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Thalamic hemi-chorea: a rare complication after receiving the adenoviral vector-based COVID-19 vaccine: a case report

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Lacunar strokes occur when a branch of a large cerebral artery is blocked. The thalamus is often affected, causing uncontrollable motions. A 72-year-old previously healthy man presented with involuntary motions in the right limbs, which were present at rest, and exacerbated during voluntary actions. He had received the first dose of the adenoviral vector-based coronavirus disease 2019 vaccine (ChAdOx1 nCoV-19) 9 days ago. Severe thrombocytopenia and elevated levels of lactate dehydrogenase, ferritin, C-reactive protein, and D-dimer were found, without any evidence of connective tissue disease. Electromyography demonstrated typical choreiform movements, and the brain magnetic resonance imaging indicated a small high signal lesion on the left side of the thalamus. Detection of the immunoglobulin G antibodies against platelet factor 4 in the blood, negative heparin-induced platelet activation (HIPA) test, and positive modified HIPA test confirmed the thalamic stroke due to the vaccine-induced prothrombotic immune thrombocytopenia (VIPIT). He was admitted to the intensive care unit and received nadroparin, sodium ozagrel, edaravone, methylprednisolone, and haloperidol. His hemi-chorea improved gradually over 2 weeks, and he was discharged after 21 days with rehabilitation advice. VIPIT due to the ChAdOx1 nCoV-19 is a novel immune-mediated response that needs clinicians' awareness and further investigations.

Keywords: SARS-CoV-2, COVID-19 vaccine, Thrombosis, Hemi-chorea, Lacunar stroke, Immunoglobulin G antibodies against platelet factor 4, Case report

Introduction

Lacunar strokes account for approximately 20%–30% of all ischemic strokes, which are small non-cortical lesions with 3–20 mm diameter. Lacunar strokes are produced by occlusion of a branching artery from a large cerebral artery, most commonly from the circle of Willis (including branches from the middle cerebral artery, anterior cerebral artery, posterior cerebral artery, or the basilar artery). The affected sites are most commonly the basal ganglia (globus pallidus, putamen, thalamus, and caudate), the pons, and the subcortical white matter (internal capsule and corona radiate). The primary underlying pathophysiological process is lipohyalinosis (thickening of the media of small vessels, accompanied by fibrinoid deposition) and micro-atheroma formation (an atheromatous arterial lesion within the brain parenchyma). Other mechanisms include small vessel arteriopathy (amyloid angiopathy and cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy), embolism, vasculitis, infections, and vasospasm [1-3].

Cerebrovascular attacks are the cause of secondary movement disorders which are rare manifestations (1%–4%) and mainly occur when affecting the deep structures of the brain like the basal ganglia (44%) and thalamus (37%). Thalamus is an important sub-cortical structure that receives its blood supply via the branches of the posterior cerebral artery, basilar artery, and posterior communicating artery. Thalamus is made up of various nuclei that relay information between the cerebral cortex and brainstem, cerebellum, and spinal cord, and any damages may lead to abnormal involuntary movements. Post-thalamic stroke movement disorders can be either hyperkinetic or hypokinetic and present as changes in neurotransmitter concentration and post-stroke modulation. Thalamic strokes can lead to dystonia, chorea, tremor, myoclonus, oromandibular dyskinesias, and asterixis, which may be isolated or in combination with other manifestations. Chorea is defined as involuntary, irregular, purposeless, non-rhythmic, and non-patterned movements that flow randomly from one part of the body to another. Hemi-chorea usually is an acute onset movement disorder that occurs due to vascular damage (stroke) in the thalamus and basal ganglia [4].

So far, vaccination, along with health protocols, has been the most important procedure in controlling the coronavirus disease 2019 (COVID-19) pandemic, which significantly reduced the prevalence, morbidity, and mortality worldwide. We presented a rare case of cerebrovascular thrombotic attack 9 days after receiving the first dose of the adenoviral vector-based COVID-19 vaccine (ChAdOx1 nCoV-19). We believe that this is a novel immune-mediated response to the vaccine that needs more research for rapid identification, diagnosis, treatment, and broadcasting of possible recommendations or changes in the vaccine.

Case Report

A 72-year-old Caucasian male was referred to the emergency ward with sudden onset headache, dizziness, and involuntary movements in his right arm and leg. Involuntary movements presented at rest, exacerbated during voluntary actions, could not be controlled by mental concentration, were prominent in the distal part of the right limbs, and affected the arm more severely than the leg. He had a history of laparoscopic cholecystectomy at the age of 61 years and had received the first dose of the ChAdOx1 nCoV-19 vaccine 9 days ago. No other medical history was detected, and his vital signs were in normal ranges. The fine finger movements of his right hand were affected; therefore, cerebellar function tests (such as finger-to-nose testing) were difficult to evaluate. He tilted to the right when standing, and as a result of severe gait instability, he was unable to walk without assistance. Cognitive assessment was almost standard (Mini-Mental State Examination score=24) with a mild decrease in abstractive and constructive performance. Other neurological and cognitive assessments were normal. The significant laboratory assessment results are presented in Table 1. The blood examinations for connective tissue diseases, echo-Doppler, and magnetic resonance angiography showed no abnormal findings. Surface electromyography demonstrated several synchronized grouping discharges in the right musculus brachioradialis and musculus extensor carpi that appeared irregularly and had a relatively long duration (>1 second). Indeed, the frequency and amplitude of the grouping discharges increased remarkably under the calculation task and showed that these patterns were consistent with typical choreiform movements (Fig. 1). Initial diffusion-weighted images (DWI) in brain mag-

Table 1. Significant laboratory findings

Laboratory assessments	Results	Reference range
Nasopharyngeal SARS-CoV-2 RT-PCR test	Negative	-
Hematology		
White blood cell (/mm^3)	12,500	3,500–10,000
Red blood cell (million/mm^3)	5	3.9–5.5
Hemoglobin (g/dL)	13.5	12–16
Hematocrit (%)	38.5	34.7–46.7
Mean corpuscular volume (fL)	88	81–100
Mean corpuscular hemoglobin (pg)	29.1	27–34
Mean corpuscular hemoglobin concentration (g/dL)	32.8	31.5–35.7
Platelet (/mm^3)	42,000	150,000–450,000
International normalized ratio	1.2	1–1.2
Partial thromboplastin time (sec)	29	25–35
Fibrinogen (g/L)	2.2	2–4
Biochemistry		
Lactate dehydrogenase (U/L)	288	135–214
Ferritin (ng/L)	369.9	10–291
D-dimer (mg/L)	600	100–250
Serology		
C-reactive protein (mg/L)	17	Up to 8
Erythrocyte sedimentation rate (mm)	15	2–20
Immunoglobulin G antibodies to platelet factor 4	3.4[a)]	-

SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; RT-PCR, reverse transcription-polymerase chain reaction.
[a)]Measured by enzyme-linked immunosorbent assay.

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netic resonance imaging (MRI) demonstrated a small lesion with high signal intensity at the left side of the thalamus that indicated an acute phase of lacunar infarction (Fig. 2A). His assessment based on the diagnostic and therapeutic algorithm in patients with thrombocytopenia/thrombosis following the AstraZeneca COVID-19 vaccine, detecting the immunoglobulin G antibodies against platelet factor 4 (IgG PF-4) in the blood, negative heparin-induced platelet activation (HIPA) test, and positive modified HIPA test presented the vaccine-induced prothrombotic immune thrombocytopenia (VIPIT) [5]. He was admitted to the intensive care unit (ICU) because of the thrombotic thalamic stroke and VIPIT. Nadroparin at 90 U/kg/day, sodium ozagrel at 160 mg/day, edaravone at 60 mg/day, methylprednisolone at 1 g/kg, and haloperidol at 0.75 mg/day were immediately prescribed. After 2 weeks, warfarin was started at the initial dose of 0.125 mg/kg/day and was titrated by monitoring prothrombin time (PT) levels for the next 3 months. His hemi-chorea improved gradually during 2 weeks, and on a follow-up brain MRI study, his left thalamic lesion had disappeared on DWI, but it remained as a chronic lesion on T2-weighted imaging (T2-WI). A chronic deficiency of cerebral blood flow was detected in T2-WI by the diffuse and pale lesions with high signal intensity in the bilateral basal ganglia and remarkable brain atrophy in the

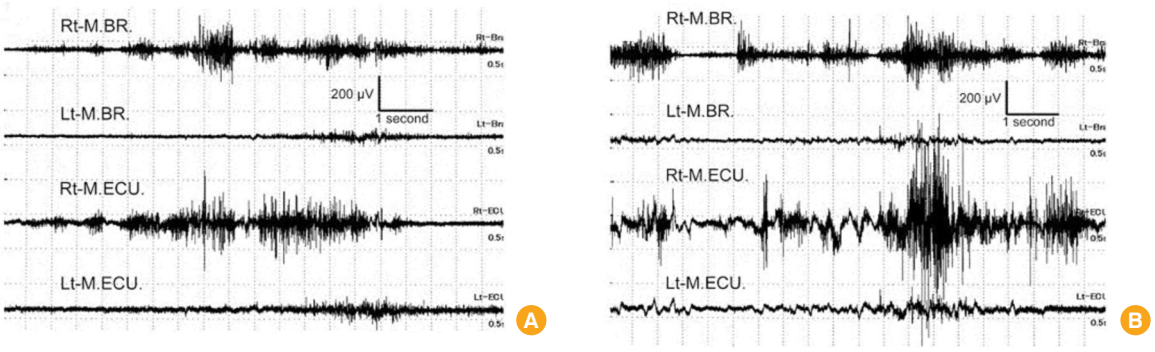

Fig. 1. Surface electromyography recordings at rest (A) and under the calculation task (B) demonstrate several synchronized grouping discharges in the right (Rt) musculus brachioradialis (M.BR.) and musculus extensor carpi ulnaris (M.ECU.). These grouping discharges appear irregularly and have a relatively long duration (>1 second). In addition, the frequency and amplitude of the grouping discharges increase remarkably under the calculation task. Lt, left.

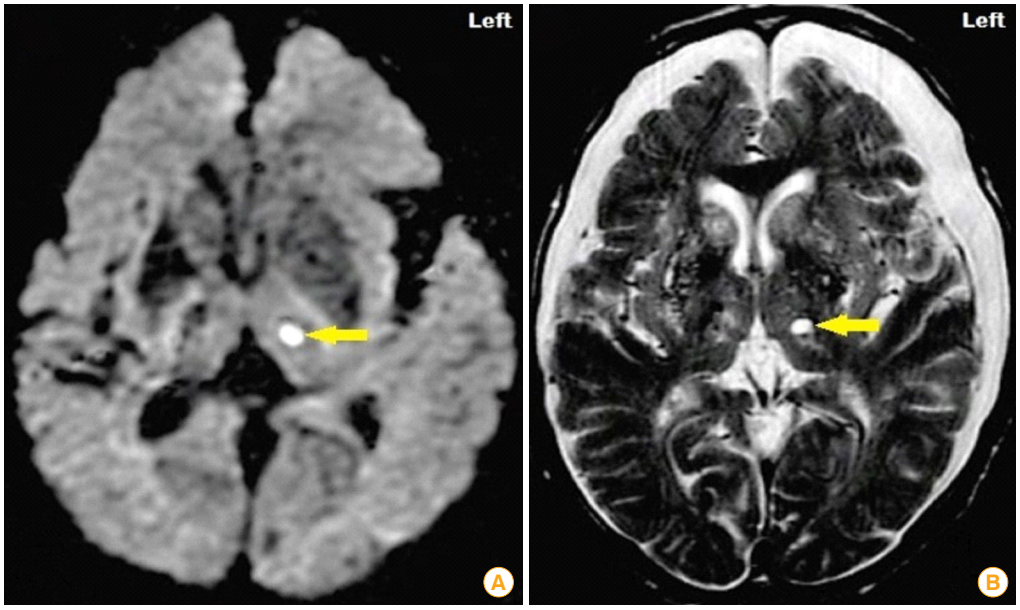

Fig. 2. Brain magnetic resonance imaging. (A) Axial section of the initial diffusion-weighted image (repetition time [TR]=6,000 ms, echo time [TE]=100 ms), performed on admission (arrow). (B) Axial section of the follow-up T2-weighted imaging (TR=4,500 ms, TE=90 ms), performed 2 weeks after admission (arrow).

bilateral frontotemporal lobes (Fig. 2B). The patient was discharged after 21 days with a satisfactory clinical condition and was recommended to receive regular rehabilitation and exercise. The patient gave written informed consent for publication of the researches details.

Discussion

COVID-19 mainly affects the respiratory system, ranging from mild flu-like symptoms to severe acute respiratory syndrome. In a subset of patients with yet unknown causes, COVID-19 has a particularly tempestuous course characterized by inflammatory cytokine response (storm) and multi-organ failure and may be potentially fatal. Extra respiratory multi-systemic complications such as neurologic, thrombotic, hematologic, cardiovascular, renal, liver, musculoskeletal, dermatologic, psychological, and gastrointestinal have all been reported in the medical literature. The risk of both venous and arterial thromboembolism is significantly increased in COVID-19 patients. Even after discharge, recovery, or vaccination, thromboembolism is one of the most common causes of sudden or undetected morbidity or mortality. The mechanisms leading to these complications are increasingly being studied. However, there is a lack of data about the disease course once the patient has had clinical and/microbiological recovery [5-7].

The safe implementation of vaccines is very important, and now many cases of unusual thrombotic or hemorrhagic or both events, especially following the ChAdOx1 nCoV-19 vaccine, have been reported. Concern about neurological complications from COVID-19 vaccines escalated in the fall of 2020 when many cases of transverse myelitis and Guillain-Barré syndrome manifested after receiving the Oxford/AstraZeneca vaccine [2,8] After that, many European countries (such as Austria, Norway, and Denmark) reported unusual thrombotic or hemorrhagic or both events in healthy persons following vaccination with the ChAdOx1 nCoV-19 vaccines. These unpredictable complications led to a temporary or permanent cease in using these vaccines in many countries [8,9]. The Society of Thrombosis and Haemostasis Research (Gesellschaft für Thrombose und Hämostaseforschung e.V.) presented an essential pathomechanism that 4 to 16 days after vaccination with the ChAdOx1 nCoV-19 vaccine, the formation of antibodies against platelet antigens (against the platelet factor 4) occur as an inflammatory reaction and immune stimulation. Without heparin involvement, these antibodies (IgG PF-4) subsequently cause massive platelet activation via the Fc receptor, thrombus formation, and severe thrombocytopenia like heparin-induced thrombocytopenia (HIT). A HIT mimicry mechanism, named VIPIT, was demonstrated in four patients with a sinus/cerebral vein thrombosis after vaccination with AstraZeneca COVID-19 vaccine. There have been reports of unusual thrombotic or hemorrhagic or both events following the ChAdOx1 nCoV-19 vaccine and the possibility of specific immune-mediated thrombocytopenia in the literature. However, it is unclear as to why this immunogenic thrombosis mainly manifests in cerebral vessels [5,8,9].

In this case, clinical presentations, neurological examinations, surface electromyography, and diffusion-weighted MRI demonstrated thromboembolic thalamic stroke in a 72-year-old previously healthy man, 9 days after receiving the first dose of the ChAdOx1 nCoV-19. Severe thrombocytopenia in a patient with a thromboembolic thalamic stroke was a significant finding. We managed this case based on the diagnostic and therapeutic algorithm in patients with thrombocytopenia/thrombosis following the AstraZeneca COVID-19 vaccine. Detecting the IgG PF-4 in the blood, negative HIPA test, and positive modified HIPA test presented the VIPIT as a predisposing or main case of the thromboembolic thalamic stroke. We admitted the patient to the ICU and treated him immediately with nadroparin, sodium ozagrel, edaravone, methylprednisolone, and haloperidol. His hemi-chorea improved gradually during 2 weeks, but on the follow-up brain MRI, he had a chronic lesion with deficiency of cerebral blood flow in the bilateral basal ganglia and remarkable brain atrophy in the bilateral frontotemporal lobes. Warfarin was started in replace of nadroparin and was titrated by monitoring PT levels for the next 3 months. Finally, we discharged him after 21 days with advice to rehabilitation exercise and follow-up [5].

In conclusion, thromboembolic thalamic stroke with severe thrombocytopenia, presence of the IgG PF-4 in the blood, negative HIPA test, and positive modified HIPA, 4–16 days after receiving the first dose of the ChAdOx1 nCoV-19 vaccine, represent the novel immune-mediated responses to the vaccine similar HIT mimicry mechanism, named VIPIT [5,8,9]. Our patient may be immunized against severe acute respiratory syndrome coronavirus 2, but he lost some of his best motor and cognitive functions. We believe that VIPIT due to the ChAdOx1 nCoV-19 needs more extensive investigations in the future and has great importance for clinicians worldwide

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for rapid identification, diagnosis, and treatment of similar cases.

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References

1. Gore M, Bansal K, Asuncion RM. Lacunar stroke. Treasure Island (FL): StatPearls Publishing; 2021.
2. Das AS, Regenhardt RW, Feske SK, Gurol ME. Treatment approaches to lacunar stroke. J Stroke Cerebrovasc Dis 2019;28:2055-78.
3. Venkataraman P, Tadi P, Lui F. Lacunar syndromes. Treasure Island (FL): StatPearls Publishing; 2020.
4. Gupta N, Pandey S. Post-thalamic stroke movement disorders: a systematic review. Eur Neurol 2018;79:303-14.
5. Oldenburg J, Klamroth R, Langer F, et al. Diagnosis and management of vaccine-related thrombosis following AstraZeneca COVID-19 vaccination: guidance statement from the GTH. Hamostaseologie 2021;41:184-9.
6. Shahali H, Ghasemi A, Farahani RH, Nezami Asl A, Hazrati E. Acute transverse myelitis after SARS-CoV-2 infection: a rare complicated case of rapid onset paraplegia. J Neurovirol 2021;27:354-8.
7. Darvishi M, Shahali H. Overt hematochezia : a rare gastrointestinal presentation in patients with corona virus disease 2019. Med J Armed Forces India 2021;77(Suppl 2):S494-8.
8. Schultz NH, Sorvoll IH, Michelsen AE, et al. Thrombosis and thrombocytopenia after ChAdOx1 nCoV-19 vaccination. N Engl J Med 2021;384:2124-30.
9. Blauenfeldt RA, Kristensen SR, Ernstsen SL, Kristensen CC, 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;19:1771-5.