Serotype-Specific Antibody Responses of Calves Infected Naturally with Bovine Rotavirus

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Rotaviruses cause neonatal diarrhea in many species of animals and have been recognized as a major etiological agent of neonatal calf diarrhea [5, 8, 19]. Epidemiological observation indicates that recurrent or sequential outbreaks of calf diarrhea caused by bovine rotavirus (BRV) are common for herds, even for certain individuals in a herd [2, 7, 10, 17, 20, 21]. The authors reported the existence of at least two major serotypes of BRV (designated as BRV-1 and BRV-2) that do not show cross-protection against the sequential infection with heterologous serotype each other in calves [11, 13, 14]. The homologous serotype as BRV-2, strain KK-3 appeared to be prevalent in the United Kingdom and the United States of America (personal communication from Dr. Snodgrass, D. R., 1989). Furthermore other serotypes of BRV have been reported in many countries [3, 4, 9, 15, 18, 22]. These data imply us to elucidate the role of the existence of BRV serotypes on the epidemiology of this infection, including such as the recurrence of this disease. The purpose of this study is to ascertain actual condition of BRV infection by monitoring the serotype-specific antibodies against BRV in sera successively obtained from ten calves over a period of five months.

The study was carried out on a male Holstein beef herd at Hokkaido from September 1982 to February 1983. The calves in this herd had been commonly suffered from intermittent diarrhea over a series of years, though the association with rotaviral and any other infections had not been examined. The calves were introduced into the herd from more than a farm at the age of less than one-week old, and were reared in pens. After this they were fed with milk substitute. Hay and grain were also provided. Serum samples were successively obtained from ten calves (designated as calves Nos. 1 to 10) which were

randomly selected from several pens in the herd, for seven times at 2- to 4-week intervals from the age of one- to 19-week old. The serum samples were stored at -20°C until serological examination. Serotype-specific antibody was assayed by serum neutralization test using BRV-1 and BRV-2, II-2 and KK-3 strains, respectively [11, 13]. The serum neutralization test was performed in roller tube cultures of MA-104 cells (an established fetal rhesus monkey kidney cell line) on a basis of inhibition of the cytopathic effect as previously described [12, 13]. Production of the serum neutralizing (SN) antibodies against each serotypes of BRV was estimated as being significant when the antibody titer rose more than four times except the colostral antibody. The time at the infection was determined according to the significant rise of the titers.

As shown in Fig. 1, the SN antibody titers against either serotypes in each calves independently fluctuated in eight out of ten calves, though coincidentally fluctuated in the remaining two calves (calves Nos. 1 and 2) until the age of 19-week old. All the calves possessed the SN antibodies against either of the two serotypes at the age of one-week old that were recognized as colostral ones. At this age, however, some of the calves lacked, or if possessed had extremely lower titer of the antibody against one of the serotypes than the other (calves Nos. 6, 8, 9 and 10). These colostral antibodies declined before the age of 3- to 5-week old. In the some of the calves, however, the antibody titers at the initial level continued for 5 to 10 weeks (calves Nos. 7, 8 and 10), or declined slowly taking for more than 10 weeks (calves Nos. 4, 5 and 9). After the decline of the colostral antibodies, both of the SN antibodies against these two serotypes were significantly produced at 4- to 15-week intervals in calves Nos. 6, 7 and 10. Furthermore, the second significant increase of the homologous antibodies against one of the serotypes was again observed after the age of 11- to 15-week old, which were shown in calves Nos. 3 and 4 for BRV-1, and Nos. 6, 8 and 10 for BRV-2, respectively.

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Fig. 1. Fluctuation of the serum neutralizing antibody titers against bovine rotavirus serotypes in calves.

As mentioned above, the SN antibodies against both serotypes were detected from all of the calves in this herd, and each antibody titers fluctuated independently for nearly 5 months in

eight out of ten calves. Since no cross-reaction was observed in convalescent calf sera between these serotypes from the results in the previous studies [13, 14], it was considered that the calves

in this study had been independently infected with either of the serotypes. The results indicated that both of the serotypes were prevalent in a single herd, and the calves were infected with both of them early in their lives.

After the decline of the colostral antibodies, significant increase of the SN antibodies against both serotypes was observed in calves Nos. 6, 7 and 10 at 4- to 15- week intervals, suggesting sequential infections with the heterologous serotypes of BRV. In the previous experiment, we demonstrated that an active immunity directed to one of these serotypes is ineffective against sequential infection with the heterologous serotypes [14], as also previously suggested by the others [22]. The results in this study suggested that sequential infection with heterologous serotype at a considerable intervals are common in bovine population, as indicated in human's [6, 16, 23].

The second significant increase of the SN antibodies against the homologous serotypes at the age of 11- to 15-week old was shown in calves Nos. 3 and 4 for BRV-1, and Nos. 6, 8 and 10 for BRV-2, respectively. This indicates the recurrence of the infection with a single serotype in bovine population as suggested by the others [7, 17], though no information about the clinical manifestation was available in the present study. In the previous experiment, we demonstrated long-term persistence of BRV despite the presence of the homologous antibody in serum and suggested transient nature of the local immune response in BRV infection [14]. Recently Besser, T. E. *et al.* [1] suggested that the SN antibody titer in the small intestinal lumina closely correlated with the calves' serum titer on BRV infection. This indicates that the serum antibody level indirectly reflects the immune response at the intestine itself. Consequently, it was comprehensible that the decrease of the SN antibody titer come from the first active immunity to the one of the serotypes might be followed by re-infection with exotic BRV, or by successive antigenic stimulation with persistently infected BRV.

In calves Nos. 1 and 2, the fluctuation of the SN antibody titers to both serotypes was coincided each other. The reason why the SN antibody titers in these calves coincidentally fluctuated is obscure. It is considered that the calves might be infected with both of the sero-

types simultaneously, or with new serotype of BRV which could be cross-reactive with both BRV-1 and BRV-2.

Recurrence of the BRV infection is still being a major epidemiological problem, in particular on a basis of the immunoprophylaxis of this infection. Although BRV infection is extremely complicated, we consider that the present results suggested the possible mechanisms of the recurrence of this disease, in which re-infection with either heterologous or homologous serotypes of BRV is common in bovine population, even in a single calf.

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要 約

自然感染牛における牛ロタウイルス型特異抗体の推移（短報）：村上洋介・西岡信義・江口正志・国安主税（農林水産省家畜衛生試験場）——1 集団保育場で10頭の子牛から生後19週まで定期的に血清を採取し、牛ロタウイルス1型及び2型に対する中和抗体の推移を調べた。その結果、両血清型ウイルスの浸潤度は高くそれぞれ独立した感染を起こすこと、同一個体においても異型、同型ウイルスによる連続あるいは再感染が起こることなどが示唆された。