Case Report

Autopsy-based Investigations of Sudden Deaths after SARS-CoV-2 Vaccination: A Report of 15 Cases in Shiga, Japan

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Abstract

In Japan, 1,513 deaths after the first or second SARS-CoV-2 vaccination were reported from February 2021 to February 2022. However, the Ministry of Health, Labour and Welfare (MHLW) did not adequately explain the causal relationship between these deaths and vaccination, leading to vaccine hesitancy and distrust of the ministry. We report the autopsy results for 15 deaths that occurred within 1 week after receiving the first or second SARS-CoV-2 vaccination in Shiga Prefecture. Eleven cases were vaccinated with Comirnaty and 3 with mRNA-1273. The name of the vaccine was unknown in 1 case. There were 4 cases without any morphological changes which were presumed to be sudden cardiac deaths. There were 3 cases each of intracranial hemorrhage and infectious disease. Three other cases had morphological changes that caused sudden cardiac death. One death was due to cancer and another to trauma. In 7 cases, symptoms of the disease that caused death preceded vaccination. We report 2 representative cases of deaths that were basically caused by factors other than vaccination. Case 1 was a 60-year-old man who died within 24 h of his first vaccination. Even though less than a day had elapsed from the time of death to its discovery, the body was highly decomposed. The cause of death was diagnosed as non-clostridial gas gangrene. The vaccination was inferred to have no causal relationship to his death because he had fever prior to vaccination. Case 2 was a 48-year-old man who died 4 h after his first vaccination. Characteristic histopathologic findings of arrhythmogenic cardiomyopathy were observed at autopsy. Among the deaths reported by the MHLW, it is possible that a causal relationship to vaccination can be excluded with adequate investigation, as in these 2 cases. However, the autopsy rate in Japan is quite low. Therefore, physicians involved in diagnosing death should rethink the process for death diagnosis and the death investigation system itself.

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—Key words—

COVID-19, mRNA-vaccine, adverse events

Introduction

The coronavirus disease 2019 (COVID-19) pandemic, which lasted for over 3 years, had a huge impact worldwide. International travel was restricted and many cities implemented lockdowns or strict curfews. From the end of 2020, medical resources in Japan became so scarce that some patients died at home because they could not access adequate medical care[1]. The situation was a disaster, with livelihoods severely limited and even the medical care system collapsing. In addition, COVID-19 has a significant impact on workers: Azevedo et al. reported that 50% of hospitalized COVID-19 patients required more than 30 days to return to work and their performance has declined after returning to work[2]. Therefore, controlling the spread of COVID-19 spread is important in occupational medicine. The rapid development of SARS-CoV-2 vaccines was greeted with hope that they would turn the tide of the pandemic. Vaccination is effective not only for reducing the severity of illness and mortality in individuals but also for reducing the likelihood of community transmission by achieving herd immunity[3]. Therefore, it is considered important to rapidly increase the vaccination

Table 1 Details of the 15 cases of death within 7 days after SARS-CoV-2 vaccination in Shiga Prefecture.

Case number	Age, years	Sex	Vaccine	Dose	Duration from vaccination to death	Cause of death
1	87	F	Comirnaty	1st	≤24 h	Right thalamic hemorrhage
2	75	F	Comirnaty	1st	≤24 h	Left cerebral hemorrhage
3	90	F	Comirnaty	1st	7 days	Peritonitis
4	81	F	Comirnaty	2nd	7 days	Subarachnoid hemorrhage
5	72	M	Comirnaty	1st	3 days	Pancreatic cancer
6 (Case 1)	60	M	Comirnaty	1st	≤24 h	Gas gangrene
7	58	M	Unknown	1st	2 days	Traumatic asphyxia
8	89	F	Comirnaty	2nd	3 days	Retropharyngeal abscess
9	38	M	mRNA-1273	2nd	3 days	Sudden cardiac death
10	58	M	Comirnaty	2nd	5 days	Sudden cardiac death
11	52	M	Comirnaty	1st	3 days	Acute myocardial infarction
12 (Case 2)	48	M	Comirnaty	1st	≤24 h	Arrhythmogenic cardiomyopathy
13	44	M	mRNA-1273	1st	3 days	Acute myocardial infarction
14	38	M	Comirnaty	2nd	6 days	Sudden cardiac death
15	28	M	mRNA-1273	2nd	2 days	Sudden cardiac death

rate in the community.

SARS-CoV-2 vaccination began in Japan in February 2021, with priority given to healthcare providers and elderly people, followed by the general population aged ≥12 years. As of March 2022, more than 80% of the population had received at least 2 doses[4]. Although the safety and efficacy of the vaccines were demonstrated in multiple studies[5–7], some people remain reluctant to get vaccinated. Common reasons for vaccine hesitancy are concerns about safety or side effects, including death due to vaccination[8]. In Japan, 1,513 deaths have been reported after the first or second vaccination through February 2022[9]. Some cases were sensationalized by the media and created the impression that the deaths were caused by the vaccine. However, the Ministry of Health, Labour and Welfare (MHLW) did not adequately explain the causal relationship between these deaths and vaccination, resulting in further vaccine hesitancy and distrust of the entities that promoted vaccination.

Japan is reported to be among the countries with lowest vaccine confidence[10]. This can be traced back to the human papillomavirus (HPV) vaccine crisis of 2013, which resulted in an extremely low vaccination rate for the next 7 years[11]. Evidence of the HPV vaccine's safety and efficacy had been amply demonstrated in many other countries before it became a routine vaccination in Japan. However, multiple symptoms were reported among the vaccinated girls, including complex regional pain syndrome, orthostatic dysregulation, chronic fatigue syndrome, autoimmune disorder, and primary ovarian insufficiency. Consequently, additional studies were conducted to examine the association between these symptoms and the HPV vaccine, including the Nagoya Study[12]. The results showed that none of the symptoms were causally related to the vaccine and public vaccination resumed in April 2022[13]. However, issues surrounding the HPV and SARS-CoV-2 vaccines have engendered distrust in efforts to promote vaccination in Japan[14]. This is a concerning situation because vaccine hesitancy might hinder the ability to maintain herd immunity for serious diseases such as polio and Japanese encephalitis.

To restore trust and continue vaccination efforts in Japan, it is necessary to clarify the details of the deaths that occurred in people after they received the SARS-CoV-2 vaccine and to properly communicate the causal relationships. We report the autopsy results for 15 cases of sudden death in people soon after receiving the first or second SARS-CoV-2 vaccine in Shiga Prefecture.

Materials and Methods

From May to December 2021, 17 sudden deaths reported to police were found to be post-vaccination. All 17 deaths underwent autopsy by forensic experts and the cause of death was decided based on autopsy results. We excluded 2 cases from the present case series because the time from vaccination to death exceeded 1 week.

Detailed characteristics of all cases are shown in Table 1. There were 10 men and 5 women. Mean age was

61.2 years and median age was 58.0 years. Nine died after receiving their first vaccination and 6 after their second. Eleven were vaccinated with Comirnaty (BNT162b2 or tozinameran, Pfizer-BioNTech) and 3 with mRNA-1273 (Moderna). The name of the vaccine was unknown in 1 case. One death was due to traumatic asphyxia related to a traffic accident. Others were deaths from diseases. Four cases lacked morphological changes and were presumed to be sudden cardiac deaths. There were 3 cases each of intracranial hemorrhage and infectious disease. Three other cases of sudden cardiac death had morphological changes: 1 case of arrhythmogenic cardiomyopathy and 2 cases of acute myocardial infarction with obvious intracoronary thrombus or myocardial necrosis.

In 7 cases (Cases 3, 5, 6, 8, 11, 12, 13), symptoms of the disease that caused death preceded vaccination. In all 15 cases, the details of the autopsy and the opinions of the forensic physician who performed the autopsy were reported to the MHLW adverse reaction study group. However, the conclusions regarding the causal relationship with vaccination were deemed "unassessable" in all cases.

Here, we report 2 representative cases in which death was caused by factors other than the vaccine.

Case 1

A 60-year-old man was living alone. Although his body temperature recorded on the pre-vaccination medical examination form was 37.1℃, he received his first vaccination as scheduled. He sent a message to a friend at 11 pm later that day. His friend found him dead at home the following day.

Even though less than a day had elapsed from the time of death to its discovery, the body was highly decomposed and bloated by emphysema. In the autopsy performed 60 h after death, no obvious injury was observed but the skin was gray with bullae and some of the epidermis had peeled off due to decomposition. Internal organs were also necrotized with liquefactive changes. Histopathological examination showed multiple bacteria in the interstitial spaces of all tissues. Blood culture was positive for *Enterococcus faecium, Morganella morganii, Klebsiella variicola,* and *Bacteroides fragilis*.

The cause of death was diagnosed as non-clostridial gas gangrene based on the characteristic findings on the body surface and internal organs. Although the body showed overall decomposition, the skin and muscles of the upper arm at the injection site were not significantly different from other parts of the body. The fever present before vaccination also indicated that the infection preceded the vaccination.

Case 2

A 48-year-old man suddenly collapsed and briefly lost consciousness while doing desk work the day before his first SARS-CoV-2 vaccination. Examination by the family doctor revealed that his vital signs and electrocardiogram were within normal limits, and he received his vaccination the next morning as scheduled. He was found dead in his bed 4 h after the vaccination. He had complained of chest discomfort 5 years earlier and undergone cardiac catheterization, but no abnormality was found.

Autopsy was performed 20 h after his death and the body showed no signs of injury. The heart weighted 440.9 g and measured 16.0 × 11.5 × 5.5 cm. A high amount of fatty tissue was observed in the myocardium of the right ventricle and septum macroscopically. On histopathological examination, more than 60% of the right myocardium was replaced with fibrofatty tissue and the outer layer of the left ventricular free wall was also fibrotic.

The cause of death was diagnosed as arrhythmogenic cardiomyopathy based on the characteristic histopathological findings. The episodes of chest discomfort 5 years earlier and fainting on the day before death were likely caused by the arrhythmogenic cardiomyopathy as well.

Discussion

We reported two cases of sudden death shortly after SARS-CoV-2 vaccination. The cause of death in Case 1 was gas gangrene and there were signs of fever prior to vaccination; therefore, we considered his death to be unrelated to the vaccination. There may be some discussion about whether it was appropriate to vaccinate him while he had a fever. His body temperature measured just prior to vaccination was 37.1℃, which is within normal range for some people; therefore, it would be difficult to suspect a serious infection and stop the vaccination. The cause of death in Case 2 was sudden cardiac death due to arrhythmogenic cardiomyopathy. Be-

cause arrhythmogenic cardiomyopathy is an inherited disorder, it was inferred that SARS-CoV-2 vaccination had no causal relationship with the death, although the stress of vaccination could have triggered the arrhythmia. He might have died suddenly even if he had not been vaccinated, given that he had fainted the day before, likely due to arrhythmia.

These two cases show that deaths immediately following vaccination are not necessarily vaccine-related. If someone dies immediately after being vaccinated, people tend to link the death to the vaccination, especially when death occurs soon afterward. However, sudden deaths occurred even before the beginning of SARS-CoV-2 vaccination. Berdowski et al. reported an incidence of 52.5 per 100,000 person-years of out-of-hospital cardiac arrests in Asia as of 2009[15]. Based on this frequency, about 671 of the 1.13 million people vaccinated between March 2021 and March 2022 in Shiga Prefecture would be expected die suddenly within the following 12 months. It is quite possible that such events would happen by chance within a few days after the vaccination.

It is true that some cases of sudden death caused by diseases that were common in the past may occur today as complications of vaccination. Therefore, the cause of death in such cases should be carefully considered in order to determine whether the vaccination was a contributing factor. Myocarditis and pericarditis are known complications of SARS-CoV-2 vaccination in young males[16], and thrombosis and thrombocytopenia have also been suggested to have an association with SARS-CoV-2 vaccination[17]. Although Klein et al. reported that the risk of hemorrhagic or ischemic stroke does not rise within 21 days after vaccination[6], there have also been reports of hypertension occurring after vaccination[18][19]. Thus, it is undeniable that intracranial hemorrhages and cardiac sudden deaths are caused by vaccination-induced hypertension. To discuss causal relationships between diseases and vaccines, it is necessary to compare the incidence between vaccinated and unvaccinated groups or between pre- and post-vaccination, as was done in the Nagoya Study[12]. To this end, it is important to collect detailed information on any deaths after vaccination and to determine whether the causes of death are appropriate for the circumstances.

Between May 2021 and March 2022, MHLW received reports of 1,430 deaths after vaccination with Comirnaty, 82 deaths after vaccination with mRNA-1273, and 1 death after vaccination with Vaxzevria (ChAdOx1 nCoV-19, AstraZeneca), corresponding to 7.8 cases per million for the Comirnaty vaccine and 2.1 cases per million for the mRNA-1273 vaccine[8]. We performed autopsies on 17 people, including 2 who had died more than 1 week after vaccination. The number of autopsies corresponds to 7.49 cases per million vaccinations, which appears to cover a large proportion of the post-vaccination deaths in Shiga Prefecture. The causes of death in the 15 cases reported in this study were adequately diagnosed at autopsy and provide important data for discussing the causal relationship between disease and the vaccines.

However, in 99% of the 1,513 deaths reported by MHLW, the association with SARS-CoV-2 vaccination was deemed "unassessable"[9] because the diagnosis of the cause of death was considered debatable due to insufficient investigation. Autopsy was performed in only 128 cases (7.02%) and postmortem computed tomography was performed in only 22%. Some of the cases in which autopsy and computed tomography were not performed may have been unrelated to vaccination, as in the 2 cases we have presented here. The death investigation system in Japan, with its low autopsy rate and inadequate diagnosis of cause of death[20], hinders proper understanding of vaccination.

Vaccine promotion is a public health issue. For the public to properly understand vaccines, it is important to investigate adverse events including any cause of death in people who have recently been vaccinated. Therefore, physicians involved in diagnosing death should rethink the process for diagnosing the cause of death and the death investigation system itself. The Japanese Society of Legal Medicine issued a statement in July 2022 that autopsy of post-vaccination sudden death is strongly recommended[21].

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SARS-CoV-2 ワクチン接種後の突然死に関する解剖調査：滋賀県における 15 症例の報告

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―キーワード―
COVID-19，mRNA ワクチン，有害事象

日本では，2021 年 2 月から 2022 年 2 月の間に 1 回目および 2 回目の新型コロナウイルスワクチン接種後，1,513 人が死亡したと発表されている．しかし，厚生労働省はその死因とワクチン接種との因果関係について適切に説明していない．この事は，ワクチンそのものとワクチン接種を行っている政府への不信感を引き起こし，ワクチン忌避に繋がっている．我々は滋賀県でワクチン接種後に 1 週間以内に突然死した 15 症例について報告する．

接種されたワクチンは，11 症例がコミナティで 3 症例が mRNA-1273，1 症例は不明であった．解剖の結果，4 症例では死因となり得る形態異常を認めず，心臓性突然死と推測された．頭蓋内疾患と感染症がそれぞれ 3 症例ずつあった．3 例には心臓性突然死を起こす形態学変化を認めた．癌と外傷による死亡が 1 症例ずつあった．7 症例はワクチン接種に先駆けて死因と関連する症状が確認されていた．ワクチン接種以外に死亡の原因があると考えられた代表的な 2 症例について紹介する．【症例 1】1 回目のワクチン接種後 24 時間以内に死亡した 60 歳男性である．死亡から発見まで 1 日以内であるにも関わらず，高度の腐敗と気腫を認めた．ガス壊疽による死亡と診断し，ワクチン接種前から発熱の症状があったことから，死亡とワクチン接種との因果関係は認めないと推測した．【症例 2】1 回目のワクチン接種後 4 時間後に死亡した 47 歳男性である．解剖により，不整脈原性右室心筋症の特徴的な病理組織所見を認めた．

厚生労働省から報告された 1,513 人のワクチン接種後死亡の中にも，この 2 症例のように，精査すればワクチン接種との関連性が否定できる症例があるかもしれない．しかし，日本の解剖率は非常に低く，充分な死因究明が為されているとは言い難い．死亡診断に係る全ての医師が，各々の死因を診断する過程と死因究明制度そのものについて再考する時である．

［COI 開示］本論文に関して開示すべき COI 状態はない

（日職災医誌，71：224―229，2023）