HCV RNA rebounding change in patients encountering dengue fever

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Objective: It is evident that dengue virus (DENV), or hepatitis C virus (HCV), has viral interference with other viruses, e.g. DENV and Chikungunya virus, or HCV and hepatitis B virus (HBV). However, the interaction between DENV and HCV is still unexplored. Kaohsiung is an endemic area for both DENV and HCV. We aimed to investigate HCV RNA serial changes in patients with dengue fever (DF).

Methods: After reviewing a total of 1192 dengue-confirmed patients during 2014-15, we found out 515 cases with HBsAg and anti-HCV data. Those with positive anti-HCV were further checked for HCV RNA using the preserved blood samples collected during DF. Furthermore, HCV RNA-positive ones would be arranged at least one subsequent follow-up of HCV viral loads after DF episode. Another age-, sex-, HCV genotype-matched controls without DF were also enrolled for observing viral kinetic in natural course.

Results: HCV prevalence was 6.21% (32/515) in these DF patients. HBV/HCV coinfection rate was 21.9% (7/32) in HCV patients. Positive HCV RNA was noted in 14 cases (43.8%). HCV with viremia or not during DF did not determine dengue-related complications (dengue hemorrhagic fever or severe dengue). Of 14 HCV RNA-positive cases, 11 were rechecked for HCV viral loads after DF with a median interval of 23 months (range 12-35) and the serial changes of HCV viral loads among the 11 cases were shown in **Figure 1**. Analysis revealed the average post-DF HCV RNA level was significantly higher than that during DF [5.43 (±0.77) vs 3.09 (±1.24) log IU/ml, p= 0.003]. Compared with 11 HCV/DENV cases, 33 HCV controls demonstrated a mild decrease in HCV RNA level after a median follow-up period of 26.5 months (range 14-75). The △HCV RNA (later level - previous level) was -0.27 (±0.76) log in HCV controls, versus 2.34 (±1.15) log in HCV/DENV cases (p< 0.001, **Table 1**). Our Con1 cell line experiment supported that DENV could infect HCV Con1 cells successfully and HCV-NS5A expression reduced while DENV-NS1 protein increased (**Figure 2**).

Conclusions: Lower HCV viral loads during DF implied that DENV might have interference with HCV directly or indirectly. Clinicians should be aware of HCV viral rebounding change after DF.

Figure 1. HCV RNA serial changes in patients with dengue fever

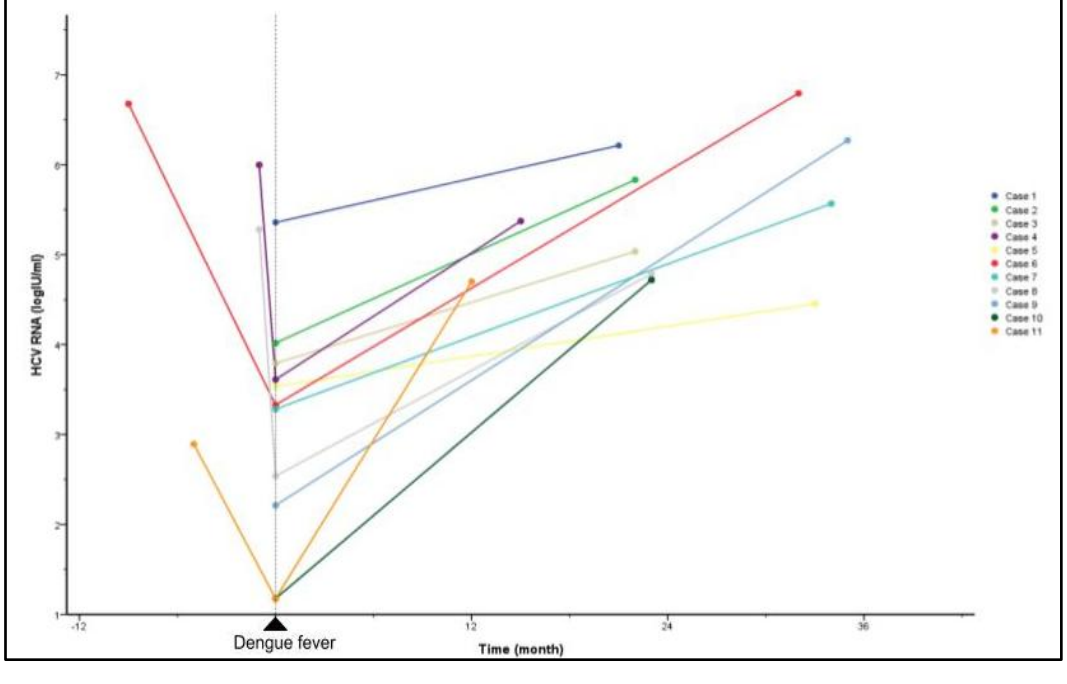

Table 1. The comparison of HCV RNA changes between 11 HCV/DENV cases and 33 HCV controls

	HCV/DENV (n=11)	HCV Control (n=33)	*p*
Age, years, mean(±SD)	59.7(±14.2)	60.2(±13.3)	0.916
Male, n(%)	6(54.5%)	18(54.5%)	1.000
HCV genotype-1/2, n/n	7/4	22/11	1.000
HCV RNA follow-up interval, months	23.0(21.1-33.0)	26.5(18.3-42.0)	0.283
The changes of viral loads			
△HCV RNA, log IU/ml, mean(±SD)	2.34(±1.15)	-0.27(±0.76)	<0.001
△HCV RNA, >0.5 log, n(%)	11(100.0%)	2(6.06%)	<0.001

△HCV RNA= (follow-up RNA level) - (initial RNA level); | △HCV RNA | = the absolute value of △HCV RNA; HCV RNA follow-up interval shown as median (IQR)

Figure 2. The reciprocal expression of DENV1-NS1 and HCV-NS5A in Con1 cell line experiment