〈Original Article〉

Incidence of aseptic meningitis following the Torii strain-derived dried live attenuated mumps vaccine

Hideaki Kumihashi[1], Munehide Kano[1,*] and Satoko Ohfuji[2]

[1] Global Vaccine Business Unit, Takeda Pharmaceutical Co., Ltd.,
2–1–1 Nihonbashi-Honcho, Chuo-ku, Tokyo, 103–8668, Japan;
[2] Department of Public Health, Osaka City University Faculty of Medicine,
1–4–3 Asahimachi, Abeno-ku, Osaka 545–8585, Japan

(Received for publication July 24, 2018)

In Japan, the high incidence of aseptic meningitis associated with a mumps vaccine strain led to the discontinuation of measles-mumps-rubella vaccine administration in 1993, interrupting routine mumps immunization. Voluntary immunization with monovalent mumps vaccines later resumed, and many Japanese pediatricians claim that the incidence of aseptic meningitis following immunization with monovalent mumps vaccines (“postvaccinal aseptic meningitis incidence”) has decreased. However, there are no reports verifying this contention. To investigate changes in the annual postvaccinal aseptic meningitis incidence, we assessed the annual incidence of aseptic meningitis following vaccination with Torii strain from 2004 to 2015. Our incidence estimates are based on the number of spontaneous reports regarding suspected cases of adverse reactions due to Torii strain-derived mumps vaccine and the number of vaccine shipments from Takeda Pharmaceutical Company Limited. During this period, there were a total of 4,610,080 vaccine shipments and 127 suspected cases of aseptic meningitis, yielding a mean annual postvaccinal aseptic meningitis incidence of 2.8 ± 1.0 cases/100,000 doses (lowest annual incidence: 1.3 cases/100,000 doses [2005]; highest annual incidence: 4.4 cases/100,000 doses [2007]). The annual incidence did not change significantly between 2004 and 2015. The cause for the possible decrease in comparison with incidence around 1990 requires further investigation.

*Corresponding author, Tel.: +81–3–3278–3624, Fax: +81–3–3278–2502, E-mail: munehide.kano@takeda.com

Introduction

Mumps is designated as a category V sentinel-reporting infectious disease in Japan, and major epidemics of mumps have occurred every 4 to 5 years[1]. The main symptom of mumps is painful salivary glands swelling on one or both sides, and the main complications include aseptic meningitis, deafness, orchitis, and oophoritis[2]. The incidence of aseptic meningitis and deafness due to natural mumps infection is approximately 1% to 5%[2,3] and 0.01% to 0.5%[4~6], respectively.

In Japan, voluntary immunization with monovalent mumps vaccines began in 1981, and subsequently the widespread immunization with measles-mumps-rubella (MMR) vaccines derived from standardized strains began in April 1989. However, concerns that aseptic meningitis associated with a mumps vaccine strain was occurring at an incidence of at least 1/2,000[7,8] led to the use of MMR vaccines being discontinued in April 1993. Voluntary immunization with monovalent mumps vaccines was resumed in 1994, and two monovalent mumps vaccine products derived from Hoshino and Torii strains are currently used in Japan[4]. Vaccination is indicated for children aged ≥12 months and administered as one subcutaneous dose[9], and the vaccination rate is approximately 30%[10]. Recently, some practicing physicians in Japan made statements suggesting that the incidence of aseptic meningitis following immunization with monovalent mumps vaccines has decreased over the past several years[11]. According to the post-marketing survey of the Hoshino strain-derived mumps vaccine, the incidence of aseptic meningitis was 8.8 cases/100,000 doses (134 cases/1.53 million doses) during 1994–2004 and 3.8 cases/100,000 doses (107 cases /2.83 million doses) during 2005–2012, suggesting a significant decrease in each period[11]. However, no reports have been published that verify these speculated changes in the annual incidence of aseptic meningitis with the Torii strain-derived mumps vaccine.

In Japan, the Pharmaceuticals and Medical Devices Agency (PMDA) collects safety information, such as adverse drug reactions, infections caused by use of pharmaceuticals and medical devices and adverse events caused by medical devices from companies and healthcare professionals. That information is stored into a database for scientific analysis and investigation. Findings from investigations are reported to the Ministry of Health, Labour and Welfare, and would result in administrative actions to ensure the safe use of pharmaceuticals and medical devices[12].

This study was conducted using the Japanese Adverse Drug Event Report database (JADER) compiled by the PMDA. It contains data on reports of adverse events that occur after the administration of medicinal products including vaccines licensed in Japan. The data are submitted according to Japanese regulations for medicinal products from all sources including companies, healthcare professionals, or non-healthcare professionals (e.g., patients, vaccine recipients, and guardians) to the PMDA since April 2004[13].

Here, we retrieved the number of suspected cases of adverse reactions due to Torii strain-de-

rived mumps vaccine (Dried Live Attenuated Mumps Vaccine, “Takeda”) from the JADER posted on the PMDA website. Based on this number and the number of vaccine shipments from Takeda Pharmaceutical Company Limited, we estimated the annual incidence of aseptic meningitis following vaccination with Torii strain for the 12 years from 2004 to 2015.

Materials and Methods

Vaccine

At present, mumps is outside the scope of the routine vaccination program in Japan, so only those whose parents request it receive a vaccination against mumps. Individuals aged 12 months or more who have never had mumps are allowed to receive the mumps vaccine, regardless of gender or age; however, it is considered preferable to receive one dose of mumps vaccine between the ages of 24 and 60 months[9]. In this study, we investigated a Torii strain-derived dried live attenuated mumps vaccine produced by Takeda Pharmaceutical Company Limited. Each single vaccine dose contains 5,000 $CCID_{50}$ or more of live attenuated mumps virus (Torii strain), stabilizers (lactose hydrate, monopotassium L-glutamate, dibasic sodium phosphate, and potassium dihydrogenphosphate), and antibiotics (kanamycin and erythromycin). This product, manufactured by Takeda Pharmaceutical Company Limited, was the only Torii strain-derived mumps vaccine available during the study period.

Study period and information collection

Data that accumulated in JADER over the 12-year period from April 2004 to March 2015 on the adverse reactions following immunization with Torii strain-derived mumps vaccine were analyzed in this study. Data before March 2004 were not included in JADER. Information on the “reporting year,” “date of vaccine administration,” “adverse reaction/adverse event,” “date of onset,” “gender” were obtained for each adverse reaction.

Annual number of aseptic meningitis cases following vaccination with the Torii strain

In the list of cases in JADER, all cases with any of the following adverse reaction terms were regarded as “aseptic meningitis cases” for this study: “aseptic meningitis,” “mumps meningitis,” “viral meningitis,” and “meningitis.” All of these cases were included in the analysis, regardless of the time from vaccination to the onset of aseptic meningitis.

Annual number of administered Torii strain-derived vaccine doses

As the monovalent mumps vaccine is purchased as needed, very few doses are likely to be discarded as unused in medical institutions. Therefore, in this study, it was assumed that all doses shipped during the study period were administered and that the number of vaccine shipments

each year was equivalent to the number of vaccine doses administered that year.

Statistical analysis

To calculate the annual incidence of postvaccinal aseptic meningitis per 100,000 doses, the annual number of aseptic meningitis cases was divided by the annual number of doses shipped and then multiplied by 100,000. Chi-squared tests were performed to evaluate the statistical significance of differences in the annual incidence of aseptic meningitis. In addition, to examine the disproportionality of aseptic meningitis cases among all adverse events in the period from 2004 to 2015, we divided the 12-year survey period into two phases, the early 6-year phase (2004–2009) and the late 6-year phase (2010–2015), and compared the proportions of aseptic meningitis between the two phases by the chi-squared test. The incidence of aseptic meningitis was also evaluated by gender, and the number of elapsed days from vaccination. Differences in the incidence of aseptic meningitis by gender were tested for significance using a chi-squared test. The number of days elapsed from vaccination were counted as the number of days starting from vaccination to the onset of adverse reactions, and the median, minimum, maximum, and mode were calculated. The mode was also determined for the time elapsed from vaccination based on a time unit of 10 days.

A two-sided significance level of 0.05 was used for all statistical tests. Statistical analyses were performed using SAS version 9.3 software (SAS Institute Inc., Cary, NC, USA).

Results

Changes in the annual incidence of aseptic meningitis following vaccination with the Torii strain

The 127 cases identified as aseptic meningitis during the period 2004–2015 comprised 99 cases of aseptic meningitis, 12 cases of mumps meningitis, 9 cases of meningitis, and 7 cases of viral meningitis.

The mean annual incidence of aseptic meningitis following vaccination with the Torii strain was 2.8 ± 1.0 cases/100,000 doses, ranging from a minimum of 1.3 cases/100,000 doses in 2005 to a peak of 4.4 cases/100,000 doses in 2007. Over this 12-year period, the annual incidences of aseptic meningitis following vaccination with the Torii strain were not significantly different, suggesting that the incidence did not change during this time (Table 1).

Of patients with adverse reactions, the percentage of those with aseptic meningitis was 64.4% (47/73 cases) in the early phase (2004–2009) and 58.8% (80/136 cases) in the late phase (2010–2015); these percentages were not significantly different ($p=0.43$). Therefore, the percentage of aseptic meningitis cases among patients with adverse reactions was also stable from the viewpoint of the early and late phases.

Table 1. Annual incidence of aseptic meningitis following vaccination with the Torii strain from 2004 to 2015

Year	Vaccine doses	Total number of adverse events	Number of aseptic meningitis cases	Ratio of aseptic meningitis cases (%)	Number of cases/100,000 vaccine doses
2004	235,044	10	7	70.0	3.0
2005	237,573	9	3	33.3	1.3
2006	275,150	15	9	60.0	3.3
2007	250,440	11	11	100	4.4
2008	283,674	16	12	75.0	4.2
2009	290,867	12	5	41.7	1.7
2010	398,886	16	14	87.5	3.5
2011	489,251	24	18	75.0	3.7
2012	520,048	17	9	52.9	1.7
2013	549,268	33	13	39.4	2.4
2014	514,956	18	9	50.0	1.8
2015	564,923	28	17	60.7	3.0
Total	4,610,080	209	127	60.8	2.8 ± 1.0 *0.20*

Comparisons of the numbers of aseptic meningitis cases following vaccination with the Torii strain between males and females

Of the 127 patients who developed aseptic meningitis following vaccination with the Torii strain, there were 83 males, 41 females, and 3 individuals with an unrecorded gender (Table 2).

Assuming that the number of males receiving the vaccine was the same as that of females, the incidence of postvaccinal aseptic meningitis in males was significantly higher (2.0-fold; $p=0.03$) than that in females.

Table 2. Comparison of the annual number of aseptic meningitis following vaccination with the Torii strain between males and females

Year	Male	Female	Unknown	Total
2004	4	3	0	7
2005	3	0	0	3
2006	7	2	0	9
2007	5	6	0	11
2008	10	2	0	12
2009	4	1	0	5
2010	11	3	0	14
2011	12	6	0	18
2012	5	3	1	9
2013	8	5	0	13
2014	5	4	0	9
2015	9	6	2	17
Total	83	41	3	127
p-value		0.03		

Suspected cases of adverse reactions following vaccination with the Torii strain from 2004 to 2015

From 2004 to 2015, 40 types of suspected adverse reactions were reported in 209 cases after vaccination with the Torii strain (Table 3).

The three most commonly reported adverse reactions, in descending order, were aseptic meningitis, encephalitis, and fever. These three adverse reactions and aseptic meningitis alone accounted for 71% and 61%, respectively, of all cases.

Number of days from vaccination to the onset of aseptic meningitis

We were able to calculate the number of days from vaccination to the onset of aseptic meningitis in 102 of the 127 cases of aseptic meningitis following vaccination with the Torii strain. The median time was 23 days (range: 4 to 67 days), and the mode, composed of 11 cases, was 25 days (Figure 1).

When based on a time unit of 10 days, the mode of the time from vaccination to the onset of aseptic meningitis was the period from 17 to 26 days, which occurred in 69 cases (54.3%). Aseptic meningitis has been reported to develop two to three weeks after mumps vaccination[2]; however, our results suggest that a follow-up observation should be required for recipients of the Torii strain-derived vaccine at or greater than three weeks after vaccination.

Outcome of aseptic meningitis cases following vaccination with the Torii strain

The 127 patients who developed aseptic meningitis following vaccination with the Torii strain in the 12-year period from 2004 to 2015 had the following outcomes: 58 patients (45.7%) recovered, 40 patients (31.5%) were still recovering, no patients (0%) recovered with sequelae, 1 patient (0.8%) did not recover, and 28 patients (22.0%) had an unrecorded outcome.

Discussion

Evaluations and analyses of the safety of mumps vaccines are often fraught with problems and limitations[14]. Because spontaneous reporting often leads to failed reporting and, consequently, an underestimation of cases, a prospective cohort study generally produces a more accurate assessment; however, this type of analysis is not always possible. Although the present study relied on spontaneous reporting, and therefore has limitations in this regard, no significant change in the aseptic meningitis incidence was observed over the 12-year period, regardless of whether comparisons were performed for the annual incidence or the disproportionality of aseptic meningitis cases between the early and late phases. This finding suggests that, at least for the duration of the study period, consistency was maintained in the quality of the mumps vaccine, the criteria for reporting adverse reactions and operation, and the incidence of aseptic meningitis associated

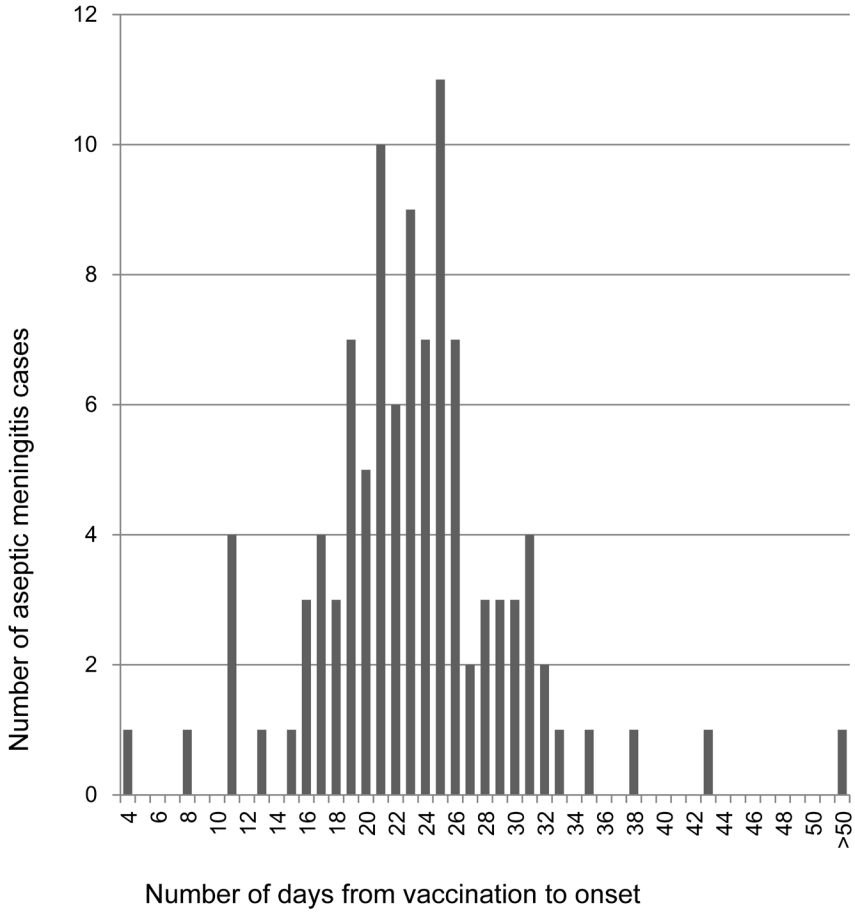
Table 3. Number of suspected cases of adverse reactions following vaccination with the Torii strain from 2004 to 2015

Adverse reaction terms	Number of reported cases	%
Aseptic meningitis	127	60.8
Encephalitis	13	6.2
Fever	8	3.8
Acute disseminated encephalomyelitis	5	2.4
Febrile convulsion	5	2.4
Anaphylactic reaction	3	1.4
Acute pancreatitis	3	1.4
Seizure	3	1.4
Parotid gland enlargement	3	1.4
Encephalopathy	3	1.4
Immune thrombocytopenic purpura	2	1.0
Inappropriate antidiuretic hormone secretion	2	1.0
Gait disturbance	2	1.0
Rash	2	1.0
Thrombocytopenic purpura	2	1.0
Loss of consciousness	2	1.0
Sjogren’s syndrome	1	0.5
Viral meningoencephalitis	1	0.5
Shock	1	0.5
Nephrotic syndrome	1	0.5
Decreased hemoglobin	1	0.5

Table 3. Continued

Adverse reaction terms	Number of reported cases	%
Orchitis mumps	1	0.5
Upper gastrointestinal hemorrhage	1	0.5
Generalized tonic-clonic seizure	1	0.5
Shock hemorrhagic	1	0.5
Laryngitis	1	0.5
Sepsis	1	0.5
Unilateral deafness	1	0.5
Aggravated condition,	1	0.5
Diabetes mellitus	1	0.5
Parotitis	1	0.5
Liver disorder	1	0.5
Pneumococcal meningitis	1	0.5
Decreased platelet count	1	0.5
Clonic convulsion	1	0.5
Deafness	1	0.5
Tachycardia	1	0.5
Purpura	1	0.5
Headache	1	0.5
Disseminated intravascular coagulation	1	0.5
40 types of adverse reactions (total)	209	100

Fig. 1. Case distribution for time from vaccination with the Torii strain to aseptic meningitis onset

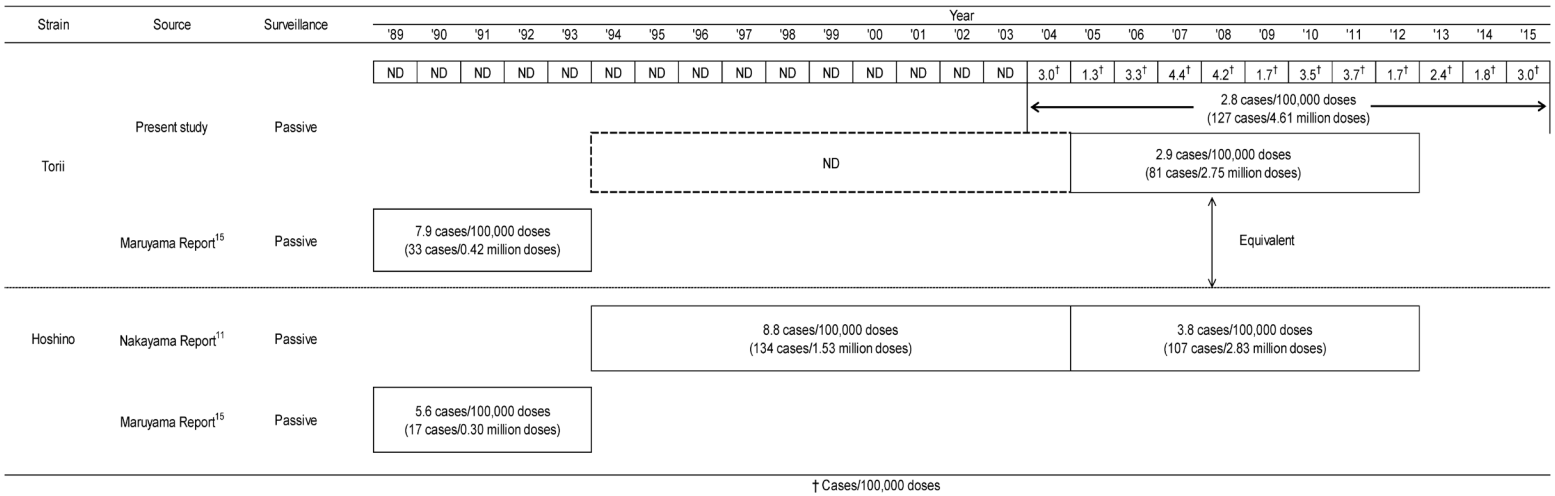


The number of cases of aseptic meningitis following vaccination with the Torii strain is shown for various lengths of time from vaccination with the Torii strain to the onset of aseptic meningitis.

with Torii strain, which under these conditions was 2.8 ± 1.0 cases/100,000 doses. The yearly incidence did not change significantly during this time. The difference of incidence of aseptic meningitis by vaccine lot number could not be analyzed in this study because the vaccine lot number is not described in JADER.

To verify the speculated decrease in the incidence of aseptic meningitis following mumps vaccination during the several decades, it is preferable to analyze long-term follow-up data collected using a uniform research method. Existing research conducted in Japan on the incidence of aseptic meningitis following vaccination with the Torii strain includes a prospective cohort study on the MMR vaccine containing the Torii strain-derived mumps vaccine produced by Takeda Pharmaceutical Company Limited[7,8], a prospective cohort study on the Torii strain-derived monovalent mumps vaccine[3], and a passive surveillance study of the Torii strain-derived monovalent

Fig. 2. Post-vaccination aseptic meningitis incidence in the present study, the Maruyama Report, and the Nakayama Report



ND, no data.

mumps vaccine based on nationwide spontaneous reports[15]. However, the research time for each of these studies was only three to four years in the period from 1990 to the first half of 2000.

Maruyama *et al.* reported that the incidence of aseptic meningitis following immunization with the Torii strain-derived monovalent mumps vaccine produced by Takeda was 7.9 cases/100,000 doses in the period from 1989 to 1993[15]. We consider the comparison between the present study using JADER data and the report by Maruyama *et al.* to be valid because both the study by Maruyama *et al.* and the JADER data were derived from passive surveillance based on nationwide spontaneous reports (Figure 2).

Results of this comparison showed that the incidence of aseptic meningitis following mumps vaccination in the period from 2004 to 2015 was lower than that following immunization with the Torii strain-derived monovalent mumps vaccine around 1990, i.e., the former was 1/2.8 of the latter.

Regarding the difference between the Hoshino strain and Torii strain, the postvaccinal reactions may vary because different attenuation methods are used to produce the vaccine strains[4]. However, according to the Nakayama Report, the incidence of aseptic meningitis associated with the Hoshino strain was 3.8 cases/100,000 doses during 2005–2012, while that associated with the Torii strain during the same period in this study was 2.9 cases/100,000 doses[11], revealing no significant difference between the two strains. The incidence of aseptic meningitis following vaccination with the Hoshino strain was 8.8 cases/100,000 doses (134 cases/1.53 million doses) during 1994–2004 and 3.8 cases/100,000 doses (107 cases/2.83 million doses) during 2005–2012, revealing a significant reduction[11]. The risk of aseptic meningitis following vaccination is not considered to be as high as that reported before 2003, regardless of whether the Hoshino strain or Torii strain is used (Figure 2).

In Japan, aseptic meningitis following mumps vaccination is regarded as an adverse reaction caused by the vaccine. However, strict virological verification is not performed in all cases, meaning that unverified cases should be considered to reflect “suspected aseptic meningitis caused by vaccination.” The 127 patients identified as aseptic meningitis cases in the present study included those with mumps meningitis (12 patients), meningitis (9 patients), and viral meningitis (7 patients), in addition to those with aseptic meningitis (99 patients). A causal relationship with the vaccine strain was verified in 12 cases, but remained unverified in the other 115 cases, which is a limitation of the present study. A definitive virological diagnosis can be achieved by an identification test that mainly distinguishes between vaccine strains and wild-type strains. The reason for performing this identification test is that some cases of aseptic meningitis are known to be caused by mingling of wild-type strains[16], but this test is only performed in certain cases. In addition, enteroviruses account for approximately 80% of the pathogens that can cause community-acquired aseptic meningitis, while the mumps virus accounts for only about 10%[17]. Therefore, aseptic meningitis caused by mingling of pathogens is more likely to be caused by enterovi-

ruses than by the mumps virus. However, an identification test of the mumps virus is only performed in certain cases, and a definitive virological diagnosis of enteroviruses is rarely performed. For accurate safety assessment of mumps vaccines with regard to aseptic meningitis, a definitive virological diagnosis of enteroviruses, in addition to an identification test of the mumps virus, should be performed in all patients with postvaccinal aseptic meningitis.

There were more boys than girls in the population that developed aseptic meningitis. The male : female ratio for these 10 patients was 9 : 1, as previously reported by Nagai *et al.*[3]. In Japan, because immunization with the monovalent mumps vaccine is voluntary, neither the injection history nor the injected number by gender is tracked, so, unfortunately, we cannot comment about them here. One likely reason for the higher number of cases reported among boys is that, because of concern about orchitis, guardians of boys in Japan may have a higher awareness of the importance of mumps vaccination, resulting in a higher vaccination rate among boys. However, there is also a gender difference in the incidence of aseptic meningitis following natural infection (wildtype strain), with the male : female ratio reported as 3 : 1[2]. This suggests that the mumps virus has a higher affinity for the central nervous system in males than in females, which may also contribute to raising the incidence of aseptic meningitis in boys.

Prognosis of postvaccinal aseptic meningitis is generally good[4], there was no case of sequelae and one case was unrecovered in this study. However, 22% of the outcomes are “unknown”, which is considered a limitation of this study due to spontaneous reports.When recommending the voluntary mumps vaccination, it is necessary to properly explain to guardians the risk for developing adverse reactions, including aseptic meningitis potentially associated with vaccination, as well as the risk of natural mumps infection if they decline the vaccination. The findings of the present study contribute to medical practice in Japan by providing useful information to Japanese pediatricians for explaining to the guardians of potential vaccine recipients as they weigh the pros and cons of electing to have their child vaccinated with the mumps vaccine.

Conflict of Interest

Hideaki Kumihashi and Munehide Kano are employees of Takeda Pharmaceutical Company Limited.

References

1) National Institute of Infectious Diseases, Japan. Mumps (infectious parotitis) in Japan, as of September 2016. Infectious Agents Surveillance Report (IASR). 2016; 37: 185–6. Available at 〈http://www.nih.go.jp/niid/en/iasr-vol37-e/865-iasr/6843-440te.html〉 Accessed April 12, 2017.
2) Rubin SA, Plotkin SA: Mumps vaccine. In: Plotkin S, Orenstein W, Offit P, editors. Vaccines. 6th Edition. Philadelphia: Saunders; 2013. p. 419–46.
3) Nagai T, Okafuji T, Miyazaki C, *et al.*: A comparative study of the incidence of aseptic meningitis in symptomatic natural mumps patients and monovalent mumps vaccine recipients in Japan. Vac-

cine. 2007; 25: 2742–7.
4) National Institute of Infectious Diseases, Japan. Otafukukaze ni kansuru fakuto shiito (July 7, 2010). Available at〈http://www.mhlw.go.jp/stf2/shingi2/2r9852000000bx23-att/2r9852000000bybc.pdf〉Accessed April 12, 2017. Japanese.
5) Hashimoto H, Fujioka M, Kinumaki H, *et al.*: An office-based prospective study of deafness in mumps. Pediatr Infect Dis J. 2009; 28: 173–5.
6) Aoyagi N, Kodama A, Koike M, *et al.*: Hearing loss due to mumps. Shonika. 1996; 37: 1273–9. Japanese.
7) Ueda K, Miyazaki C, Hidaka Y, *et al.*: Aseptic meningitis caused by measles-mumps-rubella vaccine in Japan. Lancet. 1995; 346: 701–2.
8) Kimura M, Kuno-Sakai H, Yamazaki S, *et al.*: Adverse events associated with MMR vaccines in Japan. Acta Paediatr Jpn. 1996; 38: 205–11.
9) Takeda Pharmaceutical Company Limited. Package insert of dried live attenuated mumps vaccine (Torii strain). 14th ed. Revised in Oct. 2016. Available at〈https://www.takedamed.com/mcm/medicine/download.jsp?id=105&type=ATTACHMENT_DOCUMENT〉Accessed April 12, 2017. Japanese.
10) Baba K, Okuno Y, Tanaka-Taya K, *et al.*: Immunization coverage and natural infection rates of vaccine-preventable diseases among children by questionnaire survey in 2005 in Japan. Vaccine. 2011; 29: 3089–92.
11) Nakayama T: Vaccine Q&A for general Physicians and Pediatricians 4) Is the incidence of post-mumps vaccination aseptic meningitis decreased? (Mumps Vaccine sesshugo no mukinseizuimakuen no hindo ha hette imasuka.) Vaccine Journal. 2016; 4: 26–7. Japanese.
12) Society for Regulatory Science of Medical Products. Systems for collection and analysis of information on adverse reaction etc. In: Society for Regulatory Science of Medical Products, editors. Drug approval and licensing procedures in Japan 2016. Tokyo: Jiho, Inc.; 2016. p. 669–761.
13) Pharmaceuticals and Medical Devices Agency. Post-marketing safety measures. Available at〈http://www.pmda.go.jp/english/safety/index.html〉Accessed April 12, 2017.
14) National Institute of Infectious Diseases, Japan. Notifications of adverse events after mumps vaccination, April 2013-June 2016. Infectious Agents Surveillance Report (IASR). 2016; 37: 203–4. Available at:〈http://www0.nih.go.jp/niid/idsc/iasr/37/440e.pdf〉Accessed April 12,17.
15) Maruyama H, Tomizawa I: Germlessness meningitis generation status after MMR vaccination and correspondence. Clin Viro. 1994; 22: 77–82. Japanese.
16) Sawada A, Yamaji Y, Nakayama T: Mumps Hoshino and Torii strains were distinguished from circulating wild strains. J Infect Chemother. 2013;19:480–5.
17) National Institute of Infectious Diseases, Japan. Virus isolation/detection from aseptic meningitis cases, 1999–2015. Infectious Agents Surveillance Report (IASR). Available at〈https://www.niid.go.jp/niid/ja/iasr/511-surveillance/iasr/tables/1493-iasrtv.html〉Accessed February 15, 2017 Japanese.