Presence of multiple dengue serotypes in various body compartments in different time points of single clinical episodes

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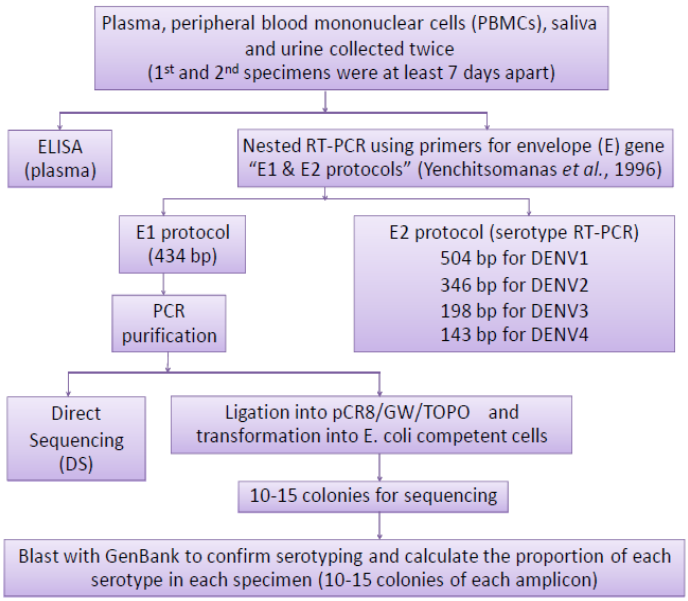
Introduction and Purpose

The wide-spread of dengue virus in hyperendemic areas can cause multi-serotype infections transmitted by mosquitoes. There have been many reports about this phenomenon in many countries, including Thailand. However, the results focused only in a single time point and specimen. Previously, our group research demonstrated clearly multi-serotype infections in various body compartments (plasma/serum, PBMCs, saliva, buccal brushes and urine) during febrile period by RT-PCR using specific primers for each serotype and showed the persistence of DENV2 in urine and PBMCs, which serotype in each specimen was not changed. Here we presented not only persistent infection but also showed multi-serotype infections in different specimens and time points in 3 interesting cases . Moreover, the benefit of using cloning and sequencing techniques could find the "hidden serotype", which promoted multi-serotype infections.

Methods



Results

All three patients were secondary infection (IgM:IgG <1.8) and were diagnosed as DHF grade II (Dengue guidelines, 2009). Multi-serotype infections occurred in all 3 patients.

Code	Clinical diagnosis	Days of fever	Febrile period				Convalescent period			
			Plasma	PBMCs	Saliva	Urine	Plasma	PBMCs	Saliva	Urine
N33	DHF II	6	DEN4 (100%) [7]	DEN4 (100%) [7]	DEN4 (100%) [7]	DEN4 (72.73%) DEN2 (27.27%) [7]	- [18]	- [18]	- [18]	DEN4 (100%) [18]
N34	DHF II	6	- [8]	DEN1 (100%) [8]	DEN1 (100%) [8]	DEN1 (100%) [8]	- [14]	- [14]	- [14]	DEN1 (83.33%) DEN3 (16.67%) [14]
N40	DHF II	4	DEN1 (100%) [4]	DEN1 (100%) [4]	- [4]	DEN1 (100%) [4]	- [21]	DEN1 (8.33%) DEN2 (91.67%) [21]	- [21]	- [21]

- = negative result
( ) = % of each serotype of DENV (total clones of each serotype/total of all selected clones)
[ ] = the day of illness that each specimen was collected

Table : The results of 3 patients positive for multi-serotype infections. N40 clearly shows different serotypes in 2 periods whereas N33 and N34 show the "hidden" serotypes in febrile urine (N33) and convalescent urine (N34), respectively.

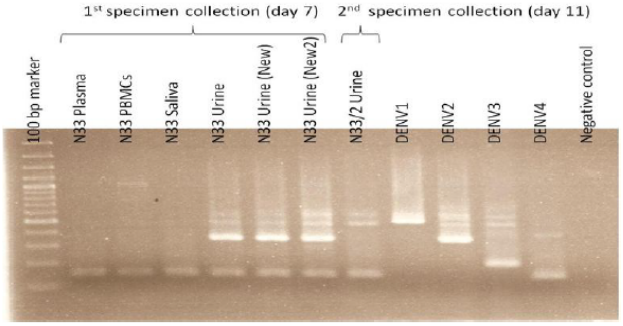


Figure : 2% gel electrophoresis of E2 RT-PCR products (serotype detection) of N33 specimens. The specimens were 11 days apart. The experiment was performed 3 times and the results were consistent .

Conclusion

Our finding suggests that multi-serotype infections occur both in the same and in the different periods of infection. Pathogenesis of this phenomenon is complicated. We hypothesize that this may be from concurrently multi-serotype-infected, or certain serotype(s) could earlier infect the host and hide/persist. Then it was later on reactivated to join the newly-infected serotype. Further investigation is needed to elucidate these findings.

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