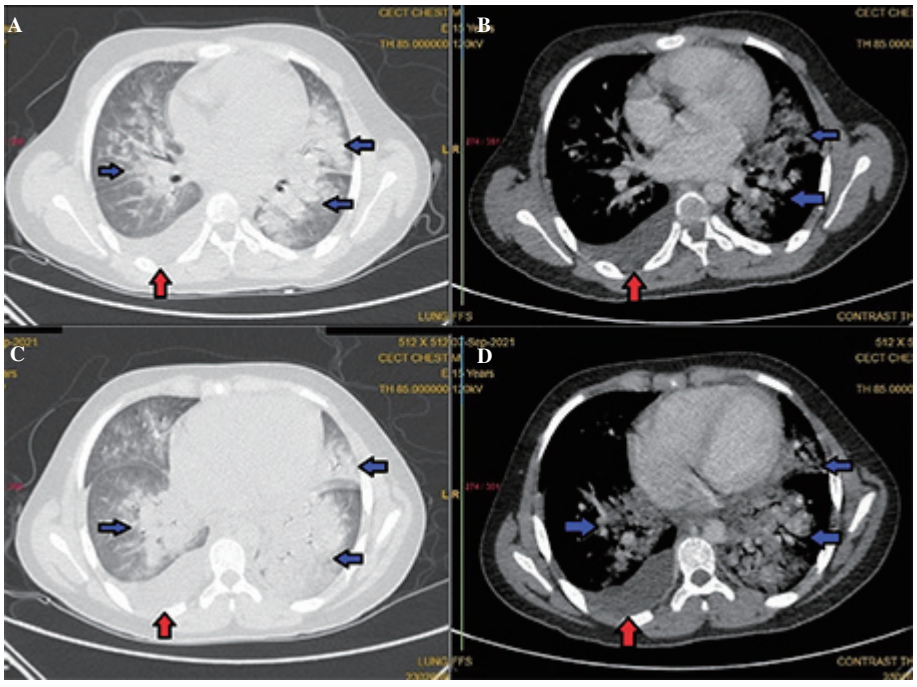

Figure 1. Computed tomography (CT) scan of the thorax in a 15-year-old male patient with dengue haemorrhagic fever. A and C: Axial sections of high-resolution CT scan of the thorax with blue arrows indicating bilateral peribronchovascular consolidations and ground glass opacities (left>right) and red arrows indicating mild pleural effusion on the right side. B and D: Axial sections of CT scan of the thorax with contrast with blue arrows indicating bilateral peribronchovascular consolidations and ground glass opacities (left>right) and red arrows indicating mild pleural effusion on the right side.

radiographic lung infiltrates, anaemia, and hypoxemic respiratory distress. This clinicopathologic condition is distinguished by the accumulation of intra-alveolar red blood cells arising primarily from alveolar capillaries but also from precapillary arterioles and postcapillary venules. DAH must be distinguished from localised pulmonary bleeding, which is typically caused by chronic bronchitis, bronchiectasis, malignancy, or localised infection[5].

2. Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

3. Case report

A 15-year-old male presented with a five-day history of fever, headache, retro-orbital pain and myalgia. He had no cough, breathlessness, abdominal pain, nausea or vomiting. On examination, the patient was dehydrated, tachycardic with petechiae on bilateral arms and legs. Lab investigations revealed hemoglobin of 15.1 g/dL (haematocrit 45.4), platelets 35 000/dL, total leucocyte count was 3 300/dL, renal function tests were normal, aspartate aminotransferase was 149 units/L, albumin 2.7 g/dL, prothrombin time was 15.4 s and international normalized ratio (INR) was 1.3, C-reactive protein was 56 mg/L and ferritin was 1 896 ng/mL. Dengue NS1 was positive.

On the 2nd day, the patient developed multiple episodes of

Table 1. Clinical and laboratory parameters in a 15-year-old male patient with dengue haemorrhagic fever.

Parameters	Reference range	Day 1	Day 2	Day 3	Day 7	Day 11
Hemoglobin (g/dL)	13.2-16.6	15.1	10.7	8.4	10.2	10.8
Total leukocyte count (cells/dL)	4 000-11 000	3 300	3 200	2 800	3 200	4 100
Platelets (cells/dL)	150 000-450 000	35 000	16 000	42 000	54 000	62 000
Aspartate aminotransferase (U/L)	8-33	149	136	154	86	52
International normalized ratio (INR)	<1.1	1.3	1.4	1.7	1.5	1.1
Oxygen saturation (SpO_2)/ Fraction of inspired oxygen (FiO_2) (%/%)	>95/21 (room air)	98/21 (room air)	90/21 (room air)	90/100 (invasive ventilatory support)	94/70 (invasive ventilatory support)	94/60 (8 litres of O_2 *via* face mask)
Respiratory rate (/min)	12-16	16	34	38	32	26
Positive end-expiratory pressure (cm of H_2O)	-	-	-	12	8	-

hemoptysis. He developed breathlessness and tachypnea (RR 34/min); oxygen saturation (SpO_2) was 90% at room air. Chest auscultation revealed bilateral fine crepitations. Haematocrit dropped to 32.1 and platelets were 16 000/dL. High-resolution computed tomography thorax revealed bilateral peribronchovascular consolidations and ground glass opacities, predominantly in the left lung with mild bilateral pleural effusions (right>left) (Figure 1). The patient underwent bronchofibroscopy, which showed the presence of blood-tinged secretions coming from bilateral lungs. Arterial blood gas was suggestive of type-1 respiratory failure with severe ARDS. The above clinical, laboratory and radiological findings were suggestive of DAH.

On the third day of admission, patient was shifted to the intensive care unit and was transfused with two units of packed red blood cells, one unit of single donor platelets and four units of fresh frozen plasma. Intravenous tranexamic acid and vitamin K were added. Inotropes were started as blood pressure fell to 70/40 mmHg. He was intubated in view of respiratory distress and falling oxygen saturation levels. Intravenous antibiotics were started to prevent secondary infections. Haematocrit and platelet levels continued to drop over the next few days necessitating further transfusion of multiple units of packed red blood cells and single donor platelets along with intravenous calcium gluconate. Serum electrolyte levels were monitored daily and corrected as required. Patient required high positive end-expiratory pressure (PEEP) to maintain oxygenation levels. On the 7th day of admission, haematocrit levels stabilized and oxygenation levels improved (Table 1). Hemoglobin and platelet levels were maintained above 10 g/dL and 50 000/dL respectively and the patient was weaned off ventilatory support on the 11th day. The patient continued to require oxygen supplementation and he was discharged once it was arranged at home. Incentive spirometry and regular follow-up for pulmonary function tests were advised. Three months after discharge, the patient did not require oxygen supplementation and is able to carry out daily routine activities.

4. Discussion

The clinical presentation of dengue is varied ranging from non-specific febrile illness to dengue haemorrhagic fever and dengue shock syndrome[10]. A provisional diagnosis of DHF can be made based on the presence of a high fever with an acute onset, a positive tourniquet test, and hemoconcentration (a haematocrit increase of 20% or more) or thrombocytopenia[3].

Our patient fulfilled the WHO criteria for DHF since he presented with fever, haemorrhagic tendencies (petechiae and hemoptysis), thrombocytopenia and pleural effusion. Pleural effusion and pneumonitis are uncommon pulmonary manifestations in DHF, and pulmonary haemorrhage is even rarer. Hemoptysis has been reported in 1.4% of dengue infections. In DHF patients, the pathogenesis of bleeding is not well understood. The abnormalities in the coagulation cascade, thrombocytopenia, platelet dysfunction, disseminated intravascular coagulation, and vascular defects are thought to be part of a multifactorial process. Vascular permeability has been thought to be mediated by histamine release[3]. High-resolution computed tomography findings of our patient were suggestive of DAH, which may impede oxygen transfer, and resulting in hypoxemia. In this setting, the diffusion capacity of the lung for carbon monoxide may be increased, and serial increases in the diffusion capacity of the lung for carbon monoxide may indicate progressive alveolar hemorrhage. Interstitial fibrosis and restrictive changes may develop after recurrent episodes of DAH. Less commonly, patients may exhibit spirometric changes indicating airflow obstruction[5].

The treatment is directed at establishing the diagnosis, providing respiratory support, and preventing progression of microcirculation damage, typically with corticosteroids and immunosuppressive agents[6]. However, such treatment is potentially harmful when DAH is due to nonimmune causes such as infections[7]. In DHF, the treatment remains mainly supportive.

Acute hypoxemic respiratory failure is the most immediate life-threatening complication of DAH. When severe DAH results in ARDS, it is crucial to maintain an acceptable level of oxygenation using high levels of FiO_2 and PEEP. Although no consensus exists regarding the optimal PEEP levels for DAH, they should be adjusted according to the severity of respiratory failure and lung recruitability. To control active bleeding and prevent lung collapse in patients with DAH, a high PEEP and permissive hypercapnia have been used[8].

To achieve rapid haemostasis, coagulopathy should be closely monitored and corrected as soon as possible. Platelet counts greater than 50 000/L and a prothrombin time-international normalised ratio less than 1.5 are commonly accepted targets. Platelet transfusions, vitamin K supplementation, cryoprecipitates, and fresh frozen plasma should all be supplemented, depending on the cause. To arrest the bleeding, various prothrombotic treatments have been used with varying degrees of success, including anti-fibrinolytics, particularly the lysine analogues tranexamic acid and epsilon aminocaproic acid, thrombin, and factor Ⅶa[9].

5. Conclusions

DAH is a very rare presentation of DHF and the mainstay of treatment remains meticulous management of fluid and electrolyte balance with supportive care. The successful management of these

patients requires a high index of suspicion, prompt evaluation, and appropriate therapy. DAH, although very rare, should always be considered in a patient with dengue who presents with hemoptysis.

Conflict of interest statement

The authors declare that there is no conflict of interest.

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Authors' contributions

PD and PG performed the clinical diagnosis and treatments of the patient. NSS and CNH supervised the laboratory analysis and interpretation. NSS obtained the informed consent. PG, NSS and CNH monitored the patient, collected data and drafted the manuscript. PD revised and prepared the final version of the manuscript. All authors have read and approved the final manuscript.

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