ScientificScholar®
Knowledge is power
Publisher of Scientific Journals

www.surgicalneurologyint.com

Surgical Neurology International

Editor-in-Chief: Nancy E. Epstein, MD, Clinical Professor of Neurological Surgery, School of Medicine, State U. of NY at Stony Brook.

SNI: Neurovascular

Editor
Kazuhiro Hongo, MD
Shinshu University, Matsumoto, Japan

SNI
Open Access

Case Report

Intracranial aneurysm rupture within three days after receiving mRNA anti-COVID-19 vaccination: Three case reports

Sotaro Oshida[1], Yosuke Akamatsu[2], Yoshiyasu Matsumoto[1], Taro Suzuki[1], Takuto Sasaki[1], Yuki Kondo[1], Shunrou Fujiwara[3], Hiroshi Kashimura[2], Yoshitaka Kubo[3], Kuniaki Ogasawara[3]

[1]Department of Neurosurgery, Iwate Prefectural Ofunato Hospital, Ofunato, [2]Department of Neurosurgery, Iwate Prefectural Chubu Hospital, Kitakami, [3]Department of Neurosurgery, Iwate Medical University, Yahaba, Iwate, Japan.

E-mail: *Sotaro Oshida - soshida@iwate-med.ac.jp; Yosuke Akamatsu - akamatsu@iwate-med.ac.jp; Yoshiyasu Matsumoto - yoshiyasu.matumoto@gmail.com; Taro Suzuki - igg4related@yahoo.co.jp; Takuto Sasaki - www.takuto1208@gmail.com; Yuki Kondo - imed1218@icloud.com; Shunrou Fujiwara - shunfuji@iwate-med.ac.jp; Hiroshi Kashimura - hkashimura@icloud.com; Yoshitaka Kubo - yokubo@iwate-med.ac.jp; Kuniaki Ogasawara - kuogasa@iwate-med.ac.jp

***Corresponding author:**
Sotaro Oshida,
Department of Neurosurgery,
Iwate Prefectural Ofunato
Hospital, Ofunato, Iwate, Japan.

soshida@iwate-med.ac.jp

Received : 16 November 2021
Accepted : 05 March 2022
Published : 31 March 2022

DOI
10.25259/SNI_1144_2021

Quick Response Code:

ABSTRACT

Background: Although neurological adverse events have been reported after receiving coronavirus disease 2019 (COVID-19) vaccines, associations between COVID-19 vaccination and aneurysmal subarachnoid hemorrhage (SAH) have rarely been discussed. We report here the incidence and details of three patients who presented with intracranial aneurysm rupture shortly after receiving messenger ribonucleic acid (mRNA) COVID-19 vaccines.

Case Description: We retrospectively reviewed the medical records of individuals who received a first and/or second dose of mRNA COVID-19 vaccine between March 6, 2021, and June 14, 2021, in a rural district in Japan, and identified the occurrences of aneurysmal SAH within 3 days after mRNA vaccination. We assessed incidence rates (IRs) for aneurysmal SAH within 3 days after vaccination and spontaneous SAH for March 6–June 14, 2021, and for the March 6–June 14 intervals of a 5-year reference period of 2013–2017. We assessed the incidence rate ratio (IRR) of aneurysmal SAH within 3 days after vaccination and spontaneous SAH compared to the crude incidence in the reference period (2013–2017). Among 34,475 individuals vaccinated during the study period, three women presented with aneurysmal SAH (IR: 1058.7/100,000 person-years), compared with 83 SAHs during the reference period (IR: 20.7/100,000 persons-years). IRR was 0.026 (95% confidence interval [CI] 0.0087–0.12; $P < 0.001$). A total of 28 spontaneous SAHs were verified from the Iwate Stroke Registry database during the same period in 2021 (IR: 34.9/100,000 person-years), and comparison with the reference period showed an IRR of 0.78 (95%CI 0.53–1.18; $P = 0.204$). All three cases developed SAH within 3 days (range, 0–3 days) of the first or second dose of BNT162b2 mRNA COVID-19 vaccine by Pfizer/BioNTech. The median age at the time of SAH onset was 63.7 years (range, 44–75 years). Observed locations of ruptured aneurysms in patients were the bifurcations of the middle cerebral artery, internal carotid-posterior communicating artery, and anterior communicating artery, respectively. Favorable outcomes (modified Rankin scale scores, 0–2) were obtained following microsurgical clipping or intra-aneurysm coiling.

Conclusion: Although the advantages of COVID-19 vaccination appear to outweigh the risks, pharmacovigilance must be maintained to monitor potentially fatal adverse events and identify possible associations.

Keywords: Adverse events, mRNA COVID-19 vaccine, Ruptured aneurysm, Subarachnoid hemorrhage

INTRODUCTION

Since late 2019, coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has spread rapidly and infected millions worldwide. The intensity and rapidity of SARS-CoV-2 transmission have led to substantial morbidity and mortality, putting considerable pressure on public health systems. Japan started administering vaccines to healthcare workers on February 17, 2021, and subsequently began a campaign of broad inoculation of the general public to ameliorate the effects of the pandemic.[21]

The Ministry of Health, Labour, and Welfare (MHLW) in Japan reported that t, as of May 7, 2021, a total of 39 people had died after receiving COVID-19 vaccinations.[10] As a result, fatal postvaccination events should be a focus of evaluation to identify those individuals for whom vaccination, including the second dose of a vaccine, might be contraindicated. Among the 39 fatal events identified after vaccination, seven individuals died of hemorrhagic stroke, including subarachnoid hemorrhage (SAH) in 3 (7.7%). All three of these cases involved women who died after the first dose of messenger ribonucleic acid (mRNA) vaccine.[10]

A previous systematic review[16] and a meta-analysis[21] have characterized the safety profile of the Pfizer-BioNTech COVID-19 (BNT162b2) vaccine (Pfizer, Philadelphia, PA), identifying common reactions in the short-term of mild-to-moderate pain at the injection site, fatigue, and headache. The incidence of serious adverse events appears to have been low and was similar between vaccine and placebo groups.[16,21] In addition, SAH has rarely been reported to date. The present study investigated three patients presenting with aneurysmal SAH relatively soon after mRNA COVID-19 vaccination.

CASE DESCRIPTION

We retrospectively reviewed the electronic medical records of all individuals who received a first and/or second dose of BNT162b2 mRNA COVID-19 vaccine between March 6, 2021 and June 14, 2021 (COVID-19 pandemic, 100 days), in the Kenou area (Kitakami City, Hanamaki City, Tono City, and Nishiwaga Town) and Kesen area (Ofunato City, Rikuzentakata City, and Sumita Town), both of which are rural districts in Iwate Prefecture, Japan. The reason for enrolling cases from March 6, 2021, was that vaccination in these rural areas began on this date. From among, these individuals, those presenting with SAH within 3 days after vaccination when side effects of mRNA vaccination appeared to be persistent were included,[13] and the overall incidence rate (IR) of SAH in these districts during the study period was verified using the Iwate Stroke Registry database.[1] The Institutional Ethics Committee reviewed and approved the study protocol. In addition, records of the overall incidence of SAH from March 6 to June 14 during each of the consecutive years of 2013–2017 were investigated, providing a 500-day reference period for the Kenou and Kesen areas.[2] Patients or their family members provided informed consent before participation, in accordance with the Declaration of Helsinki. SAH was diagnosed using computed tomography (CT). CT angiography or digital subtraction angiography (DSA) was performed to diagnose the cause of SAH in all cases. Preoperative neurological condition was evaluated using the World Federation of Neurological Surgeons grading scale for SAH (WFNS grade). In addition, results of laboratory tests including coagulation tests and inflammatory markers (hemoglobin, platelet count, C-reactive protein, fibrinogen, and creatinine) were reviewed. Clinical outcomes of patients were assessed using the modified Rankin scale (mRS) score as of past follow-up.

IRs are reported per 100,000 person-years [Table 1]. Results from regression analyzes are reported as IR ratios (IRRs) with 95% confidence intervals (CIs) and interpreted as the difference in the IR of aneurysmal SAH within 3 days after vaccination and spontaneous SAH compared with the reference period (2013–2017).[7,11] All models were tested for goodness-of-fit using both deviance goodness-of-fit and Pearson goodness-of-fit. P-values were obtained using the χ^2 statistic. *P*-value <0.05 was considered indicative of a significant difference in ratio. For the CI of the incidence ratio, MedCalc uses the "exact Poisson method."[11,18]

Among 34,475 individuals vaccinated between March 6, 2021, and June 14, 2021, three cases presented with intracranial aneurysm rupture in the 3 days after vaccination.

Table 1: The incidence and IRs for aneurysmal SAH within 3 days after vaccination and spontaneous SAH for March 6–June 14, 2021, and for the March 6–June 14 intervals of a 5-year reference period of 2013–2017, and IRRs compared with the incidence of SAH of reference period of 2013–2017.

	Total incidence (Kenou)	IR	IRR (95%CI)	*P*-value
2013–2017				
Total (500 days)	83 (68)	20.7		
2013	23 (18)	28.6		
2014	21 (15)	26.1		
2015	8 (8)	10.0		
2016	11 (8)	13.7		
2017	22 (19)	27.4		
2021				
Total (100 days)	28 (22)	34.9	0.78 (0.53–1.18)	0.204
Within 3 days after vaccination	3 (1)	1058.7	0.026 (0.0087–0.12)	<0.001

IR: Incidence rate (per 100,000 person-years), SAH: Subarachnoid hemorrhage, IRR: Incidence rate ratio, 95%CI: 95% confidence interval

The IR of spontaneous SAH calculated using the person-year method with an observation period of 3 days following COVID-19 vaccination was 1058.7 per 100,000 person-years. All three individuals were women, with a median age of 63.7 years (range, 44–75 years). Two patients had histories of hypertension and dyslipidemia, while the other had no history of illness. The median interval from vaccination to onset of SAH was 2 days (range, 0–3 days). Preoperative WFNS grade was I or II in all cases. Saccular aneurysms were diagnosed using three-dimensional CT angiography or DSA in all cases. The aneurysms arose at the bifurcation of the middle cerebral artery (MCA), internal carotid-posterior communicating artery (IC-Pcom), or anterior communicating artery (Acom) in one case each. Microsurgical neck clipping was performed in two of the studied patients and aneurysmal rupture was confirmed intraoperatively. Endovascular coiling was performed in the remaining patient. Clinical outcomes at last follow-up were favorable (mRS score, 0 or 2), after a median follow-up of 57.7 days (range, 24–102 days). The demographic characteristics, clinical features, laboratory data, neuroimaging findings, and treatment course for the three patients are summarized in [Table 2].

On the other hand, a total of 85 cases of ruptured aneurysms were encountered in these study areas during the same period of March 6–June 14 during the 5 years reference period before the COVID-19 pandemic (2013–2017).[2] The IR of spontaneous SAH in the reference period as calculated using the person-year method was 21.2/100,000 person-year. The incidence of aneurysmal SAH within 3 days following vaccination thus seemed higher, with an IRR of 0.026 (95% CI 0.0087–0.12; $P < 0.001$) compared to the crude incidence in the 2013–2017 reference period. Moreover, 28 individuals including the three cases after vaccination among the 293,192 target populations in these rural areas presented with intracranial aneurysm rupture during the same period in 2021.[1] Twenty-four of those 28 individuals were women, with a median age of 67.1 years (range, 30–92 years). The incidence of spontaneous SAH during the same period in 2021 calculated using the person-year method was 35.7/100,000 person-years. The incidence of spontaneous SAH during the same period in 2021 thus seemed similar, with an IRR of 0.78 (95% CI 0.53–1.18; $P = 0.204$) compared to the crude incidence for the 2013–2017 reference period.

Table 2: Summary of demographic characteristics, clinical features, laboratory investigations, neuroimaging findings, and treatments in the three studied cases.

	Case 1	Case 2	Case 3
Age (years), sex	44, female	72, female	75, female
Ethnicity	Asian	Asian	Asian
Past medical history	None	Hypertension, dyslipidemia	Hypertension
Regular medications	None	Amlodipine besylate, rosuvastatin calcium	Amlodipine besylate, candesartan cilexetil
Family history	None	None	None
Smoking history	None	None	None
Interval from vaccination to onset (days)	0	3	3
Initial symptoms	Headache	Headache	Headache
Preoperative WFNS	Grade II	Grade I	Grade I
Laboratory parameters on Admission			
Platelets ($\times 10^9$/L)	415	221	266
Hemoglobin (g/dl)	11.5	14.4	12.3
Fibrinogen (mg/dl)	205	304	420
CRP (mg/L)	0.03	0.03	0.24
Creatinine (mg/dl)	0.52	0.45	0.53
Localization of aneurysm	Left MCA	Left IC-Pcom	Acom, left MCA
Treatment	Clipping, removal of ICH, decompressive craniectomy	Coiling	Clipping
Clinical outcome at past follow-up (timing)	mRS 2 (102 days)	mRS 0 (24 days)	mRS 0 (47 days)
Prognostic symptoms	Impaired visual acuity of the left eye, minor executive function, and acalculia	None	slight motor aphasia

WFNS: World federation of neurosurgical societies grading scale for subarachnoid hemorrhage, CRP: C-reactive protein, MCA: Middle cerebral artery, IC-Pcom: Internal carotid-posterior communicating artery, Acom: Anterior communicating artery, ICH: Intracranial hemorrhage, mRS: Modified Rankin scale

Illustrative cases

Case 1

A 44-year-old woman who had no medical history presented with severe headache 4 h after receiving the second dose of the BNT162b2 mRNA COVID-19 vaccine. On admission, she was unconscious (Glasgow coma scale [GCS] 4). Initial CT of the head revealed diffuse SAH in the basal cistern, thin subdural hematoma, intracranial hematoma (blood volume, 34.3 ml; 33 mm × 52 mm × 40 mm), and communicating hydrocephalus [Figure 1]. Three-dimensional CT

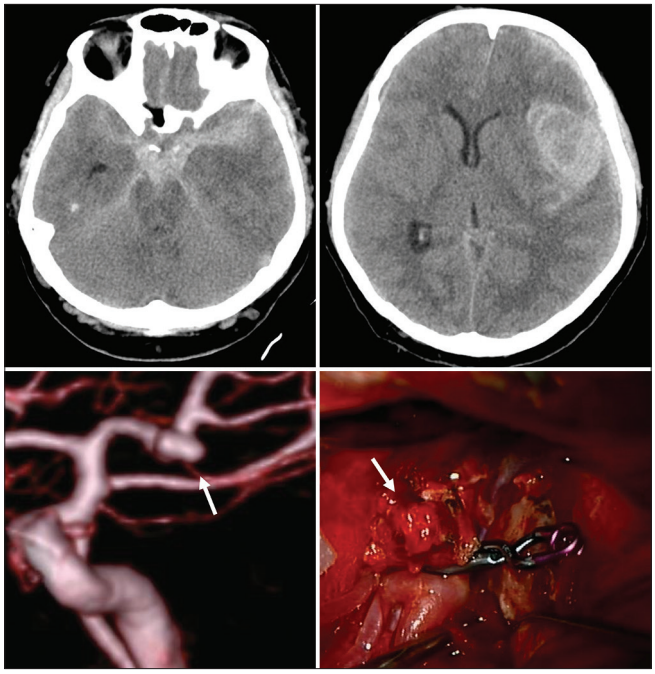

Figure 1: Computed tomography (CT) shows subarachnoid hemorrhage (upper, left) and left Sylvian hematoma (upper, right). Preoperative CT angiography demonstrates a saccular aneurysm (white arrow) (lower, left). Intraoperative images of post clip ligation indicating rupture of the aneurysm (white arrow) (lower, right).

angiography showed a saccular aneurysm arising from a bifurcation in the left MCA [Figure 1]. Following the placement of spinal drainage for acute hydrocephalus, level of consciousness gradually improved to GCS 14 (WFNS Grade II). The patient then underwent aneurysmal neck clipping and decompressive craniectomy on the 2nd day of SAH. MCA aneurysm was confirmed as the bleeding point intraoperatively [Figure 1]. Cranioplasty was performed 34 days later. The patient was transferred to a rehabilitation hospital 49 days later with minor executive function disorder, acalculia and impairment of visual acuity due to Terson syndrome and mRS Score 3. At follow-up 102 days after stroke onset, minor executive function disorder and acalculia had gradually improved with rehabilitation, and she was discharged with mRS Score 2.

Case 2

A 72-year-old woman with arterial hypertension and dyslipidemia presented with severe headache 3 days after receiving the first dose of BNT162b2 mRNA COVID-19 vaccine. She was fully alert (GCS score 15) on arrival at the emergency department. Initial CT of the head revealed thin SAH in the basal cistern (Fisher II) [Figure 2]. Three-dimensional CT angiography showed a saccular aneurysm arising from the IC-Pcom bifurcation [Figure 2]. The patient underwent intra-aneurysm coil embolization on the 1st day

Figure 2: Computed tomography demonstrates subarachnoid hemorrhage (upper). Oblique view of the left carotid injection shows internal carotid-posterior communicating artery aneurysm with a daughter sac (white arrow) (lower, left). Postoperative angiography reveals complete obliteration of the aneurysm (white arrow) (lower, right).

of SAH [Figure 2]. The postoperative course was uneventful and the patient was discharged with mRS Score 0 on postoperative day 24.

Case 3

A 75-year-old woman with arterial hypertension and dyslipidemia presented with severe headache 3 days after receiving a first dose of BNT162b2 mRNA COVID-19 vaccine. She was fully alert (GCS score 15) on admission. Initial cranial CT revealed thin SAH in the interhemispheric cistern (Fisher II) [Figure 3]. SAH was also detected on fluid-attenuated inversion recovery magnetic resonance imaging [Figure 3]. Three-dimensional CT angiography showed a saccular aneurysm arising from the bifurcation of the Acom and MCA [Figure 3]. The patient underwent microsurgical clipping of both Acom and MCA aneurysms through a left pterional approach the day after admission. Intraoperatively, the Acom aneurysm was confirmed as the cause of the SAH. The patient developed mild motor aphasia due to damage to the left caudate head and was transferred to a rehabilitation

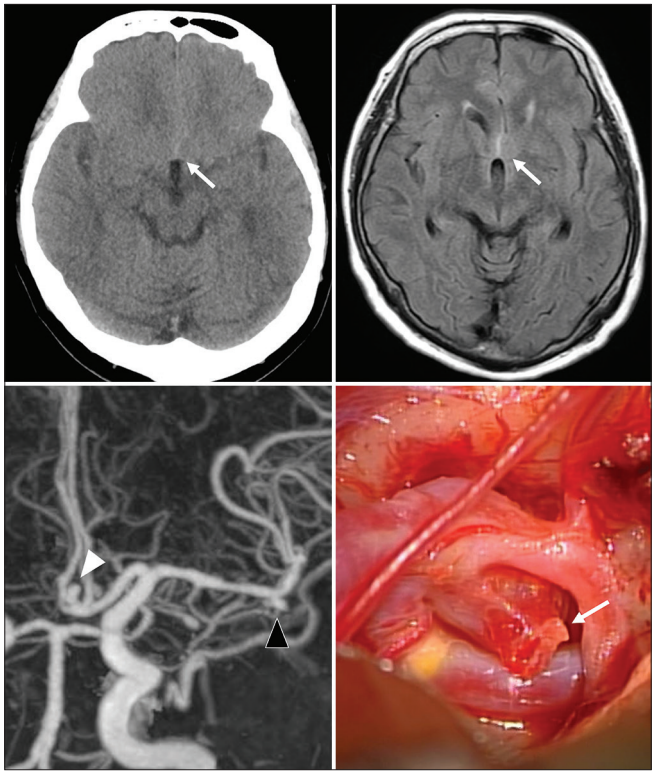

Figure 3: Computed tomography (CT) (upper, left) and magnetic resonance imaging (upper, right) demonstrate subarachnoid hemorrhage (white and black arrows). Aneurysms were confirmed by CT angiography (white and black arrowhead) (lower, left) and were confirmed as the bleeding source intraoperatively (white arrow) (lower, right).

hospital with mRS score 1. At follow-up after 47 days, the aphasia had gradually improved with rehabilitation and the patient was discharged with mRS Score 0.

DISCUSSION

We have reported here three cases of intracranial aneurysm rupture shortly after receiving the BNT162b2 mRNA COVID-19 vaccine. Three patients developed aneurysmal SAH within 3 days following vaccination in our district. Although the sample size of the present preliminary data was limited, the IR for aneurysmal SAH calculated using the person-year method with an observation period of 3 days following COVID-19 vaccination was 1058.7/100,000 person-years. On the other hand, the IR for spontaneous SAH calculated using the person-year method from 2013 to 2017 was 20.7/100,000 person-years. This IR for Iwate corresponded with an IR of 20.25/100,000 person-year in Japan.[9] The incidence of aneurysmal SAH within 3 days following vaccination thus seemed higher, with an IRR of 0.026 (95%CI 0.0087–0.12; $P < 0.001$) compared to the incidence 2013–2017 reference period. On the other hand, 28 individuals (including the three cases after vaccination), among the 293,192 target populations in these rural areas during the same period in 2021, presented with intracranial aneurysm rupture.[1] The IR of spontaneous SAH calculated using the person-year method with the same observation period in 2021 was 35.7/100,000 person-years. The incidence of spontaneous SAH during the same period in 2021 thus seemed similar, with an IRR of 0.78 (95% CI 0.53–1.18; $P = 0.204$) compared to the incidence 2013–2017 reference period. In addition, a previous study reported that the age-specific IR was highest for women aged 80–84 years, at 93.4/100,000 person-years in Iwate, Japan.[14] Nevertheless, the vaccinated individuals in our cohort were relatively younger (median age, 63.7 years) and presented a high IR of SAH (1058.7/100,000 person-years). Therefore, the possibility of an association between the high IR of aneurysmal SAH and BNT162b2 mRNA COVID-19 vaccination cannot be excluded from the study. Although the previous studies have supported the safety of vaccination using mortality rates,[7,8,10,21] since patients with SAH show a high morbidity rate of approximately 37% as well as a mortality rate of 22.2%,[15] discussing the incidence of aneurysmal SAH after BNT162b2 mRNA COVID-19 vaccination may be important.

The mRNA contained in the Pfizer-BioNTech vaccine is translated into the viral spike protein, eliciting antibody production.[8] However, mRNA could also bind to receptors, potentially inducing pro-inflammatory cascades.[13,20] Although the development of COVID-19 vaccines has raised concerns about cerebrovascular disease, particularly cerebral venous thrombosis in patients vaccinated with the AstraZeneca vaccine, Janssen vaccine, or Pfizer-BioNTech vaccine,[3-5,12,19] the present three cases did not display thrombocytopenia or thrombus formation during the postoperative courses. Two patients underwent uneventful surgical clipping without bleeding tendencies. None of the present three cases showed any indication of induced immune thrombotic thrombocytopenia. We may also have to focus on the sex imbalance in the incidence of SAH following BNT162b2 mRNA COVID-19 vaccination. The patients with SAH described in this report were all women. Moreover, as reported by the MHLW in Japan, all deaths due to SAH in those who received an mRNA vaccine have involved women.[4] As recently reported in a retrospective cohort study from Italy, overall antibody titers were significantly higher in women than in men following administration of the BNT162b2 mRNA COVID-19 vaccine.[17] Immunoreactivity following vaccination or the onset of SAH was not evaluated in the present cases; however, since inflammatory response in the saccular cerebral aneurysm wall (mainly in the form of T-cell and macrophage infiltration) is known to be associated with aneurysm rupture,[6] a relationship between stronger

immune responses in women and aneurysm rupture events cannot yet be ruled out.

As a limitation of this study, attention should be paid to interpret the statistical results with deeply considering the limited period, region, and number of patients. Further studies as a require to confirm the findings of the present study.

CONCLUSION

We have reported the cases of three women with intracranial aneurysm rupture shortly after undergoing BNT162b2 mRNA COVID-19 vaccination. Although we believe that the advantages of COVID-19 vaccination outweigh the risks, continuous pharmacovigilance is necessary to monitor for potentially fatal adverse events and identify any possible associations.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Committee of the Iwate Stroke Registry, Kubo N, editors. The database of Iwate Stroke Registry 2021. Iwate (Japan); 2021.
2. Committee of the Iwate Stroke Registry, Kubo N, editors. The Report of Iwate Stroke Registry 2013-2017. Iwate (Japan); 2020.
3. Dias L, Soares-Dos-Reis R, Meira J, Ferrao D, Soares PR, Paster A, *et al*. Cerebral venous thrombosis after BNT162b2 mRNA SARS-CoV-2 vaccine. J Stroke Cerebrovasc Dis 2021;30:105906.
4. European Medicines Agency. COVID-19 Vaccine Janssen: Link between the Vaccine and the Occurrence of Thrombosis in Combination with Thrombocytopenia. Amsterdam, Netherlands: European Medicines Agency; 2021. Available from: https://www.ema.europa.eu/en/medicines/dhpc/covid-19-vaccine-janssen-link-between-vaccine-occurrence-thrombosis-combination-thrombocytopenia [Last accessed on 2021 Nov 18].
5. European Medicines Agency. Vaxzevria (Previously COVID-19 Vaccine AstraZeneca): Link between the Vaccine and the Occurrence of Thrombosis in Combination with Thrombocytopenia. Amsterdam, Netherlands: European Medicines Agency; 2021. Available online: https://www.ema.europa.eu/en/medicines/dhpc/vaxzevria-previouslycovid-19-vaccine-astrazeneca-link-between-vaccineoccurrence-thrombosis [Last accessed on 2021 Nov 18].
6. Frösen J, Piippo A, Paetau A, Kangasniemi M, Niemela M, Hernesniemi J, *et al*. Remodeling of saccular cerebral artery aneurysm wall is associated with rupture: histological analysis of 24 unruptured and 42 ruptured cases. Stroke 2004;35:2287-93.
7. Gee J, Marquez P, Su J, Calvert GM, Liu R, Myers T, *et al*. First month of COVID-19 vaccine safety monitoring United States, December 14, 2020-January 13, 2021. MMWR Morb Mortal Wkly Rep 2021;70:283-8.
8. Gubernot D, Jazwa A, Niu M, Baumblatt J, Gee J, Moro P, *et al*. US population-based background incidence rates of medical conditions for use in safety assessment of COVID-19 vaccines. Vaccine 2021;39:3666-77.
9. Ikawa F, Morita A, Nakayama T, Goto Y, Sakai N, Iihara K, *et al*. A register-based SAH study in Japan: High incidence rate and recent decline trend based on lifestyle. J Neurosurg 2020;27:1-9.
10. Ministry of Health, Labour and Welfare. Summary of Death Cases after the Administration of COVID-19 Vaccines. Ministry of Health, Labour and Welfare; 2021. Available from: https://www.mhlw.go.jp/content/10906000/000778304.pdf [Last accessed on 2021 Oct 20].
11. Mohammad MA, Koul S, Olivecrona GK, Götberg M, Tydén P, Rydberg E, *et al*. Incidence and outcome of myocardial infarction treated with percutaneous coronary intervention during COVID-19 pandemic. Heart 2020;106:1812-8.
12. Muir KL, Kallam A, Koepsell SA, Gundabolu K. Thrombotic thrombocytopenia after Ad26.COV2.S vaccination. N Engl J Med 2021;384:1964-5.
13. Naaber P, Tserel L, Kangro K, Sepp E, Jurjensen V, AdamsonA, *et al*. Dynamics of antibody response to BNT162b2 vaccine after six months: A longitudinal prospective study. Lancet Reg Health Eur 2021;10:100208.
14. Omama S, Yoshida Y, Ogasawara K, Ogawa A, Ishibashi Y, Ohsawa M, *et al*. Incidence rate of cerebrovascular diseases in northern Japan determined from the Iwate stroke registry with an inventory survey system. J Stroke Cerebrovasc Dis 2013;22:317-22.
15. Pandey AS, Gemmete JJ, Wilson TJ, Chaudhary N, Thompson BG, Morgenstern LB, *et al*. High subarachnoid hemorrhage patient volume associated with lower mortality and better outcomes. Neurosurgery 2015;77:462-7.
16. Polack FP, Thomas SJ, Kitchin N, Absalon J, Gurtman A, Lockhart S, *et al*. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. N Engl J Med 2020;383:2603-15.
17. Resta C Di, Ferrari D, Viganò M, Moro M, Sabetta E, Minerva M, *et al*. The gender impact assessment among healthcare workers in the SARS-CoV-2 vaccination an analysis of serological response and side effects. Vaccines 2021;9:522.
18. Sahai H, Khurshid A. Statistics in Epidemiology: Methods, Techniques, and Applications. Boca Raton: CRC Press; 1996. p. 172-4.
19. See I, Su JR, Lale A, Woo EJ, Guh AY, Shimabukuro T, *et al*. US case reports of cerebral venous sinus thrombosis with thrombocytopenia after Ad26.COV2. S vaccination, March 2 to April 21, 2021. JAMA 2021;325:2448-56.
20. Talotta R. Do COVID-19 RNA-based vaccines put at risk of

immune-mediated diseases? In reply to "potential antigenic cross-reactivity between SARS-CoV-2 and human tissue with a possible link to an increase in autoimmune diseases. Clin Immunol 2021;224:108665.

21. The Japan Times. Japan gives First COVID-19 Vaccinations to Tokyo Health Workers; 2021. Available from: https://www.japantimes.co.jp/news/2021/02/17/national/vaccination-rollout-begins [Last accessed on 2021 Nov 18].
22. Yuan P, Ai P, Liu Y, Ai Z, Wang Y, Cao W, *et al*. Safety, tolerability, and immunogenicity of COVID-19 vaccines: A systematic review and meta-analysis. medRxiv 2020;2020:20224998.

How to cite this article: Oshida S, Akamatsu Y, Matsumoto Y, Suzuki T, Sasaki T, Kondo Y, *et al*. Intracranial aneurysm rupture within three days after receiving mRNA anti-COVID-19 vaccination: Three case reports. Surg Neurol Int 2022;13:117.