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Case Report



Ischemic stroke following COVID-19 vaccination

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Abstract

Following the coronavirus disease 2019 (COVID-19) vaccination, complications are expected. In this regard, coagulopathy after COVID-19 vaccination has been reported. Here, we report a rare case of ischemic stroke subsequent to receiving the Beijing Bio-Institute of Biological Products - Coronavirus (BBIBP-CorV) vaccine (Sinopharm). Ten days after receiving the first dose of the BBIBP-CorV vaccine, a 76-year-old woman showed right central hemifacial weakness, balance disorder, and right hemisensory involvement with normal muscle force. Although the magnetic resonance imaging assessment revealed an acute lacunar stroke in her left thalamus, laboratory findings were normal. Based on our report, ischemic stroke may be a post-complication of BBIBP- CorV vaccination. However, further studies are needed to confirm this finding.

Introduction

Coronavirus disease 2019 (COVID-19) has become a global health issue. 1,2 Despite numerous efforts, there is no definite efficient treatment for the disease.³ In this respect, the vaccination is the most effective and best approach for avoiding COVID-19.4 Vaccines against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) have been licensed and utilized around the world.^{4,5} Beijing Bio-Institute of Biological Products (BBIBP) developed Sinopharm vaccine (BBIBP-CorV) is defined as an inactivated SARS-CoV-2 with alum adjuvant.⁶ The virus undergoes the beta-propiolactone treatment in the Sinopharm vaccine. Beta-propiolactone binds to the viral RNA and precludes it from replication. The alum adjuvant can also assist to boost the immune response induced by the vaccines. In two clinical trials, no serious adverse events were reported within 28 days after vaccination in all participants.^{7,8} However, there is still a concern over the side effects of vaccination in the general population.

Calling attention, it has been documented that COVID-19 exerted some neurological manifestations. Ischemic and hemorrhagic strokes, as two well-known types of stroke, can be observed following COVID-19. COVID-19-associated coagulopathy is considered one of the severe coagulation disorders induced by an excessive

inflammatory response.

After COVID-19 vaccination, thrombotic events of the cerebral venous system, which may be attributed to a hypercoagulable state, have been reported. 9-11 Ischemic stroke has also been reported after COVID-19 vaccination. In a large number of studies, the middle cerebral and internal carotid arteries were mostly involved after COVID-19 vaccination, 12-16 while this study displayed a different involvement of the vasculature, in which the small penetrating arteries caused an infarction, reflecting the rare entity of this case. To date, only one report of ischemic stroke after the first dose of vaccination with BBIBP-CorV was reported in Morocco. 17 Here, we reported a case of left thalamic lacunar ischemic stroke 10 days after receiving the first dose of the COVID-19 vaccine BBIBP-CorV.

Furthermore, our case report has a limitation of coincidence of stroke and COVID-19 vaccination that could not be ruled out.

Case Report

In June 2021, a 76-year-old female patient presenting with right central hemifacial weakness, balance disorder (slight deviation to the right side while walking), right hemisensory disturbance, and normal muscle force

visited the clinic about 12 hours after the abrupt onset of the symptoms. She had received the first dose of the BBIBP-CorV vaccine 10 days prior to the onset of the symptoms. The patient had a history of hypertension and type 2 diabetes mellitus. She also underwent coronary artery bypass graft surgery (CABG), and was on Metoprolol (25 mg/12 h), Losartan-H (50 mg/12.5 mg/d), aspirin (80 mg/d), metformin (500 mg/12h), and atorvastatin (20 mg/d). On physical examination, there were a blood pressure of 160/80 mm Hg, a pulse rate of 82/min, a respiratory rate of 15/min, a temperature of 36.5 °C, and a blood glucose of 182 mg/dL. On neurological examination, the Babinski reflex, deep tendon reflexes, and finger-to-nose examination were normal, followed by normal cranial nerve examinations except for that of the facial nerve.

A physical examination of the patient did not show any signs and symptoms in favor of COVID-19. Laboratory results also showed a normal platelet count. Other laboratory parameters, including complete blood count, blood urea nitrogen (BUN), creatinine (Cr), electrolytes, liver function test, fibrinogen, D-dimer, lipid profile, and C-reactive protein (CRP) were normal. Diffusionweighted magnetic resonance imaging (DW-MRI) represented an acute lacunar stroke in the left thalamus. The fluid-attenuated inversion recovery MRI showed also disseminated white matter microvascular involvement and brain atrophy. Color Doppler ultrasound imaging revealed no remarkable stenosis of the carotid artery with normal blood flow. Echocardiography showed an ejection fraction of 50%, mild left ventricular hypertrophy, mild tricuspid regurgitation, mild mitral regurgitation, and normal pulmonary pressure echocardiography (29 mm Hg). The National Institutes of Health Stroke Scale (NIHSS) and modified Rankin Scale (mRS) were 5 and 2, respectively. The therapeutic regimen consisted of Ticagrelor (180 mg stat followed by 90 mg/12 h), Aspirin (80 mg/d), Losartan-H (50 mg.12.5 mg/12 h), metoprolol (25 mg/12 h), metformin (500 mg/12 h), and rosuvastatin (20 mg/day). Gabapentin 100 mg/12 h and vitamin B1 (300 mg/d) were also administered to preclude paresthesia. The patient showed improvement in her symptoms 5 days after the treatment. Informed consent was obtained from the patient for the report. This report was approved by the ethics committee of Semnan University of Medical Sciences.

Discussion

A vaccine has the potential to provoke the immune response, however, some undesirable side effects can be detected. Common side effects may include pain at the injection site, fever, headache, myalgia, arthralgia, and feeling unwell.¹⁸ Even so, more serious and rare side effects may occur. Thrombotic events of the cerebrovascular system following COVID-19 vaccination may occur in the venous system.9-11 Therefore, an association between vaccination and ischemic stroke was suspected. The post-complication observed following the COVID-19 vaccination in our case has been rarely described in previous literature. Elaidouni et al also reported a Moroccan case of ischemic stroke after the first dose of BBIBP-CorV vaccination in a 36-year-old man without past medical history.¹⁷ The authors found involvement of superficial and deep right parietal arteries two days after the vaccination and in line with this report the laboratory findings were normal. In contrast, our 76-year-old patient suffered from an acute lacunar stroke in the left thalamus due to the involvement of penetrating arteries with normal laboratory findings.

Several differential diagnoses are considered in cases with thrombotic events after COVID-19 vaccination. Vaccine-induced immune thrombotic thrombocytopenia (VITT) is identified as a life-threatening condition. It is a pro-thrombotic disorder that clinically resembles heparin-induced thrombocytopenia spontaneous (HIT). 19,20 VITT has been also reported following the ChAdOx1 nCoV-19 (Oxford-AstraZeneca).19-22 In the current case report, an ischemic stroke occurred due to the occlusion of small deep penetrating branches of the cerebral artery. VITT may happen one or two weeks after vaccination with ChAdOx1 nCoV-19. Another report also showed a VITT induced by other adenoviral COVID-19 vaccines, such as Ad26.COV2-S (Janssen vaccine).23 However, in our case, lacunar ischemic stroke occurred 10 days after COVID-19 vaccination with Sinopharm. The pathophysiology of VITT may be related to the endogenous production of antibodies targeting platelet factor 4. These antibodies trigger a coagulation cascade and cause thrombotic complications. 22,24

HIT is a potentially devastating immune-mediated adverse drug reaction, which is believed to be strongly associated with thromboembolic complications, involving both the arterial and venous systems. In our case, since platelet counts were normal and the patient did not receive heparin, HIT would not be as a differential diagnosis.

A thrombotic stroke is characterized as an ischemic stroke that is mostly caused by atherosclerosis. Here, the patient had at least two risk factors of atherosclerosis, including hypertension and diabetes mellitus. However, the color Doppler ultrasound imaging of the carotid arteries was normal. Furthermore, the embolic stroke was almost ruled out through normal echocardiography.

Our case report has a limitation of co-incidence of stroke and COVID-19 vaccination that could not be ruled out.

Conclusion

This case report indicated a lacunar ischemic stroke following an inactivated COVID-19 vaccination. The patient showed a lacunar infarct with a normal platelet count 10 days after the vaccination. Deep understanding of these side effects induced by COVID-19 vaccination may be helpful for clinicians to promote timely diagnosis and treatment. Further studies are needed to confirm this finding.

Authors' Contribution

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Competing Interests

The authors declare no conflict of interest to concerning the present paper.

Ethical Approval

This study was approved by the ethics committee of Semnan University of Medical Sciences.

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References

- Reiss CS. Coronavirus pandemic. DNA Cell Biol. 2020;39(6):919. doi: 10.1089/dna.2020.29015.csr.
- Khan M, Adil SF, Alkhathlan HZ, Tahir MN, Saif S, Khan M, et al. COVID-19: a global challenge with old history, epidemiology and progress so far. Molecules. 2020;26(1):39. doi: 10.3390/molecules26010039.
- 3. Kaur H, Shekhar N, Sharma S, Sarma P, Prakash A, Medhi B. Ivermectin as a potential drug for treatment of COVID-19: an in-sync review with clinical and computational attributes. Pharmacol Rep. 2021;73(3):736-49. doi: 10.1007/s43440-020-00195-y.
- Lotfi H, Mazar MG, Ei NMH, Fahim M, Yazdi NS. Vaccination is the most effective and best way to avoid the disease of COVID-19. Immun Inflamm Dis. 2023;11(8):e946. doi: 10.1002/iid3.946.
- Izda V, Jeffries MA, Sawalha AH. COVID-19: a review of therapeutic strategies and vaccine candidates. Clin Immunol. 2021;222:108634. doi: 10.1016/j.clim.2020.108634.
- Lee P, Kim CU, Seo SH, Kim DJ. Current status of COVID-19 vaccine development: focusing on antigen design and clinical trials on later stages. Immune Netw. 2021;21(1):e4. doi: 10.4110/in.2021.21.e4.
- Xia S, Duan K, Zhang Y, Zhao D, Zhang H, Xie Z, et al. Effect of an inactivated vaccine against SARS-CoV-2 on safety and immunogenicity outcomes: interim analysis of 2 randomized clinical trials. JAMA. 2020;324(10):951-60. doi: 10.1001/ jama.2020.15543.
- Xia S, Zhang Y, Wang Y, Wang H, Yang Y, Gao GF, et al. Safety and immunogenicity of an inactivated SARS-CoV-2 vaccine, BBIBP-CorV: a randomised, double-blind, placebocontrolled, phase 1/2 trial. Lancet Infect Dis. 2021;21(1):39-51. doi: 10.1016/s1473-3099(20)30831-8.
- Taquet M, Husain M, Geddes JR, Luciano S, Harrison PJ. Cerebral venous thrombosis and portal vein thrombosis: a retrospective cohort study of 537,913 COVID-19 cases. EClinicalMedicine. 2021;39:101061. doi: 10.1016/j. eclinm.2021.101061.
- 10. Franchini M, Testa S, Pezzo M, Glingani C, Caruso B,

- Terenziani I, et al. Cerebral venous thrombosis and thrombocytopenia post-COVID-19 vaccination. Thromb Res. 2021;202:182-3. doi: 10.1016/j.thromres.2021.04.001.
- Goldman M, Hermans C. Thrombotic thrombocytopenia associated with COVID-19 infection or vaccination: possible paths to platelet factor 4 autoimmunity. PLoS Med. 2021;18(5):e1003648. doi: 10.1371/journal.pmed.1003648.
- Al-Mayhani T, Saber S, Stubbs MJ, Losseff NA, Perry RJ, Simister RJ, et al. Ischaemic stroke as a presenting feature of ChAdOx1 nCoV-19 vaccine-induced immune thrombotic thrombocytopenia. J Neurol Neurosurg Psychiatry. 2021;92(11):1247-8. doi: 10.1136/jnnp-2021-326984.
- Blauenfeldt RA, Kristensen SR, Ernstsen SL, Kristensen CCH, Simonsen CZ, Hvas AM. Thrombocytopenia with acute ischemic stroke and bleeding in a patient newly vaccinated with an adenoviral vector-based COVID-19 vaccine. J Thromb Haemost. 2021;19(7):1771-5. doi: 10.1111/jth.15347.
- Garnier M, Curado A, Billoir P, Barbay V, Demeyere M, Dacher JN. Imaging of Oxford/AstraZeneca® COVID-19 vaccine-induced immune thrombotic thrombocytopenia. Diagn Interv Imaging. 2021;102(10):649-50. doi: 10.1016/j. diii.2021.04.005.
- Walter U, Fuchs M, Grossmann A, Walter M, Thiele T, Storch A, et al. Adenovirus-vectored COVID-19 vaccine-induced immune thrombosis of carotid artery: a case report. Neurology. 2021;97(15):716-9. doi: 10.1212/wnl.0000000000012576.
- De Michele M, Iacobucci M, Chistolini A, Nicolini E, Pulcinelli F, Cerbelli B, et al. Malignant cerebral infarction after ChAdOx1 nCov-19 vaccination: a catastrophic variant of vaccine-induced immune thrombotic thrombocytopenia. Nat Commun. 2021;12(1):4663. doi: 10.1038/s41467-021-25010-x.
- 17. Elaidouni G, Chetouani Z, Manal Merbouh CB, Bkiyar H, Housni B. Acute ischemic stroke after first dose of inactivated COVID-19 vaccine: a case report. Radiol Case Rep. 2022;17(6):1942-5. doi: 10.1016/j.radcr.2022.02.082.
- Rabail R, Ahmed W, Ilyas M, Rajoka MSR, Hassoun A, Khalid AR, et al. The side effects and adverse clinical cases reported after COVID-19 immunization. Vaccines (Basel). 2022;10(4):488. doi: 10.3390/vaccines10040488.
- Greinacher A, Thiele T, Warkentin TE, Weisser K, Kyrle PA, Eichinger S. Thrombotic thrombocytopenia after ChAdOx1 nCov-19 vaccination. N Engl J Med. 2021;384(22):2092-101. doi: 10.1056/NEJMoa2104840.
- Schultz NH, Sørvoll IH, Michelsen AE, Munthe LA, Lund-Johansen F, Ahlen MT, et al. Thrombosis and thrombocytopenia after ChAdOx1 nCoV-19 vaccination. N Engl J Med. 2021;384(22):2124-30. doi: 10.1056/NEJMoa2104882.
- Scully M, Singh D, Lown R, Poles A, Solomon T, Levi M, et al. Pathologic antibodies to platelet factor 4 after ChAdOx1 nCoV-19 vaccination. N Engl J Med. 2021;384(23):2202-11. doi: 10.1056/NEJMoa2105385.
- 22. Cines DB, Bussel JB. SARS-CoV-2 vaccine-induced immune thrombotic thrombocytopenia. N Engl J Med. 2021;384(23):2254-6. doi: 10.1056/NEJMe2106315.
- Muir KL, Kallam A, Koepsell SA, Gundabolu K. Thrombotic thrombocytopenia after Ad26.COV2.S vaccination. N Engl J Med. 2021;384(20):1964-5. doi: 10.1056/NEJMc2105869.
- 24. Roytenberg R, García-Sastre A, Li W. Vaccine-induced immune thrombotic thrombocytopenia: what do we know hitherto? Front Med (Lausanne). 2023;10:1155727. doi: 10.3389/fmed.2023.1155727.