Takayasu’s arteritis diagnosed/relapsed following COVID-19 vaccine: A case report with literature review

Abdul-Wahab Al-Allaf*, Maab F. Elhaj, Yousr Al-Allaf
1 Internal Medicine, Rheumatology, Hamad Medical Corporation, Doha, Qatar
2 Imperial College School of Medicine, London, United Kingdom

Abstract

COVID-19 infection has been associated with high morbidity and mortality. The vaccines for COVID-19 have been regarded as a necessity to contain the COVID-19 pandemic. Studies indicated that the vaccine is safe, however, there is still some worry about the possible side effects associated with the vaccine. Since the use of the vaccine, there has been an emergence of some case reports and cases series highlighting some temporal relationships between COVID-19 vaccination and the occurrence of some autoimmune diseases. Here we are reporting a 43-year-old female who has had an unexplained complete left vertebral artery occlusion 25 years ago. Then she was asymptomatic after that and leading a normal life. Two weeks after her AstraZeneca COVID-19 vaccine, she presented to the clinic with new symptoms of left upper limb claudication pain, which increased with simple physical activity, with weak left-hand grip and associated with dizziness. We confirmed for the first time the diagnosis of Takayasu’s arteritis based on the radiological, clinical and laboratory criteria. The patient responded very well to prednisone with remarkable improvement in her laboratory and clinical symptoms. Up to our knowledge, this is the first case of post-COVID-19 vaccine reactivation of Takayasu’s arteritis. Although it is a rare complication, it is valuable to bring to our attention this possible association.

Introduction

Vasculitis is a class of varied disorders identified by vascular wall inflammation, with complicated and poorly identified pathophysiological mechanisms [1]. Vaccine effects on the immune system are a debatable matter. There have been many vaccine-associated immunological adverse outcomes that have been mentioned in the literature; for instance, systemic lupus erythematosus has been described with the papilloma vaccine, and Guillain-Barre syndrome was described in association with the influenza vaccine and immune demyelination was reported as a consequence following the hepatitis B vaccine. Although direct causality is questionable, the association is probable [2, 3, 4]. Detection of immunological adverse consequences of COVID-19 vaccines is challenging and of important scientific and community concern [4]. In the literature, there were several cases of vasculitis reported post-vaccine. Here we are the first to report a post-COVID-19 vaccine leading to Takayasu’s arteritis reactivation.

Case Presentation

A 43-year-old lady, with a background of unexplained complete occlusion of the left vertebral artery 25 years ago was confirmed by CT angiogram after which she was stable with no complaints. She was also diagnosed with latent tuberculosis two years before this presentation, for which she was treated with anti-tuberculous medications for four months.

She presented to the clinic on the 18th of April 2021, two weeks after taking her second dose of the AstraZeneca COVID-19 vaccine with a 10-day
history of severe left upper limb pain on minimal physical activity, rated as 8/10 as per the normalized scale ratio (NRS). The pain was dull in character, continuous and increased with activities; especially overhead activities. It was also associated with left-hand grip weakness and mild dizziness. The patient reported symptoms suggestive of acid reflux disease for which she used to take pantoprazole. Upon systemic review, she described shortness of breath and easy fatiguability even with minor activities. She was initially assessed by the vascular surgery team and they recommended oral Aspirin 100 mg tablet daily and oral pentoxifylline 400 mg twice daily and referred her to a rheumatology clinic.

Upon rheumatological review, her main symptom is related to the pain in her left upper limb, which worsen by physical activities and feeling tired and lethargic. She denied oral ulcers, Sicca symptoms, weight loss, photosensitivity and night sweats. On examination, there is an absent palpable left radial pulse with a normal right radial pulse and normal blood pressure on both sides (119/82 on the left arm and 115/77 on the right side). Heart rate was 81 beats/min, respiratory rate was 18 breaths/min, and saturation (SPO2) was 99% on room air. There was no bruit in the neck or subclavian areas, with no lymphadenopathy or organomegaly.

Laboratory workup showed Erythrocyte Sedimentation Rate (ESR) at 13 mm/hr, C-Reactive Protein (CRP) of 10 mg/l, with raised White Blood cell Count (WBC) 18*10^9/l, and normal renal & liver function, lipid profile, urinary Protein Creatinine Ratio (PCR) with negative Antineutrophil Cytoplasmic Antibodies (ANCA), Anti-nuclear antibody (ANA), Rheumatoid factor (RF), Anti-cyclic citrullinated peptide (anti-CCP), hepatitis B, C and Treponema pallidum serology.

CT angiogram of the left upper limb findings revealed complete obliteration of the left subclavian artery after the origin of the left vertebral artery with severe attenuation of the proximal left subclavian artery and vertebral artery. It also showed reconstitution of the left upper limb arterial supply from cervicothoracic collaterals from the axillary artery onward with mild and irregular circumferential narrowing of the right subclavian artery with subtle wall enhancement (Fig 1A, 1B).

Figure 1A: Reconstructed images (CT Angiogram) showed complete obliteration of the left subclavian artery after the origin of the left vertebral artery with severe attenuation of the proximal left subclavian artery and vertebral artery (blue arrows) and left upper limb arterial supply from cervicothoracic collaterals from the axillary artery (green arrows).

Figure 1B: Reconstructed images (CT Angiogram) showed complete obliteration of the left subclavian artery after the origin of the left vertebral artery with severe attenuation of the proximal left subclavian artery and vertebral artery (blue arrows).
The patient was started on prednisone 30 mg oral for two weeks with tapering by 5 mg every two weeks and showed significant improvement. After tapering the steroid dose below 20 mg, her symptoms started to recur. Her steroid was increased back to 25 mg and she was started on the steroid-sparing agent Methotrexate 15 mg weekly with folic acid 5 mg weekly, 24 hours after her methotrexate dose.

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**Discussion**

To the best of our knowledge, this is the first case of post-COVID-19 vaccine Takayasu’s arteritis reactivation identified in the literature and which occurred 25 years after her initial unexplained symptoms.

Takayasu arteritis (TA) is a granulomatous inflammatory vasculitis of large vessels with rare incidence and unknown cause [5]. If untreated, usually results in fibrosis of the adventitia, media, and intimal layers of large vessel walls as a result of myofibroblast proliferation and arterial wall infiltration by macrophages, T lymphocytes and monocytes [5, 6]. This leads to arterial occlusion, aneurysmal dilatation, or significant arterial stenosis [6]. The majority of TA cases (80%-90%), have been reported in young females, aged ten to forty years [6]. It is more prevalent in Asia, with the highest incidence being in Japan with approximately 150 new cases of TA a year per million population. In contrast, in the United States of America and Europe, the incidence was found to be 1-3 new cases a year per million population [7].

Predominantly, TA impacts the aorta and its major branches; the pulmonary, subclavian, and common carotid arteries [6]. It is manifested clinically in two stages. Patients initially present with systemic manifestations such as headaches, fever, malaise, weight loss, arthralgia, carotidynia and myalgia which represent the early inflammatory pre-pulseless stage. In the later pulseless stage, patients usually present after months-years with symptoms associated with end-organ ischemia which incorporate neurological manifestations and limb claudication such as systemic arterial hypertension, absent or weak peripheral pulses, arterial bruits, and aortic regurgitation [8]. Although diagnostic criteria exist [9], the lack of specific laboratory markers and the nonspecific presentation of the disease delays the diagnosis of early pre-stenotic disease leading to life-threatening outcomes [6, 8].

In our case, we confirmed the diagnosis of the TA 25 years after the initial unexplained complete occlusion of the left vertebral artery. The primary objectives of management of TA include early diagnosis and initiation of steroid treatment intending to prevent complications such as occlusive or stenotic lesions and hypertension. As the disease primarily affects women of child-bearing ages management should include a multidisciplinary approach with the contribution of rheumatologists, vascular surgeons, obstetricians, cardiologists and anesthesiologists [7]. Some TA cases need surgical intervention and the indication and timing for surgery are very important [10].

AstraZeneca (AZD1222) vaccine was developed by Oxford University and utilizes a non-replicating adenovirus chimpanzee as a transmitter (ChAdOx1) and is altered to promote the SARS-CoV-2 S protein [11].

Multiple case reports highlighted the association between the COVID vaccine and the development or reactivation of vasculitis in literature. Abdelhamid Naitlo et al, 2021, reported a case of Henoch-Schönlein Purpura (HSP), which developed 8 days following AstraZeneca COVID-19 vaccination in a sixty-two-year-old patient [1]. Fadi Kharou et al, 2021, also reported a case of a 60-year-old male who presented 3-days following his first dose of Pfizer BioNTech COVID-19 vaccine with blurry vision, frontotemporal headaches, along with generalised weakness and diffuse arthralgia, consistent with possible temporal arteritis [4]. Moreover, Abdul-Wahab Al-Allaf et al, 2022, reported a medium vessel abdominal vasculitis associated with anterior uveitis one week following the second dose of Pfizer BioNTech COVID-19 vaccine who presented to the hospital with epigastric and right upper quadrant abdominal pain [12].

The precise post-vaccine vasculitis pathophysiology is still inadequately understood. The most revised theory is immunological, similar to the mechanism relating Polyarteritis Nodosa (PAN) to HBV Ag-Ac immune complexes [13]. In the majority of vasculitis, the causative mediator is unknown. We are proposing that the potential mechanism by which the COVID-19 vaccine triggers autoimmunity includes molecular mimicry, leading to the production of autoantibodies and there is a possible role of certain vaccine adjuvants. Previously, it has been well proposed that Influenza, hepatitis B and human papillomavirus vaccines trigger autoimmunity through molecular mimicry [2, 3, 4].

We have to keep in mind that COVID-19 infection itself could lead to the development or reactivation of autoimmune disease. It also could have significant morbidity and mortality if not prevented. The vaccine has saved many lives
and altered the course of the COVID-19 pandemic. Also, the temporal relation is not proof of causation. Accordingly, we strongly advise the COVID-19 vaccine. However, we need to raise awareness of such autoimmune disease development or reactivation soon after the COVID-19 vaccines for early diagnosis and better management and outcome.

**Conclusion**

Possible complications of COVID-19 vaccines have become of special interest to both healthcare workers and the public. Our report showed a good temporal relation between the COVID vaccination and the occurrences of TA reactivation. However, this should not be deemed to signify causality. To the best of our knowledge, we are the first group to report post-COVID-19 vaccine TA reactivation and we advise our colleagues to remain vigilant for such temporal associations so that any potential cases are promptly diagnosed, evaluated, and treated.

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**Statement of Ethics:** The case was approved by the Hamad Medical Corporation Medical Research Center, and the patient signed a written informed consent to publish her case.

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**References**