# Case Report: A Rare Case of Dengue-Triggered Very Severe Aplastic Anemia in a Pediatric Patient in Cambodia

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## ABSTRACT

### Introduction

Dengue fever is a common viral infection in tropical regions, including Cambodia. While rare, it can lead to severe aplastic anemia (AA) −, a life-threatening condition marked by bone marrow failure and pancytopenia, posing significant diagnostic and therapeutic challenges. Early recognition and treatment are crucial for improving outcomes. This case report presents a unique instance of dengue-induced very severe AA that was successfully managed with immunosuppressive therapy.

### Case Presentation

An 11-year-old Cambodian boy presented with fever, headache, myalgia, vomiting, and mild abdominal pain. Laboratory tests revealed pancytopenia, with a WBC count of $0.9 \times 10^9$/L, an absolute neutrophil count (ANC) of $0.5 \times 10^9$/L, Hb concentration of 7.3 g/dL, and platelet count of $70 \times 10^9$/L. Dengue serology was positive for both IgG and IgM, confirming the presence of dengue fever. After 16 days, the patient was afebrile for more than 9 days, but persistent pancytopenia led to a referral for hematology. Repeated laboratory investigations confirmed severe pancytopenia, with a white blood cell count (WBC) of $0.9 \times 10^9$/L, ANC of $0.08 \times 10^9$/L, a hemoglobin (Hb) concentration of 7.7 g/dL, a platelet count of $40 \times 10^9$/L, and an absolute reticulocyte count of $2.94 \times 10^9$/L, with a bone marrow exam revealing very severe aplastic anemia (AA) secondary to dengue. Biimmunosuppressive therapy with cyclosporin A (8 mg/kg/day) and prednisolone (2 mg/kg/day) was started. The patient improved significantly, with normalization of blood counts and resolution of hemorrhagic symptoms, and was discharged. Cyclosporine treatment was continued for 3 months, resulting in complete remission.

### Conclusion

Aplastic anemia secondary to dengue fever is an uncommon but serious complication. Early recognition, particularly in endemic areas, and timely initiation of immunosuppressive therapy are crucial for favorable outcomes. In resource-limited settings where ATG is not accessible, such as in Cambodia, a combination of cyclosporin A and corticosteroids can be an effective alternative, as demonstrated in this case.

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**Keywords:** Dengue fever, Aplastic anemia, Bone marrow failure, Pancytopenia, Immunosuppressive therapy

## Introduction

Dengue fever, a mosquito-borne viral illness common in tropical countries such as Cambodia, usually presents with mild symptoms but can sometimes result in serious complications. One uncommon yet potentially fatal consequence is aplastic anemia (AA), a condition characterized by bone marrow failure. Although various viral infections are known to precipitate AA, the mechanisms by which dengue virus induces this condition remain unclear. Current evidence suggests that immune-mediated processes and direct suppression of bone marrow activity may be involved [1,2]. Early recognition is crucial, as delayed diagnosis can lead to severe complications, including bleeding and infections. This report presents a pediatric case of dengue-induced severe AA successfully managed with immunosuppressive therapy, offering insights into a rare hematologic consequence of dengue fever [3].

## Case Presentation

An 11-year-old Cambodian boy, weighing 25 kg, with no significant past medical or family history, presented to the infectious disease department with a 4-day history of fever, headache, myalgia, repeated vomiting, and mild abdominal pain without diarrhea. Upon admission, laboratory investigations revealed pancytopenia, with a white blood cell count (WBC) of $0.9 \times 10^9$/L, an absolute neutrophil count (ANC) of $0.5 \times 10^9$/L, a hemoglobin level (Hb) of 7.3 g/dL, and a platelet count of $70 \times 10^9$/L. Dengue serology returned positive for both IgG and IgM antibodies, confirming the diagnosis of dengue fever on the fourth day of illness.

Initial management was initiated with supportive care, in alignment with the national dengue treatment guidelines. By day 16 of illness, the patient had been afebrile for more than 9 days, suggesting clinical recovery from dengue fever. However, persistent pancytopenia prompted a referral to the pediatric hematology department for further diagnostic evaluation. Upon arrival, physical examination revealed pallor and petechiae on the extremities. Abdominal examination revealed mild tenderness and hepatomegaly, whereas heart and lung findings were unremarkable. Repeated laboratory investigations confirmed severe pancytopenia, with a white blood cell count (WBC) of $0.9 \times 10^9$/L, an absolute neutrophil count (ANC) of $0.08 \times 10^9$/L, a hemoglobin (Hb) concentration of 7.7 g/dL, a platelet count of $40 \times 10^9$/L, and an absolute reticulocyte count of $2.94 \times 10^9$/L. The results of the other blood tests are summarized in **Table 1**. Bone marrow examination revealed findings consistent with very severe aplastic anemia (AA) secondary to dengue fever, with no evidence of myelodysplasia or malignancy **(Figure 1)**.

**Table 1.** Summarized laboratory investigations

| *Day of illness* | D4 | D16 | D33 | D64 | D108 | D136 | **Reference Range** |
|---|---|---|---|---|---|---|---|
| *Complete Blood Count* | | | | | | | |
| WBC | 0.9 | 0.9 | 1.0 | 1.4 | 4.5 | 1.2 | 5-15 x $10^9$/L |
| ANC | 0.5 | 0.08 | 0.82 | 0.32 | 3.96 | 0.26 | 1.5-8 x$10^9$/L |
| Lymphocyte | 0.4 | 0.8 | 0.15 | 1 | 0.54 | 0.9 | 6-9 x $10^9$/L |
| RBC | 2.4 | 2.5 | 3.8 | 4.6 | 4.3 | 3.2 | 4-5.2 x$10^{12}$/L |
| Hemoglobin | 7.3 | 7.7 | 11.5 | 13.8 | 12.9 | 9.8 | 11-14 g/dL |
| Hematocrit | 22 | 23 | 35 | 41 | 39 | 30 | 34-40% |
| Platelet | 70 | 40 | 193 | 196 | 103 | 116 | 200-490 x $10^9$/L |
| Reticulocyte | 2.94 | | | | | | 0.2-2% |
| MCV | 79 | 78 | 79 | 79 | 80 | 79 | 75-87 fL |
| MCHC | 27 | 26 | 26 | 28 | 29 | 26 | 31-37 mg/dL |
| RDW-VC | 13 | 14 | 12 | 14 | 14 | 13 | 12-15% |
| *Peripheral Smear* | | | | | | | |
| WBC | Normal | | | | | | |

| Day of illness | D4 | D16 | D33 | D64 | D108 | D136 | Reference Range |
|---|---|---|---|---|---|---|---|
| RBC | Normal | | | | | | |
| Platelet | Normal | | | | | | |
| **Liver enzymes** | | | | | | | |
| AST | 32 | | | | | | <31 U/L |
| ALT | 27 | | | | | | <32 U/L |
| **Renal functions** | | | | | | | |
| Urea | 39 | | | | | 40 | 10-50 mg/dL |
| Creatinine | 0.7 | | | | | 0.5 | 0.5-0.9 mg/dL |
| **Serology** | | | | | | | |
| Dengue IgG | + | | | | | | |
| Dengue IgM | + | | | | | | |

*WBC: white blood cells, ANC: absolute neutrophil count, RBC: red blood cell, MCV: mean corpuscular volume, MCHC: mean corpuscular hemoglobin concentration, RDW-VC: red cell distribution width - coefficient of variation, ALT: alanine aminotransferase, AST: aspartate aminotransferase.*
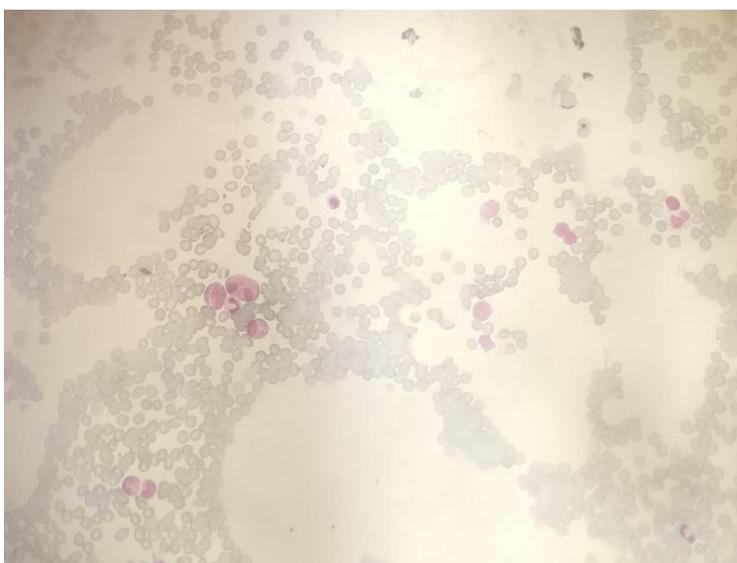


**Figure 1.** Bone marrow examination

## Management and outcomes

The management approach was carefully discussed, weighing the option of observation until spontaneous recovery versus initiating treatment. Given the severity of the pancytopenia with hemorrhagic manifestations, the decision was made to start treatment. In light of the unavailability of anti-thymocyte globulin (ATG), the patient commenced on bi-immunosuppressive therapy with cyclosporin A (8 mg/kg/day) and prednisolone (2 mg/kg/day). The patient demonstrated significant improvement, with resolution of petechiae and ecchymosis, along with marked increases in white blood cell (WBC) count, absolute neutrophil count (ANC), and platelet count. The patient was subsequently discharged. Prednisolone was tapered over 2 weeks, while cyclosporin A was continued for 3 months, at which point it was discontinued following the achievement of complete remission.

## Discussion

This case highlights a rare but serious complication of secondary dengue infection, culminating in very severe AA. The persistence of thrombocytopenia, anemia, and neutropenia beyond two weeks post-infection prompted a bone marrow examination, which confirmed the diagnosis. Viral infections, including dengue, have been implicated in the pathogenesis of bone marrow failure, primarily through the inhibition of hematopoietic cell proliferation [4]. However, the underlying mechanisms remain incompletely understood and are thought to involve both immune-mediated peripheral destruction and direct viral cytotoxicity to hematopoietic progenitor cells [4].

The progression from dengue fever to severe AA has been documented in multiple case reports. Immunosuppressive therapy—comprising anti-thymocyte globulin, methylprednisolone, and cyclosporine—is currently a viable alternative to bone marrow transplantation (BMT) and has been shown to promote hematologic recovery in affected individuals [5]. Ramzan et al. [4] reported the case of an 8-year-old girl who initially presented with persistent thrombocytopenia following dengue fever. She later developed pancytopenia, and a bone marrow biopsy confirmed the diagnosis of severe AA. The patient was successfully treated with ATG, methylprednisolone, and cyclosporine and achieved transfusion independence within six months. Similarly, Saha RP et al. [6] reported a 13-year-old boy who developed severe AA one month after dengue infection. Despite initial supportive care, he became transfusion dependent. Immunosuppressive therapy with ATG, methylprednisolone, and cyclosporine led to hematologic recovery and transfusion independence within six months.

In settings where standard treatment with ATG is unavailable, some cases have been successfully managed using bi-immunosuppressive therapy with cyclosporine and corticosteroids, leading to favorable remission. Kaur et al. [5] described a 9-year-old child who presented with fever, abdominal pain, and bleeding and was diagnosed with pancytopenia in the context of confirmed dengue infection (positive IgM, IgG, and NS1). Bone marrow examination revealed hypoplasia, and treatment with cyclosporine and corticosteroids led to hematologic improvement, mirroring the response observed in our case. Similarly, Albuquerque et al. [7] reported a 15-year-old girl who presented with anemia, gum bleeding, petechiae, and fever. Laboratory evaluation revealed severe cytopenia, and dengue IgM serology was positive. Bone marrow findings confirmed severe aplastic anemia. The patient was initially managed with intravenous immunoglobulin and methylprednisolone, followed by long-term cyclosporine therapy, resulting in a favorable clinical outcome.

## Conclusion

Aplastic anemia secondary to dengue fever is an uncommon but serious complication. Early recognition, particularly in endemic areas, and timely initiation of immunosuppressive therapy are crucial for favorable outcomes. In resource-limited settings where ATG is not accessible, such as in Cambodia, a combination of cyclosporin A and corticosteroids can be an effective alternative, as demonstrated in this case.

## Data Availability Statement

Patient health information supporting this case report is available upon request from the corresponding author, and all other relevant data are included within the manuscript.

## Consent

Informed consent was obtained from the child's parents for the publication of this manuscript.

## Funding

## Conflicts of Interest

The authors declare that they have no conflicts of interest.

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