

## Case Report

**Secondary infection in immuno-competent children with dengue:  
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**Abstract**

The occurrence of bacterial superinfection, or coinfection, in patients with dengue, has been previously reported, but the available information comes from anecdotic reports. We report clinical and pathological data of immuno-competent children diagnosed with dengue and had evidence of concurrent bacterial infections.

**Key words:** *Children, Dengue, Immuno-competent, Secondary bacterial infection*

The clinical spectrum of dengue is highly variable, ranging from a mild flu-like syndrome to severe disease, with shock and hemorrhage [1]. Dengue virus infects human endothelial cells in vitro and causes cellular activation [2]. The enhanced capillary permeability appears to be due to endothelial cell dysfunction rather than injury as electron microscopy demonstrated a widening of the endothelial tight junctions [3]. Leukopenia, thrombocytopenia, and a hemorrhagic diathesis are the typical hematologic findings in dengue virus infections. Leukopenia is apparent early in the illness and is of similar degree in both severe dengue and dengue fever with warning signs [4]. It is thought to represent a direct effect of dengue virus on the bone marrow [5]. Known leukopenia, lymphocytolysis, and immunological alterations may predispose to superadded infections in dengue, theoretically. However, bacteremia in the course of dengue infection is rarely described in the medical literature [6-12]. We report two children diagnosed with dengue who developed serious bacterial infections and one child with severe leucopenia without any bacterial infection.

**CASE REPORTS****Case 1**

A 4-year-old male child, presented with fever and fast breathing for 6 days. There was no history of headache, retro-orbital pain, vomiting, bleeding manifestation, or altered sensorium. Birth and developmental history was normal, and child was immunized for his age without any significant family history.

On examination, child had a fever (104.6°F) and tachypnea (respiratory rate 68/min) with chest retractions and nasal flaring. Blood pressure was 98/60 mmHg (75<sup>th</sup> centile). Child was underweight (11.5 kg, weight/age 72.7%) with no wasting or stunting. There were multiple petechiae (abdomen, lower limbs). On systemic examination, there was decreased movement on the right side of the chest in comparison to the left side. On auscultation, there was decreased air entry with crepitations on right infrascapular area. Within 12 h of admission, child developed jaundice and abdominal distension, suggesting ascites. Chest X-ray was suggestive of

right-sided pleural effusion. Pleural tap revealed purulent fluid full of neutrophils, protein as 3.9 g%, and sugar as 28mg% suggestive of exudative pleural effusion. Intercostal tube was put, and purulent fluid was drained out and broad spectrum antibiotics (ceftriaxone and vancomycin) were started. Initial investigations showed hemoglobin 10.8 g%, hematocrit 33.3% with leukopenia (4700/mm<sup>3</sup>) and thrombocytopenia (36,000/mm<sup>3</sup>). Liver functions tests were deranged (Table 1).

Pleural fluid culture and simultaneously drawn blood culture revealed pseudomonas species. In view of petechiae, thrombocytopenia, and dengue epidemic settings dengue serology was sent which revealed positive IgM (MAC ELISA) for dengue. Child was managed as per standard treatment protocols. Child improved; intercostal tube was removed after 5 days. Ascites and jaundice slowly resolved, and child became afebrile in next 7 days and discharged after 18 days of admission with 14 days of antibiotics.

**Case 2**

An 11-year-male child, presented with fever, rash and congested eyes for 3 days, multiple episodes of vomiting, pain abdomen and nasal bleeding for 1 day. There was no history of headache, retro-orbital pain, altered sensorium, black stool and red urine, abdominal distension, swelling over the body or decreased urine output. Birth and developmental history was normal, and child was immunized up to 5 years of age. Family history was not significant. On examination, child was febrile (102°F) with erythematous rash all over body. Blood pressure was 100/62 (75<sup>th</sup> centile). Child weighed 30 kg (weight/age 83%). On systemic examination, cardiorespiratory, abdominal, and central nervous system were found within normal limits. Investigations revealed hemoglobin 11.7 g% and pancytopenia (Table 1). A presumptive diagnosis of dengue with warning signs was kept, and child was started on standard treatment protocols. Chest X-ray was normal, and ultrasound abdomen showed gall bladder edema. Dengue serology was positive

**Table 1: Laboratory parameters of three cases**

Investigations	Case 1		Case 2		Case 3	
	Admission	Discharge	Admission	Discharge	Admission	Discharge
Hemoglobin (g%)	10.8	9.4	12.7	10.5	13.7	9.2
Hematocrit (%)	33.3	27.7	35.6	29.2	39.5	26.3
Total leucocyte counts (mm <sup>3</sup> )	4700	7800	600	1600	3900	7100
Absolute neutrophil counts	3384	3432	150	400	936	2840
Platelet counts (mm <sup>3</sup> )	36,000	56,000	20,000	66,000	28,000	64,000
Liver function test	Serum bilirubin total 5.2 mg% direct 3.8 mg%, SGPT>500	Normal	Normal		Normal	
Malarial parasite	Negative		Negative		Negative	
Widal test	Not done		Not done		<64	
Blood culture	<i>P. aeruginosa</i>		Sterile		<i>K. pneumonia</i>	
Chest X-ray	Right pleural effusion	Normal	Normal	Normal	Right pleural effusion	Normal
Ultrasound abdomen	Ascites	Normal	Gall bladder edema with ascites	Normal	Gall bladder edema	Normal
Dengue serology (IgM)	Positive		Positive		Positive	

SGPT: Serum glutamate-pyruvate transaminase, *P. aeruginosa*: *Pseudomonas aeruginosa*, *K. pneumonia*: *Klebsiella pneumonia*

for dengue virus IgM by MAC ELISA kit. Patient improved clinically (afebrile on day 4), leukocyte and platelet counts gradually increased and discharged in 5 days. There was no feature of secondary bacterial infection despite very severe leucopenia ( $600/\text{mm}^3$ ) and blood culture was sterile after 48 h of incubation which was sent on day 2 of admission in view of severe leukopenia.

### Case 3

A 7-year-old male child presented with fever (8 days), pain abdomen, and vomiting (2 days) with black color stools since 1 day. There was no history of headache, retro-orbital pain, altered sensorium, red urine, nasal bleed, or decreased urine output. Next day, patient developed abdominal distension and difficulty in breathing. On examination, child was febrile ( $101^\circ\text{F}$ ) with rash and petechiae (face and limbs), swelling over face, and cervical lymphadenopathy. Child weighed 18 kg, (weight/age 81.8%). Child had pulse rate of 97/min, respiratory rate 68/min, blood pressure 86/55 mm of Hg ( $<50^{\text{th}}$  centile). Systemic examination revealed right-sided pleural effusion with ascites.

Investigations revealed hemoglobin 13.7g%, hematocrit 39.5%, leukopenia, and thrombocytopenia (Table 1). A presumptive diagnosis of dengue was kept, and child was started on standard treatment protocols. Chest X-ray showed right-sided massive pleural effusion and ultrasound abdomen showed gall bladder edema with moderate ascites. Dengue serology was positive done by IgM Antibody (capture Elisa by Arbovirus diagnostics, NIV, Pune, India). Blood culture sent on the second day of admission showed growth of *Klebsiella pneumonia* species with sensitivity to chloramphenicol, ofloxacin, piperacillin-tazobactam and resistance to cefotaxim. Child was treated with intravenous antibiotics. Child improved in next 6 days with a gradual increase in leukocyte and platelet counts in 6 days.

### DISCUSSION

Dengue can be diagnosed by isolation of the virus, by serological tests, or by molecular methods. MAC-ELISA has become an important tool for routine dengue diagnosis, and it has a sensitivity and specificity of approximately 90% and 98%, respectively [13]. Incidence of bacteremia in

dengue infections lacks in children. Lee et al. [8] observed that 5.5% of the adult patients with dengue infection also showed bacteremia (*K. pneumonia*, *Enterococcus faecalis*). Previous reports of bacterial (*Escherichia coli*, *Salmonella* sp., *Streptococcus pneumoniae*, *Mycobacterium tuberculosis*, *Mycoplasma pneumoniae*, *Shigella sonnei*, *K. pneumonia*, *Klebsiella ozaenae*, *E. faecalis*, *Moraxella lacunata*, *Staphylococcus aureus*, *Roseomonas* sp., *Haemophilus influenza* etc.) and viral (herpes viruses) co-infections with dengue virus infection in adults are present in literature [6-12,14-17]. Such at Hongsiriwon showed occurrence of 21% co-infection in infants with dengue (4/19) [12]. However, pseudomonas co-infection has not been reported previously in children.

Leukopenia occurs early in the course of illness and is probably due to the direct effect of dengue virus on the bone marrow [5]. Theoretically immunological alterations (leucopenia, proliferation of lymphocytoid and plasmacytoid cells, lymphocytolysis, lymphophagocytosis, depletion of lymphocyte and breakdown of digestive epithelial barrier (endothelial damage or intestinal hemorrhage) which help these pathogens to enter the circulation, are possible explanations for superinfections. There seems to be a predominance of intestinal flora micro-organisms in such cases [8,17]. The bacterial infection superimposed on the dengue virus infection either occurs as a mere temporal coincidence or, more likely, occur due to immunosuppression caused by the virus [1].

In our first case, child presented with empyema and just in setting of outbreak and thrombocytopenia, we suspected dengue in which serology came positive. On the contrary, our third case presented with severe dengue not responding to usual treatment and blood culture was positive for *Klebsiella*. In the second case, we simply had severe leukopenia without findings of severe dengue or infections. Exact mechanism for secondary bacterial infection in dengue fever cannot be ascertained as all our three patients had leukopenia but with varying degree of clinical manifestation. This possibly supports the secondary mechanism of gastrointestinal epithelial breakdown.

### CONCLUSION

Clinicians should be vigilant to unusual manifestations of dengue fever, which points toward a concomitant

infection by other microorganisms, mainly bacteria. Our case series may contribute to increased awareness of these associated life-threatening infections. Here, bacterial infection was confirmed by blood culture and would never have been disclosed if the procedure had not been performed.

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