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Case Report

Report of two Cases of Acute Ischemic Stroke after ChAdOx1-S (Oxford–AstraZeneca) Covid-19 Vaccine

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Abstract :

Safety concerns regarding an elevated risk of thrombosis in vaccinated individuals by the AstraZeneca COVID-19 vaccine has been created. This case report describes two cases of acute ischemic stroke within 48 hour of vaccination by AstraZeneca COVID-19 vaccine in MAY 2021, with up to 7 days follow up. Both patients have proven risk factors for cardioembolic events; heart failure and premature atrial contractions in patient 1, atrial fibrillation and mitral valve stenosis in patient 2. We suggest that using AstraZeneca vaccine in patients with cardioembolic risk factors requires more caution.

Keywords : stroke; astrazeneca vaccine; embolic stroke

Introduction

The coronavirus disease 2019 (COVID-19) is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [1]. The risk of both venous and arterial thromboembolism is increased in COVID-19 infection [2]. Effective vaccination is the only way for the radical control of COVID-19. Several vaccines have been licensed and are currently being used in Iran to combat the COVID-19 pandemic. COVID-19 vaccine from AstraZeneca has been recently used in Iran for over 80s individuals. Safety concerns regarding an elevated risk of thrombosis in vaccinated individuals are created according to reports of cases of thrombosis among individuals vaccinated by the AstraZeneca COVID-19 vaccine in the European Union [3]. However, The European Medicines Agency (EMA) Pharmacovigilance Risk Assessment Committee reported that the vaccine is safe, effective and the benefits outweighed the risks [4]. This study reports 2 cases of acute ischemic stroke following AstraZeneca COVID-19 vaccination within 48 hours.

Case 1

An 88-year-old man presented to the emergency room due to acute-onset dysarthria after morning wake up. The patient's past medical history was significant for hypertension and heart failure which he was receiving Furosemide, Spironolactone, and Nitrocontin. The patient was vaccinated for COVID-19 (Vaccine AstraZeneca) 36 hours before the onset of symptoms. Vital signs were within normal limits. Neurological examination was positive for dysarthria and minor left facial paresis. The motor and sensation were intact in the limbs. No other focal neurologic deficit was seen in neurological examination. National Institutes of Health Stroke Scale (NIHSS) score was 2. Laboratory studies including complete blood count (CBC) and complete metabolic panel (CMP) were within normal limits. Computed tomography (CT) scan of the head showed no acute intracranial abnormality. Magnetic resonance imaging (MRI) was subsequently obtained and revealed right frontal cortical infarction in territory of the superior division of middle cerebral artery (MCA) (figure 1).

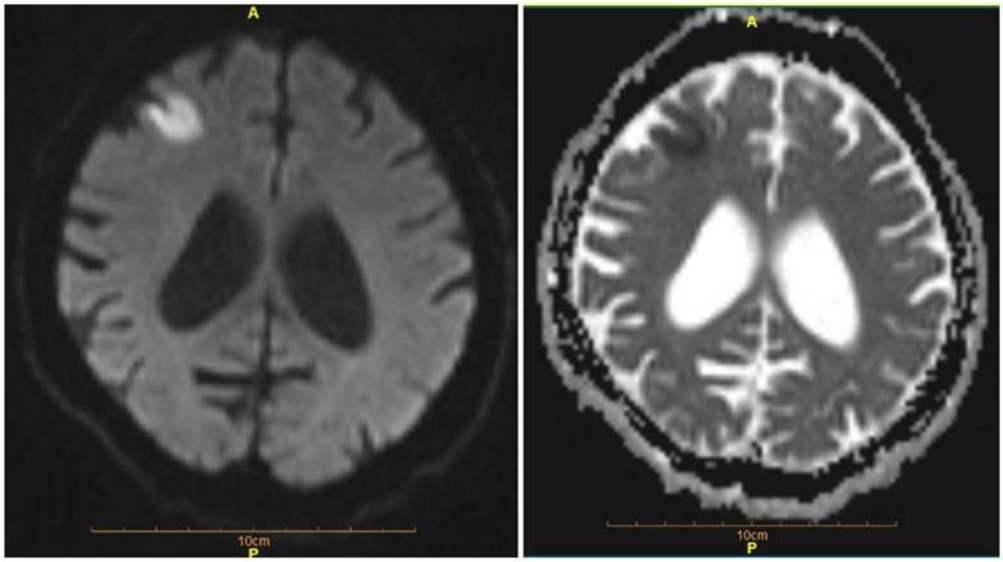

Figure 1: Axial view of a magnetic resonance image of the brain, an increased signal in diffusion-weighted imaging sequence (DWI) (A) and decrease signal in apparent diffusion coefficient (ADC) (B); consistent with Right cortical frontal acute ischemic infarction, which is in the territory of superior division of right middle cerebral artery.

Magnetic resonance venography (MRV) was normal. Dual antiplatelet therapy; clopidogrel 75 mg daily and aspirin 80 mg daily; and high-intensity statin was started. EKG showed premature atrial contractions. Echocardiography reported ejection fraction of 20%. Carotid/vertebral duplex and Transcranial Doppler (TCD) reported no significant stenosis. According to mentioned findings, with the diagnosis of embolic stroke, Aspirin and Clopidogrel were discontinued, and Warfarin was started. After international normalized ratio (INR) reached above 2, the patient was discharged. The patient was re-examined after 7 days. The INR was remained in *therapeutic* range [2,3] NIHSS score was reduced to 1 and no other thromboembolic events was happened.

Case 2

An 83-year-old man presented to the emergency room due to acute-onset dysarthria, right-sided facial droop, and right-sided hemiparesis since 6 hours ago. The patient's past medical history was significant for hypertension and chronic kidney disease which he was receiving metoprolol, losartan, furosemide, and allopurinol. The patient was vaccinated for COVID-19 (Vaccine AstraZeneca) 24 hours before the onset of symptoms. Vital signs were within normal limits. Neurological examination was positive for dysarthria, right facial paresis, right-sided hemiplegia affecting the upper and lower extremities and right–sided hemisensory loss. National Institutes of Health Stroke Scale (NIHSS) score was 10. Laboratory studies including CBC and CMP were within normal limits. CT scan of the head showed acute infarction in the left frontal region. MRI was subsequently obtained and revealed left frontal infarction with hemorrhagic transformation in territory of the superior division of MCA (figure 2).

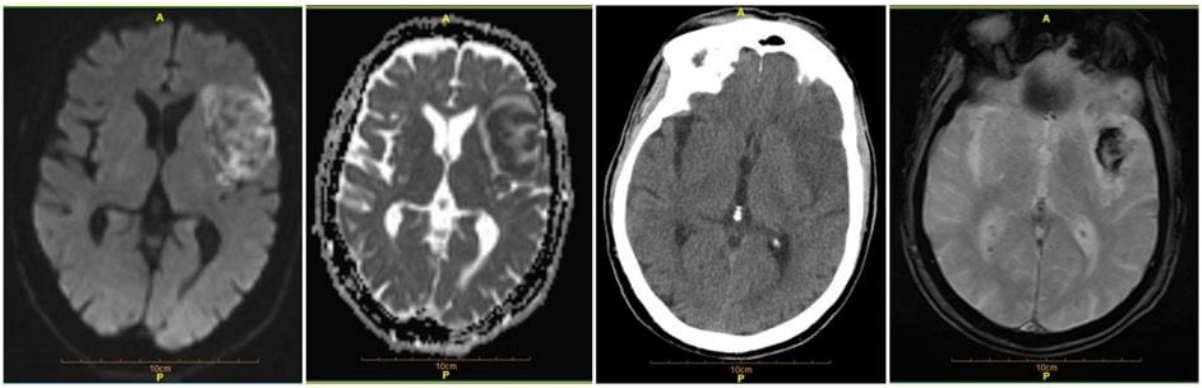

Figure 2: Axial view of a magnetic resonance image of the brain, an increased signal in diffusion-weighted imaging sequence (DWI) (A), decreased signal in apparent diffusion coefficient (ADC) (B), hypodensity in CT scan (C), and decrease signal in Gradient echo sequences (GRE); consistent with acute ischemic infarction in territory of superior division of left middle cerebral artery with hemorrhagic transformation.

MRV was normal. Aspirin 80 mg daily as well as high-intensity statin was started. EKG showed atrial fibrillation. Echocardiography revealed an ejection fraction of 55%, moderate mitral stenosis and moderate mitral regurgitation. Carotid/vertebral duplex and TCD showed no significant stenosis. According to mentioned findings, with the diagnosis of embolic stroke, aspirin was discontinued, and Warfarin was started. After INR

reached above 2, the patient was discharged. The patient was re-examined after 7 days. The INR was remained in *therapeutic* range [2.6], NIHSS score was remained 10 and no other thromboembolic events was happened.

Discussion:

Chimpanzee adenovirus encoding the SARS-CoV-2 spike glycoprotein (ChAdOx1-S)
known as Oxford–AstraZeneca vaccine is one of the several vaccines produced to combat COVID-19 infection [5]. EudraVigilance (EV) database [6] reported 54,571 adverse reaction (AR) for ChAdOx1-S. Most frequent ARs were mild to moderate in severity, including injection site tenderness, injection site pain, fatigue, headache, malaise, myalgia, and pyrexia [5].

However, severe side effects have also been reported to a limited extent, which in some cases has caused death [4,5]. One of these severe complications was an incidence of thromboembolic events [3]. According to EMA, among approximately 5 million Oxford–AstraZeneca vaccine recipients, 28 cases of thromboembolic events had been reported by March 10, 2021 [4]. These reports mainly included pulmonary embolism, cerebral venous sinus thrombosis, deep vein thrombosis, thrombophlebitis, pelvic venous thrombosis and one carotid artery thrombosis [4]. More than half of the reports were people over 85 years old. Paul Ehrlich Institute (PEI) had reported 13 cases of sinus or cerebral vein thrombosis among 1.6 million AstraZeneca recipients [3]. The Interval time between vaccination and thromboses was 4 to 16 days in 12 women, and one managed 20 to 63 years [3]. The patients also had a triad of thromboembolic events; thrombocytopenia and anti-PF4 antibodies appear to be characteristic of the Heparin-induced-thrombocytopenia (HIT), which was also reported in other reports [7-12]. The vaccination is likely to induce the formation of antibodies against platelet antigens. [3] These antibodies cause platelet activation via the Fc receptor. The same thing was happening in heparin-induced thrombocytopenia (HIT) [3]. No other mechanism has been suggested to explain these thrombotic events so far.

About 70% of patients with HIT develop thrombosis, most often vein thrombosis, but arterial thrombosis has also been reported [13]. Reports have been mostly related to venous thrombosis [7-12], and only a few cases of arterial thrombosis have been reported [7]. In this article, we describe two patients who experience arterial ischemic stroke after receiving the ChAdOx1-S vaccine. The median age was 85 years old, and both of them were male who is contradicting other articles that reports of priority of female compared to males.
Both patients have proven cardioembolic risk factors for cardiovascular [14]. Patient 1 (reduction in EF, EF=20%) and patient 2 (mitral stenosis and atrial fibrillation rhythm) were prone to cardioembolic events. By so far, they have no history of stroke or transient ischemic attack before vaccination.
We believe that HIT was not a mechanism implicated in arterial embolism or arterial thrombosis in our patients. There are reasons to support this claim. In both patients, there was no progressive platelet fall or platelet drop of more than 50%. Also, the clot formed on the first and second day after vaccination, which is contrary to the classic HIT diagnostic criteria [13]. According to the 4T criteria of determining HIT possibility [15], our patients are categorized as a low probability for HIT. Therefore, platelets Antibodies do not evaluate.

Regardless of HIT mechanism, it is unclear whether there is a specific link between the Oxford–AstraZeneca vaccine and development of thromboembolic events or its just co-accidental happening. According to presence of cardioembolic risk factors in both of our cases, it is suggested to use AstraZeneca vaccine in patients with cardioembolic risk factors with more cautions. However, further studies will be necessary to evaluate this relationship.

References:

1. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet (London, England). 2020;395(10223):497-506.
2. Connors JM, Levy JH. COVID-19 and its implications for thrombosis and anticoagulation. Blood. 2020;135(23):2033-2040.
3. Oldenburg J, Klamroth R, Langer F, Albisetti M, von Auer C, Ay C, et al. Diagnosis and Management of Vaccine-Related Thrombosis following AstraZeneca COVID-19 Vaccination: Guidance Statement from the GTH. Hamostaseologie. 2021.
4. Tobaiqy M, Elkout H, MacLure K. Analysis of Thrombotic Adverse Reactions of COVID-19 AstraZeneca Vaccine Reported to EudraVigilance Database. Vaccines. 2021;9(4).
5. Voysey M, Clemens SAC, Madhi SA, Weckx LY, Folegatti PM, Aley PK, et al. Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK. The Lancet. 2021;397(10269):99-111.
6. European Medicines Agency. EudraVigilance: European Database of Suspected Adverse Drug Reaction Reports. Available online: http://wwwadrreportseu/en/backgroundhtml (accessed on 15 March 2021).
7. Bayas A, Menacher M, Christ M, Behrens L, Rank A, Naumann M. Bilateral superior ophthalmic vein thrombosis, ischaemic stroke, and immune thrombocytopenia after ChAdOx1 nCoV-19 vaccination. Lancet (London, England). 2021;397(10285):e11.
8. Bjørnstad-Tuveng TH, Rudjord A, Anker P. Fatal cerebral haemorrhage after COVID-19 vaccine. Tidsskrift for den Norske laegeforening : tidsskrift for praktisk medicin, ny raekke. 2021;141.
9. Tiede A, Sachs UJ, Czwalinna A, Werwitzke S, Bikker R, Krauss JK, et al. Prothrombotic immune thrombocytopenia after COVID-19 vaccine. Blood. 2021.
10. 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. Journal of thrombosis and haemostasis : JTH. 2021.
11. Greinacher A, Thiele T, Warkentin TE, Weisser K, Kyrle PA, Eichinger S. Thrombotic Thrombocytopenia after ChAdOx1 nCov-19 Vaccination. The New England journal of medicine. 2021.
12. Schultz NH, Sørvoll IH, Michelsen AE, Munthe LA, Lund-Johansen F, Ahlen MT, et al. Thrombosis and Thrombocytopenia after ChAdOx1 nCoV-19 Vaccination. The New England journal of medicine. 2021.
13. Warkentin TE, Roberts RS, Hirsh J, Kelton JG. An improved definition of immune heparin-induced thrombocytopenia in postoperative orthopedic patients. Archives of internal medicine. 2003;163(20):2518-2524.

14. Pillai AA, Tadi P, Kanmanthareddy A. Cardioembolic Stroke. StatPearls [Internet]. 2020.
15. Cuker A, Gimotty PA, Crowther MA, Warkentin TE. Predictive value of the 4Ts scoring system for heparin-induced thrombocytopenia: a systematic review and meta-analysis. Blood. 2012;120(20):4160-4167.

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