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BRIEF REPORT

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Outbreak report of rotavirus gastroenteritis among remotely vaccinated travelers: A potential implication of booster vaccine for travelers to endemic countries

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ABSTRACT

In countries in which rotavirus vaccines have been introduced for young infants, the incidence of rotavirus infections has dramatically decreased. This report presents an outbreak of rotavirus gastroenteritis among travelers. Data regarding the long-term protective effect of rotavirus vaccines after years of vaccination are scarce. A Japanese group of 14 children and nine adults traveled to Malaysia over 4 weeks. During travel, 15 of 23 patients developed gastroenteritis symptoms (Figure 1). Stool samples were collected from two symptomatic patients that tested positive for rotavirus. None of the five members with a history of rotavirus gastroenteritis developed symptoms. Nine of the 10 vaccinated children developed symptoms of acute gastroenteritis without the need for hospitalization. The only child without a history of vaccination or infection developed acute gastroenteritis and required hospitalization for continuous intravenous hydration. While individuals with a history of infection did not develop acute gastroenteritis, the protective effects of vaccination against symptomatic infection did not sustain long. This indicates the potential need for a booster dose of the rotavirus vaccine for travelers to rotavirus-endemic countries.

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Introduction

Rotavirus infection was the leading cause of acute gastroenteritis in young children during the pre-vaccine era.[1] In countries in which rotavirus vaccines for young infants have been introduced into the national immunization program (NIP), the incidence of rotavirus infection has significantly reduced across all age groups, including older children and adults.[2] In Japan, rotavirus vaccines for young infants were introduced as "voluntary vaccinations" in 2011, followed by routine vaccinations in 2020. In Japan, the annual number of reported cases of rotavirus gastroenteritis was 11.04 per sentinel facility in 2016, which reduced to 0.32 per sentinel facility by 2023.[3] Although vaccine efficacy data of rotavirus vaccines during the infancy have been reported, these studies followed for a relatively short period of up to 20 months.[4] The data regarding the long-term protective effect of rotavirus vaccine of vaccination are scarce. Here, we report the rotavirus infection outbreak among Japanese travelers, most of whom were remotely vaccinated. This report was approved by the Institutional Review Board of Nara Prefectural General Medical Center (No. 944), and written informed consent was obtained from all participants.

Presentation

Study design and settings

Between late July and late August 2024, five Japanese families (14 children and nine adults) traveled from Japan to Kuala Lumpur, Malaysia, for 4 weeks. Four of the nine adults had only joined the itinerary for the last 4 days, and the five adults who traveled for the entire itinerary were all Japanese registered nurses. Four of the five families stayed in a single condominium room, and the other family stayed in a different room in the same building; however, all five families frequently gathered together and shared spaces throughout the itinerary. The children attended a language school in Kuala Lumpur during their travel periods. In the index case, a 4-y-old child with a history of rotavirus vaccination in early infancy developed fever and diarrhea on August 7, 2024. In the following 2 weeks, 15 of the 23 patients developed gastroenteritis symptoms (Figure 1). Stool samples were collected from two symptomatic patients. Rapid antigen tests were conducted for the two stool samples, and both samples were positive for rotavirus but negative for adenovirus and norovirus. Stool culture, molecular tests (e.g., PCR) or gene sequencing was not available in any patients. Stool samples of other patients were not obtained, and the diagnosis of all patients other than two patients with stool samples was made clinically (e.g., symptoms of gastroenteritis and close contact with patients with rotavirus gastroenteritis).

Symptom development among those with and without previous history of rotavirus gastroenteritis

Median age of 23 members was 7 y [interquartile range (IQR); 4–40 years], and 11 (47.8%) were female. None of the members had chronic medical comorbidities. Five members (three older children and two adults) had a history of rotavirus

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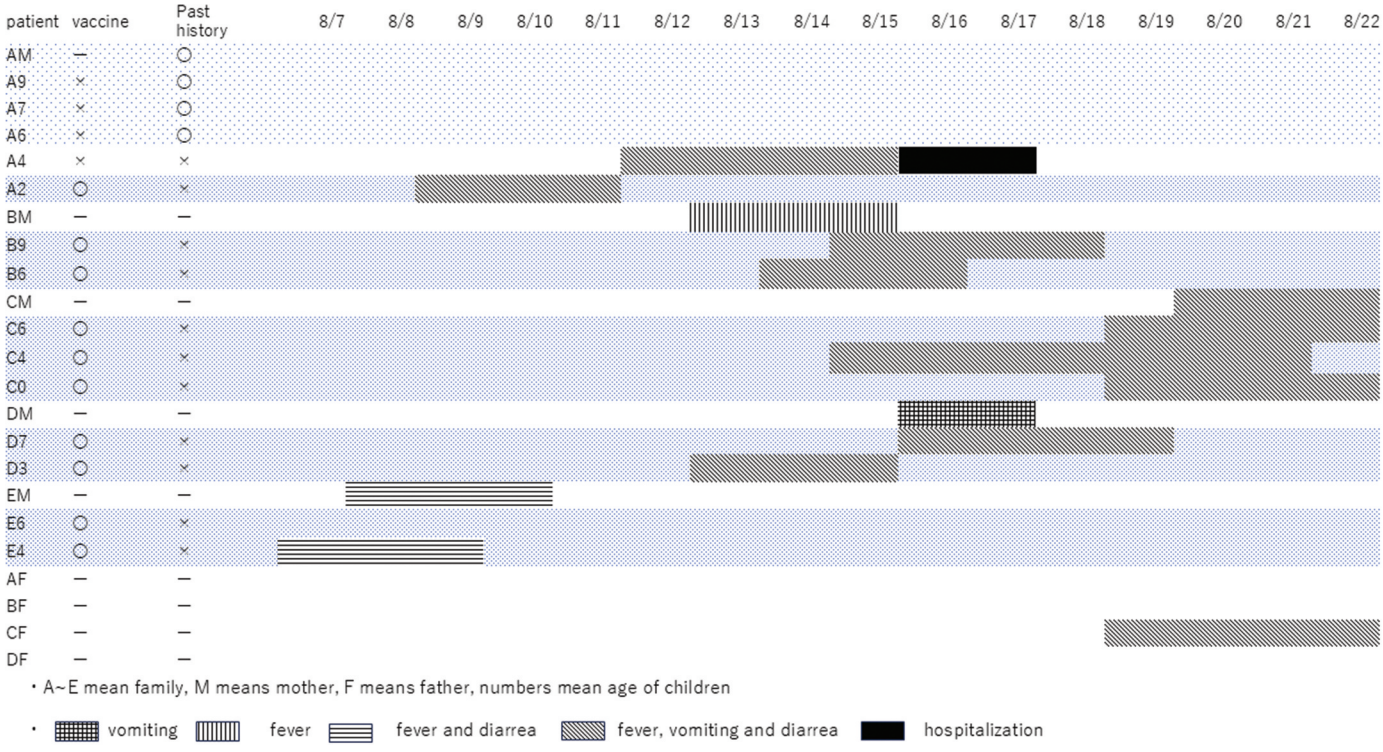

Figure 1. Clinical profile and course of symptoms in patients.

Table 1. Patients characteristics, symptoms, vaccination history and clinical symptoms Patient ID (Family/Role history of microbiologically Vaccine type Time since vaccination Symptom Rapid antigen Management.

or (years))	Age	confirmed rotavirus infection	(age of last vaccination)		test	
A/M		4 years ago	–	none	–	–
A/F		4 years ago	–	none	–	–
A/9		4 years ago	–	none	–	–
A/7		4 years ago	–	none	–	–
A/6		4 years ago	–	none	–	–
A/4	none	–	–	fever,	RV(+)	hospitalization
A/2	none	RV1	2y1m (3m)	vomiting, diarrhea fever, vomiting, diarrhea	–	ORT
B/M	none	–	–	fever	–	ORT
B/F	none	–	–	none	–	–
B/9	none	RV1	9y6m (4m)	fever, vomiting, diarrhea	–	ORT
B/6	none	RV5	6y6m (5m)	fever, vomiting, diarrhea	–	ORT
C/M	none	–	–	fever, vomiting, diarrhea	–	ORT
C/F	none	–	–	fever, vomiting, diarrhea	RV(+)	ORT, div
C/6	none	RV1	5y9m (3m)	fever, vomiting, diarrhea	–	ORT
C/4	none	RV1	4y1m (3m)	fever, vomiting,	–	ORT
C/0	none	RV1	6m (3m)	diarrhea fever, vomiting, diarrhea	–	ORT
D/M	none	–	–	vomiting	–	ORT
D/F	none	–	–	none	–	–
D/7	none	RV1	**7**y1m (3m)	fever, vomiting, diarrhea	–	ORT
D/3	none	RV1	2y11m (3m)	fever, vomiting, diarrhea	–	ORT
E/M	none	–	–	fever, diarrhea	–	none
E/6	none	RV1	6y6m (3m)	none	–	–
E/4	none	RV1	4y10m (3m)	fever, diarrhea	–	none

Abbreviations: F; father, M; mother, NA; not applied, ORT; oral rehydration therapy, RV; rotavirus, RV1; monovalent rotavirus vaccine (Rotarix®), RV5; pentavalent rotavirus vaccine (Rotateq®), -: not applicable.

gastroenteritis 4 y pre-outbreak, and none of them developed symptoms. On the other hand, 15 out of 18 members without previous history of rotavirus gastroenteritis developed symptoms associated with gastroenteritis (two out of the three asymptomatic members only joined the itinerary for 1 week).Table1).

Clinical course of remotely vaccinated children without history of rotavirus gastroenteritis

Of the 14 children, 10 children (median age of 5 y [IQR; 3–6 years] at this outbreak) were vaccinated during early infancy (median age of 3 months [IQR; 3–3 months] for last dose). One child received three doses of pentavalent rotavirus vaccines, and nine children received two doses of monovalent rotavirus vaccines. Time since the last dose of rotavirus vaccination among the 10 vaccinated children was median 64 months [IQR; 30–82 months]. Nine of the 10 vaccinated children developed symptoms of acute gastroenteritis without the need for hospitalization. The proportion of symptom development in those with a previous history of rotavirus gastroenteritis (0/5) was significantly larger than that with a history of rotavirus vaccination and without a history of rotavirus gastroenteritis (9/10) ($p = .002$ in Fisher's exact test).

Clinical course of an unvaccinated child without previous history of rotavirus gastroenteritis

The only child (4-y-old girl) without a history of vaccination or infection developed acute gastroenteritis and required hospitalization for continuous intravenous hydration. Her stool sample was positive for rotavirus by the rapid antigen test.

Discussion

This report presents the outbreak of rotavirus gastroenteritis among a Japanese traveler group, with most children vaccinated during infancy. Excluding the four members who only joined in the last week of the itinerary, 14 out of 19 members developed symptoms of gastroenteritis. Considering that all five adults who traveled with their children during the entire itinerary were registered nurses and understood the infection precaution measures, this report indicates the high transmissibility of rotavirus. The short incubation period observed in this study was consistent with the previously reported incubation period (1–2 days) of rotavirus gastroenteritis.[5] Most children (9/10) with a remote history of vaccination (median 5 years since the last dose) developed acute gastroenteritis without a need for hospitalization. This suggests that rotavirus vaccination may prevent severe disease for the long term after vaccination, however, the protective effect of vaccination against infection may not be sustained. Conversely, none of the five members with a history of rotavirus gastroenteritis developed symptoms, indicating that the protective effect of infection against recurrent infection lasted longer than that of vaccination.

Currently, rotavirus vaccines are licensed for use only in infants.[6] A meta-regression study showed that vaccine efficacy of infantile rotavirus vaccines slightly wanes over time (vaccine efficacy 82% (74–92) after 2 weeks and 77% (67–84) after 12–20 months of last dose in medium-mortality settings, respectively).[4] A prospective study showed that infants infected with rotavirus in a previous year were significantly less likely to be reinfected compared with infants not previously infected.[7] However, data regarding the duration of protection of vaccination or past infection beyond 2 y are scarcely reported. Our report suggests that the protective effect against infection may be reduced years after vaccination. Intussusception is a safety concern if implementing rotavirus vaccines in older children. Some studies have estimated that the excess risk of intussusception following rotavirus vaccination is 1–5/100,000 vaccinated infants.[7] Data on the risk of intussusception in older children following rotavirus vaccination are unavailable. Notably, most cases of intussusception have been reported to occur between 6 months and 2 y.[8] Although the effectiveness and safety of rotavirus vaccines in older children and adults should be evaluated, this report indicates that travelers without a history of rotavirus gastroenteritis or recent vaccination may receive a potential benefit from rotavirus vaccination if traveling to rotavirus-endemic countries through a protection from infection and its complications. However, it is important to acknowledge that the risk of vaccination (e.g., intussusception) is unknown in older children and adults at this moment. The benefit–risk balance of receiving a booster dose of the rotavirus vaccine if traveling to endemic countries should be evaluated to consider a wider recommendation as a traveler vaccine.

The limitations of this report include the lack of some microbiological tests (e.g., stool culture, molecular test and sequencing data) of stool samples and the need to rely on clinical diagnosis of rotavirus gastroenteritis in all but two cases. The genotype of the rotavirus in this outbreak is unknown. In Malaysia, various genotypes, including G3P [8] and G9P[8], have recently been reported.[9,10] Due to the limited number of cases, vaccine effectiveness could not be determined. However, the dissociation of incidence rates (zero out of five individuals with a history of infection vs nine out of 10 individuals with a history of vaccination who developed acute gastroenteritis) strongly suggests that vaccine effectiveness against infection wanes significantly gradually.

Overall, this report presents an outbreak of rotavirus gastroenteritis among travelers. While individuals with a history of infection do not develop acute gastroenteritis, the protective effects of vaccination may not be sustained for years. This indicates the potential need for a booster dose of the rotavirus vaccine for travelers to rotavirus-endemic countries.

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