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Hepatitis C Virus Genotype 2 May Not Be Detected by the Cobas AmpliPrep/Cobas TaqMan HCV Test, Version 1.0

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Accurate hepatitis C virus (HCV) RNA quantification is essential for the management and efficacy of treatment of chronic hepatitis C. The HCV RNA level is assessed using real-time PCR-based assays. Two highly sensitive commercial assays for HCV RNA quantification are available in many countries: the Roche Cobas AmpliPrep/Cobas TaqMan HCV assay (CAP/CTM HCV) (Roche Molecular Systems, Inc., Pleasanton, CA) and the Abbott RealTime HCV assay (ART HCV) (Abbott Molecular, Inc., Des Plaines, IL). Despite its good performance with most HCV strains, the CAP/CTM HCV test version 1.0 (v1.0) fails to detect genotype 4 strains with single nucleotide polymorphisms at positions 145 and 165 in the 5′ untranslated region (5′ UTR) (1). HCV genotype 4 is restricted to particular geographical areas, and many countries, including Japan, continue to use CAP/CTM HCV v1.0 to monitor HCV RNA quantification.

We report two Japanese patients with HCV genotype 2a in whom HCV RNA was undetectable by CAP/CTM HCV v1.0, although hepatitis C viremia was confirmed by the ART HCV test (4.0 and 5.0 $\log_{10}$ IU of HCV RNA/ml) and the Architect HCV core antigen assay (Abbott Diagnostics, Lake Forest, IL) (95 and 107 fmol/liter). This failure could be related to two or three substitutions in the putative binding site for the TaqMan probe (Fig. 1). The substitutions are at position 145, as described for HCV genotype 4 (1), and positions 158 and 169, which have not been reported previously.

Underestimation of HCV genotype 2 RNA by CAP/CTM HCV v1.0 has been reported previously (2), but failure to detect HCV genotype 2a RNA is critical as this genotype is the second most common HCV genotype. Recently, a second version of the assay, CAP/CTM HCV v2.0 (3), with redesigned primers and an addi-

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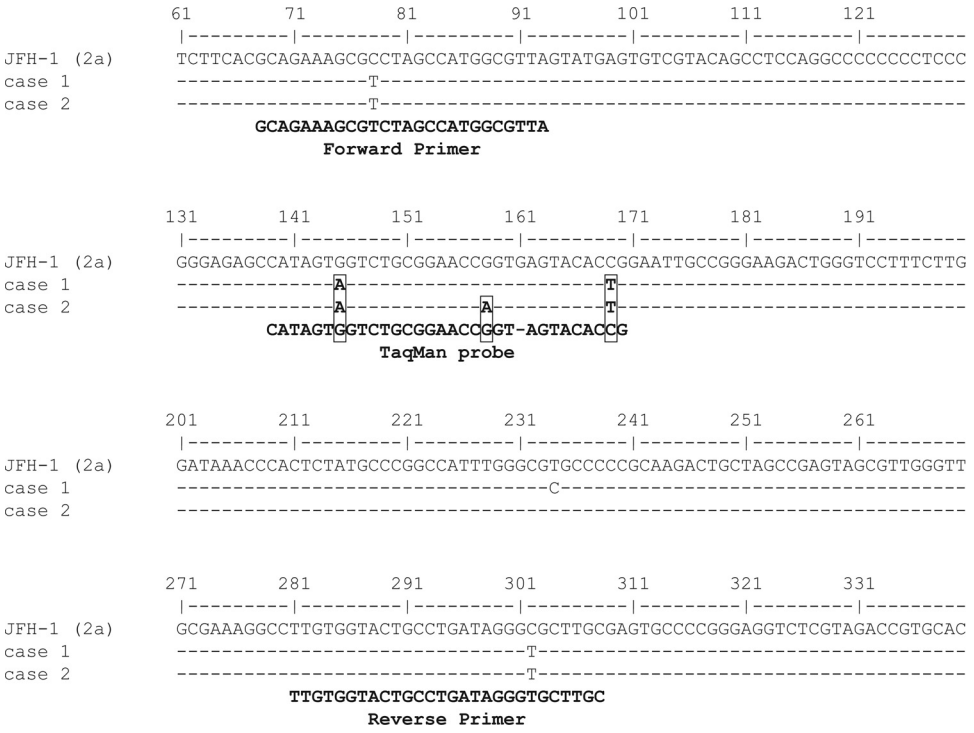

FIG 1 Alignment of HCV 5′-untranslated sequences for two patients with HCV genotype 2a, in whom HCV RNA was undetectable by the CAP/CTM HCV v1.0 assay, against the sequence of a reference HCV genotype 2a strain (JFH-1). Nucleotide substitutions were found in the patient's sequences compared to the reference sequence: G to A at position 145 and C to T at position 169 in both cases and G to A at position 158 in case 2, within the putative binding site of the TaqMan probe. Primer and probe sequences were obtained from the Japanese Patent Office (patent no. 4638388).

tional probe, has been released in Western Europe and the United States to resolve the problem of underestimation of HCV genotype 4 viral RNA (4). CAP/CTM HCV v2.0 detected and quantified the HCV genotype 2a RNA in the two specimens that were not detected by v1.0 at 4.17 $\log_{10}$ IU/ml and 5.05 $\log_{10}$ IU/ml. These values are comparable to that obtained by the Abbott RealTime HCV test. Clinicians need to be aware that the Roche Cobas TaqMan HCV test v1.0 may fail to provide a viral RNA result for genotype 2a, and if RNA results are discrepant with clinical findings, they need to confirm the HCV viral load using an alternative assay.

Nucleotide sequence accession numbers. The GenBank accession numbers for the nucleotide sequences are AB853937 for case 1 and AB853938 for case 2.

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