

Origin of rare bovine rotavirus strains detected from Japanese children

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Rotavirus (RV) is an important viral pathogen causing acute gastroenteritis (AGE) in humans. As most of infants have received the rotavirus vaccine rotavirus infections among infants and young children has since decreased significantly in developed countries [1]. Each year, the vaccine prevents an estimated 40,000 to 50,000 hospitalizations among U.S. infants and young children [2]. RV infects not only humans but also various young domestic and wild animals, such as monkeys, bovine, pigs, horses, dogs, cats, rats, chicken and deer [3-6]. *Although* nature of RV in spans of many mammals and birds, infection of RV infection in humans is virtually limited to humans. Reports of the epidemic strain in local areas are very important to investigate the pandemic from the epidemic in the region.

RV, a member of the family Reoviridae, has 11 segments of double-stranded RNA as a genome, and the viral particle is composed of the outer capsid, inner capsid and core [7]. In some group of RV the outer capsid consists of two structural proteins, VP4 and VP7, which contain neutralization antigens. The inner capsid consists of structural protein VP6. Based on the antigenicity of the inner capsid protein VP6 and genomic characteristics, RV is classified into seven groups (A–G), among which group A RV is the major etiologic agent in humans and animals. For epidemiological investigations of RV, a genetic classification system based on the outer capsid proteins VP7 (G type) and VP4 (P type) has been adopted [8].

While at least 12 G genotypes have been isolated from humans, G1, G2, G3, G4, and emerging G9 are major genotypes of human rotaviruses [3]. Several P genotypes (P[1]-[3], P[5], P[7], P[9]-[11], P[14], P[19], and P[25]) have been detected sporadically in the human population [9-11]. As human P genotypes, P [8] is the most common genotype worldwide, followed by P [4] and P [6]. Also, 6 non-structural proteins (NSP) are known [3]. In human RVs, five common G and P genotype combinations (genogroups) have been identified: G1P[8], G2P [4], G3P[8], G4P[8], and G9P[8] on the Wa-like genome constellation (I1-R1-C1-M1-A1-N1-T1-E1-H1), and G2P[4] on the DS-1-like constellation (I2-R2-C2-M2-A2-N2-T2-E2-H2). AU-1-like rotaviruses make up a third group of human RV, which is distributed at low prevalence and has a distinct gene constellation (G3-P[9]-I3-R3-C3-M3-A3-N3-T3-E3-H3).

Although G6 human rotavirus is quite rare, it is the major type among RVs from cattle. In a study of Japanese cows, 59.1% of isolates belonged to G6. The first G6P[9] strain, PA151, was isolated from an Italian child with AGE [12], followed by the Se584 strain from the United States [13], several Hungarian strains [14]. G6P[9] has subsequently been reported in Japan [15-17], Australia [18], and Tunisia [19]. Usually, bovine G6 strains were combined with P[5], P[1] and others worldwide [20].

Recently, full-genome sequences of RV strains have been increasingly analyzed in order to understand the interspecies transmission, reassortment, and evolutionary relationships between human and animal RVs. In the previous study [15,16], nearly full-length sequences of all the gene segments were determined to investigate the genetic origin of the unique human G6P[9] RVs detected in Japan. The authors [21] considered that their isolates represented reassortment events between bovine-like human rotaviruses and human/feline AU-1-like rotaviruses. G6 is a common genotype in cattle/buffalo [22], sheep [23], and goats [24,25] and has been identified sporadically or at a low prevalence in rabbits and pigs [26]. G6P [14] in Egypt [27] and G6P [9] in Burkina Faso [28] in either was reported as a rare virus. The patient from whom the unique human G6P[9] RVs detected recently in Japan did not have previous contact with obvious bovine or other sources of infection.

All other genes of the detected strain except for the NSP3 were relatively closely related to at least one of the human G6 RVs reported in Europe and the U.S. In a study from Miyagi Prefecture of Japan G6P [9] (M72S11) per sample was found from a 2-year-old toddler in 2011 [29]. Also G6P [9] have been detected from more than 3 cats of Mie Prefecture of Japan. These findings suggest that human G6 RV which had occurred by reassortment between human and feline or bovine RV are distributed worldwide, despite low prevalence. Since genotypes of a few gene segments are different among those human G6 strains, this suggests that G6 rotaviruses may occur independently in various locations or countries through reassortment among local strains.

Although infections with feline rotaviruses (FRVs) rarely cause severe illness in cats [30,31], FRVs have captured attention as perpetuating, albeit infrequent, sources of human disease. Human RV with genetic homology to FRV had been isolated from widespread geographical locations, including Japan [32,33], Israel [34], Tunisia, and United States [35]. Additionally, putative human/feline reassortant rotaviruses have been identified in children in Italy [36].

Two G and P genotypes identified combinations carried by rotaviruses circulating in the cat population were G3P[9] and G6P[9].

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Key words: rotavirus gastroenteritis, endemic strain, genotype, G6P [9], bovine rotavirus, reassortment

Received: March 05, 2018; **Accepted:** March 25, 2018; **Published:** March 29, 2018

Both G3P[9] and G6P[9] genotypes have been isolated from humans. G3P[9] is a recognized feline genotype (AU-1-like and BA222-like genotype constellations [37]. Ferine RV (G6P[9] and G3P[9]) were detected at a low prevalence (3.0%) in the cat population in the United Kingdom. G6 was the more prevalent genotype (84%) and was detected in Scotland, the Midlands, and Cornwall, which are geographically distinct regions encompassing the length of the United Kingdom [37]. This is similar to estimates from other countries including Japan but showed regional and seasonal variations. Longitudinal sampling strategies based on this prevalence could be used to investigate transmission dynamics in more detail. The absence of an association between RV infection and diarrhea in cats is in stark contrast to humans.

Infection has also been associated with diarrhea and decreased productivity in cows [38], suckling pigs, and horses. Asymptomatic infections are reported, although their importance in transmission is not well understood due to the lack of population-based studies [39]. In cows, asymptomatic individuals shed similar viral titers to those of clinically infected individuals, and the roles of virulent and avirulent strains of RV have been postulated [40]. Asymptomatic infection may be a reflection of the nature of the relationship of G6P[9] and G3P[9] with the feline host [41].

The possibility of G6 feline origin at some historical point has been proposed. With clustering of published human G6 genotypes with our feline G6 genotypes, rather than with published bovine G6 genotypes [42], it was strongly suggests that G6P[9] genotypes were examples of zoonotic or anthro-p-zoonotic transmission between cats and humans.

G6P[9] is a relatively common feline rotavirus exists at low prevalence in cat population in Japan. Transmission events between both cats or bovine and human likely existing, although they are infrequent and do not cause outbreaks of disease. The surveillance of RV in domestic pet population is important for investigating rotavirus genetic diversity, elucidating the role of asymptomatic carriage, exploring zoonotic risk, and monitoring the potential role of nonhuman rotaviruses in the evolution of RV.

Conflict of interest

No commercial relationship or potential conflict of interest related to the submission of this manuscript.

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