# Fatal subarachnoid haemorrhage in a patient with severe dengue

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## SUMMARY

**Dengue fever is one of the commonest tropical disease in the tropics. It can present with mild acute febrile illness to severe organ failure. Reported neurological complications of dengue include dengue encephalopathy, encephalitis, transverse myelitis and intracranial haemorrhage. Intracranial haemorrhage in dengue can present as subdural haematoma, extradural haematoma, intracerebral haemorrhage and subarachnoid haemorrhage. We report here a case of subarachnoid haemorrhage in a patient with severe dengue. Our patient was a 30-year-old man who presented with acute febrile illness. He subsequently developed plasma leakage and upper gastrointestinal bleeding. He then had reduced conscious level. Computed tomography of his brain showed subarachnoid haemorrhage. He eventually succumbed to his illness.**

## INTRODUCTION

Dengue fever is an important public health problem in the tropics. The incidence has increased dramatically over the past three decades.[1] The World Health Organization estimated that 390 million dengue infections occur annually with 96 million cases manifested clinically. Neurological complications occur in 1% to 5% of the dengue patients. Reported neurological manifestations of dengue include dengue encephalopathy, encephalitis, stroke, Guillain-Barre Syndrome, encephalomyelitis and intracranial hemorrhage. We report here a case of subarachnoid haemorrhage in a patient with severe dengue.

## CASE PRESENTATION

A previously healthy 30-year-old man presented with fever for 4 days associated with arthralgia, myalgia and vomiting. He denied diarrhoea, abdominal pain or bleeding tendencies. On arrival at the Hospital Lahad Datu, Sabah, Malaysia, he was alert and conscious. His blood pressure was 129/88mmHg, pulse rate was 78bpm, temperature was 36.7C. Respiratory examination showed reduced breath sounds over right hemithorax. Cardiovascular and abdominal examination were unremarkable.

His admission full blood count showed haemoglobin of 17.8g/dl, total white cell count of $5.4x10^9$/L and platelet of $19x10^9$/L. Renal profile showed acute kidney injury with urea 6.2mmol/L, creatinine 259µmol/L. His liver enzymes were deranged with alanine aminotransferase (ALT) of 4159U/L and aspartate aminotransferase (AST) of 22590U/L (Table I). His dengue NS-1 (SD Bioline NS-1) was negative and serology was positive for dengue IgM and IgG (SD Bioline Dengue Duo). Chest radiograph showed right pleural effusion. He was treated as severe dengue with plasma leakage, acute kidney injury and liver injury and admitted to intensive care unit.

10 hours into admission, he developed haematemesis. Full blood count showed haemoglobin of 12.9g/dl and platelet of $9.4x10^9$/L. He was started on infusion of intravenous pantoprazole. Emergency oesophagogastroduodenoscopy showed Forrest IIb prepyloric ulcer. He received blood product with 6units packed cell, 12units fresh frozen plasma and 10units platelet were given. He was intubated soon after for worsening respiratory distress. Over the next 2 days, his condition stabilised and entered into the recovery phase uneventfully.

On day 4 of admission, he was noted to have unequal pupils. An urgent computed tomography (CT) of the brain showed subarachnoid haemorrhage with generalized cerebral oedema (Figure 1). However, no CT angiogram (CTA) of the brain was done due to renal impairment and haemodynamic instability. Electroencephalography performed showed severe background suppression with no discernable cerebral activities. He eventually succumbed to his illness on day 6 of admission from subarachnoid haemorrhage.

## DISCUSSION

Dengue fever is endemic in South East Asian region and continue to be a public health challenge. The clinical presentation of dengue fever can vary from mild acute febrile illness to severe organ failures and death. Neurological manifestation of dengue is rare with intracranial haemorrhage (ICH) reported as an uncommon complication. DENV-2 and DENV-3 are more commonly associated with neurological complications of dengue fever.

The pathogenesis of ICH in dengue is multifactorial.[1] The postulated pathogenesis involves a complex interaction

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**Table I : Relevant Result of the Patient**

| Parameters | Results 14/12 | 15/12 | 16/12 | 17/12 | 18/12 | 19/12 | Unit | Normal Range |
|---|---|---|---|---|---|---|---|---|
| Hemoglobin | 17.8 | 9 | 8.8 | 11.5 | 10.4 | 10.4 | g/dL | 13 – 18 |
| Total White Blood Cell | 5.18 | 5.4 | 8 | 7.7 | 7.2 | 22 | 109/L | 4 – 10 |
| Platelet | 14.7 | 11.6 | 29.8 | 52 | 43 | 98 | 109/L | 150 – 400 |
| Hematocrit | 51 | 26.1 | 25.8 | 35.7 | 30.8 | 30 | | 40 - 54 |
| Sodium | 120.7 | 128.6 | 135 | 139 | 142 | 139 | mmol/L | 135 – 145 |
| Potassium | 6.2 | 5.9 | 4.8 | 4.3 | 4 | 5 | mmol/L | 3.5 – 5 |
| Urea | 20.4 | 23.1 | 27.4 | 24 | 32.3 | 17 | mmol/L | 2.8 – 7.8 |
| Creatinine | 259 | 342 | 432.2 | 425 | 505.5 | 331 | µmol/L | 90 – 110 |
| Total bilirubin | 49 | 45 | 60.9 | 89.9 | | 135 | µmol/L | 0 – 17.1 |
| ALT | 4159 | 1716 | 1227 | 867 | | 875 | U/L | <40 |
| AST | 22590 | 7831 | - | 4448 | | - | U/L | 1 – 38 |
| Alb | 34 | 30 | 32 | 34 | | 36 | g/L | 34 – 48 |
| Glo | 23 | 20 | 21 | 32 | | 32 | g/L | 20 – 35 |
| ALP | 169 | 115 | 94 | 134 | | 176 | U/L | 40 - 129 |
| PT | 13.5 | 16.2 | 15.1 | 15.3 | 16.6 | 25 | seconds | 10.7 – 13.8 |
| APTT | 55.4 | 59.4 | 33.5 | 47.7 | 31.9 | >180 | seconds | 24.6 – 37.5 |
| INR | 1.14 | 1.40 | 1.49 | 1.48 | 1.63 | 2.43 | | 1 – 1.5 |
| pH | 7.36 | 7.31 | | 7.53 | | 7.1 | | 7.35 – 7.45 |
| PCO2 | 37.2 | 42.7 | | 27 | | 45 | mmHg | 33 – 48 |
| PO2 | 43.7 | 40.6 | | 88 | | 129 | mmHg | 80 – 100 |
| HCO3 | 20.6 | 21 | | 26 | | 12.8 | mmol/L | 22 – 28 |
| Lactate | | | 3.4 | 10.9 | | | mmol/L | 0 – 2 |
| Blood culture | No growth | | | | | | | |
| Serum dengue PCR | DEN-3 | | | | | | | |

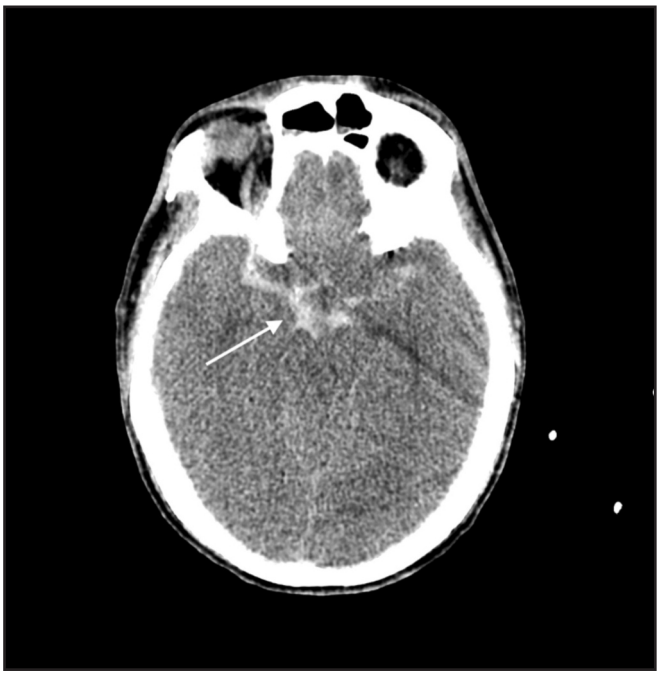

**Fig. 1:** Computed tomography of brain of the patient showing hyperdensity along the circle of Willis (arrowed) suggestive of subarachnoid hemorrhage. Basal cistern is effaced with associated cerebral edema.

between coagulopathy, thrombocytopenia, plasma leakage, vasculopathy and platelet dysfunction.[2] Besides that, host, virus factors and cytokines are also thought to play a role.[3] The presence of dengue virus in the brain together with the cytokines such as TNF alpha further enhance the immunopathological mechanism of plasma leakage and haemorrhage in dengue. Apart from that, NS-1 antigen released from dengue infected cells can have immunomodulatory effects on complement system. Activation of complement system can enhance cytokines production, which ultimately leads to bleeding and shock in dengue.[3]

Our patient was diagnosed to have severe dengue with plasma leakage and GI bleeding. He subsequently developed subarachnoid hemorrhage (SAH) in his recovery phase. We believe that his SAH could have developed earlier but was unable to detect early changes of increased intracranial pressure as he was intubated. Early symptoms and signs of SAH can be very subtle. The pathophysiology of SAH in this patient is likely to be multifactorial. Thrombocytopenia, plasma leakage, vasculopathy and disseminated intravascular coagulation could probably all have contributed to his SAH.

The diagnosis of ICH is often difficult as the symptoms of ICH can mimic the symptoms of dengue. CT brain should be done in any patient with suspicion of ICH especially in high risk groups. Previous study suggests that patients with secondary dengue with positive NS-1 antigen and IgG are at higher risk of ICH.[1] In patients presenting with severe headache and vomiting in the presence of thrombocytopenia, we should have lower threshold for brain imaging to exclude ICH. Presence of seizures, focal neurological deficits and reduced conscious level also warrant evaluation with brain imaging.

Management of ICH in dengue fever is often difficult. Surgical options have to be carefully considered as often patient have thrombocytopenia, platelet dysfunction and plasma leakage which can lead to uncontrollable bleeding and potentially harm the patient. It remains unclear if

medical or surgical management of dengue ICH is optimal, as the data to make definite recommendations remains limited currently.[4] There is also no evidence that prophylactic platelet transfusion improves outcome and there is no correlation between platelet count and bleeding in dengue patients.[5]

## CONCLUSION

In conclusion, ICH is a potentially fatal complication of dengue fever. It can present as subdural haematoma, intracerebral haemorrhage and subarachnoid haemorrhage. Clinicians should have low threshold to perform brain imaging to exclude ICH in high risk patients with consistent clinical symptoms and signs. At present, there is insufficient evidence to address optimal care and it remains a consideration on case-by-case basis.

## CONFLICT OF INTERESTS

The author declare that they have no conflict of interest.

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