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THROMBOCYTOPENIA: VACCINATION INDUCED or SPORADIC?

Anaesthesiology

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ABSTRACT

No sooner than an outbreak of 'pneumonia of unknown etiology' started from Wuhan, China, in November 2019, the entire world got engulfed by it. The causative organism was identified to be a novel beta- coronavirus named SARS CoV 2. On March 11th 2020, the WHO declared the outbreak as a 'pandemic'. Where on one hand, untiring efforts were made to curtail the spread of this highly contagious disease, on the other, challenges were encountered in developing a vaccine for the same. A successful COVID 19 vaccine should not only be potent, effective and safe but also free of any serious adverse reactions. After serial phase trials, India developed two vaccines – Astrazeneca's Covishield, manufactured by the Serum Institute in Pune, and Bharat Biotech's Covaxin. With the mammoth vaccination drive going on in the country, information of post-vaccination side-effects are pouring in from every nook and corner. The most striking of all is the incidence of the blood clotting events reported in forms of brain ischaemia. Whether they are related to vaccination or sporadic coincidence is unknown. Our institution also witnessed such cases which are being reported in this article.

KEYWORDS

COVID 19 Vaccination, Side-effects, Vaccine-induced thrombotic thrombocytopenia, mRNA vaccines

INTRODUCTION:

Coronavirus disease 2019 (COVID 19) is believed to originate from the Huanan seafood market in Wuhan, China. It was declared a pandemic by the World Health Organization (WHO) after the disease had swept over 200 countries round the globe. It is considered the most devastating one in the last 100 years after the outbreak of the Spanish Flu. This pandemic has crippled the world in terms of human health, life and economy. The medical professionals of varied countries have spent almost a year in a desperate attempt to develop a successful and effective COVID 19 vaccine. India started its first mass vaccination drive on the 16th of January 2021, shielding the healthcare professionals and the frontline workers. Till date over 60 million people in India have received the first dose of vaccine. Incidences of side-effects have also seen an upward trend with the inoculation being carried out in large numbers.

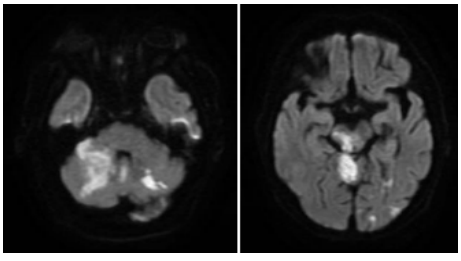
While the country has witnessed the second wave of the virus outbreak, managing the vaccine related complications is a new menace in itself. One such complication is the blood clotting event which largely present as brain infarct and acute myocardial infarction. Such cases have been documented not only in India but also abroad countries. The ongoing researches have suspected a pro-thrombotic event post vaccination responsible for such incidences. Two such cases of cerebrovascular accidents of ischaemic origin in patients having received COVID 19 vaccination were admitted in our institution, which is a tertiary care center of the state capital.

CASE REPORTS

Case 1

Mr X, 70 years old male is a known hypertensive and diabetic on regular medications for last fifteen years. He was brought to the emergency department on 5th of April '21 with sudden onset unconsciousness and left sided weakness for over four hours. On examination his GCS was E2V2M4, vital parameters within normal limit; and a saturation of 92% at room air. A history of receiving first dose of Covid vaccination on 31st of March'21 was also elicited. Routine blood and urine investigations were carried out. He also underwent MRI and MRA Brain, the reports of which were suggestive of acute infarct in right cerebellum, bilateral corona radiata and occipital region. Right Vertebral Artery could not be visualised suggesting occlusion by thrombus. Also, his blood counts showed evidence of reduced platelets. He was treated conservatively in the intensive care unit. Under strict vigilance and rehabilitation, Mr X was discharged after a period of two weeks with a GCS of E4V2M6.

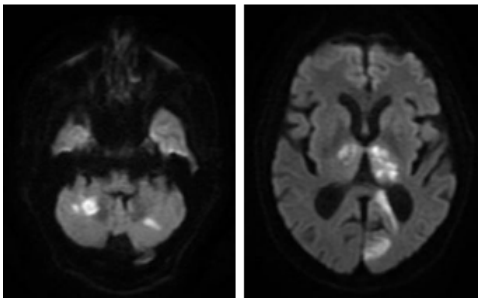
(Image 1: Ax DWI of patient of Case 1).



Case 2

Mr Y, 65 years old male with no known comorbidity presented to the emergency department on 8th of April '21, intubated and receiving oxygen through Bain's circuit. The attendants briefed that the patient had a sudden onset of slurring of speech, grunting sound vocally and decreased consciousness, eight hours ago. He was taken to the nearest PHC, where he became unconscious, was intubated and provided respiratory support. He had received his first shot of Covid vaccine on the 2nd of April '21. On arrival to our hospital for further management, his GCS was found to be E1VTM1, pupils dilated and non-reactive to light, however vitals were maintained. Standard investigations were carried out. MRI Brain showed acute infarct in cerebellum, thalamus, midbrain and pons suggestive of basilar artery thrombus; also the platelet showed mild decline in numbers. The patient was put on mechanical ventilation and counselling for organ donation was done. Attendants refused and the patient was discharged against medical advice.

(Image 2: Ax DWI of patient of Case 2).



DISCUSSION:

Coronavirus disease 2019 (COVID-19), the illness caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has been responsible for the continued morbidity and mortality faced by the

globe in the last couple of years. Various measures were owned by different countries to contain the spread of this contagious disease; however, the most crucial one of paramount importance was vaccinating the mass to develop herd immunity against this viral illness. This lead to the development of vaccines at an unprecedented speed, subjected to hastened clinical phase trials. In India, both the vaccines, Covaxin and Covishield were engineered using an Adenovirus-based (AdV) platform to deliver the mRNA molecule - coding for the spike protein of SARS-CoV-2. Vaccination triggers the immune system resulting in the production of neutralizing antibodies against SARS-CoV-2. (1)

During the later days of February 2021, when mass vaccination was occurring across the continents, a new clinical syndrome characterized by thrombosis at atypical sites combined with thrombocytopenia was observed in multiple patients, days after being inoculated. The identification of this rare but potentially lethal clinical entity raised concerns amongst the mass leading to reconsideration of the vaccination strategies in many countries (2). The entity was termed as 'vaccine induced immune thrombotic thrombocytopenia (VITT)', of which cerebrovascular thrombotic events were found to contribute the most percentage- wise. As per the American Society of Hematology, VITT is defined as a clinical syndrome characterized by all of the below described abnormal laboratory and radiologic abnormalities occurring in individuals 4 to 30 days after vaccination COVID vaccines.

- Development of thrombosis at uncommon sites includes cerebral venous sinus thrombosis (CSVT)/splanchnic venous thrombosis.
- Mild to severe thrombocytopenia. However, a normal platelet count does not exclude the possibility of this syndrome in its early stages.
- Positive antibodies against platelet factor 4 (PF4) identified by enzyme-linked immunosorbent assay (ELISA) assay. (3)

The pathogenesis of vaccine-induced thrombotic thrombocytopenia is not well established at this time. However, given its clinical presentation and biochemical similarities to heparin-induced thrombocytopenia, which is a prothrombotic and potentially life-threatening condition, a similar immune-mediated response induced by these adenoviral vector vaccines has been postulated (4). The following are the proposed hypotheses: (i) the role of antibodies against platelet factor 4 (PF4), (ii) the direct interaction between adenoviral vector and platelets, (iii) the cross-reactivity of antibodies against SARS-CoV-2 spike protein with PF4, (iv) cross-reactivity of anti-adenovirus antibodies and PF4, (v) interaction between spike protein and platelets, (vi) the platelet expression of spike protein and subsequent immune response, and (vii) the platelet expression of other adenoviral proteins and subsequent reactions. It is also plausible that thrombotic thrombocytopenia after the COVID-19 vaccine is multifactorial (5).

Based on the treatment guidelines by the British Society of Haematology (BSH), Society of Thrombosis and Haemostasis Research (GTH), and American Society of Hematology (ASH), patients suspected of VITT typically had platelet nadir ranging from 9,000 to 1,07,000. No correlation has been demonstrated between the onset of this reaction and laboratory evaluation, for example, of markers of clotting function, such as PT or aPTT. However, the identification of a weak reduction in platelet number should generate unjustified alarmism and medical intervention (6).

In accordance with the above discussion, both the patients received at our tertiary care centre had a history of receiving Covid vaccine within the time frame of 4 – 30 days. The imaging (MRI Brain) of the patients were evident of thrombotic event and their laboratory reports (platelet count) were also consistently low. The availability of ELISA test of antibodies against platelet factor 4 (PF4) is not available in this region so we could not convincingly term them as a cases of 'Vaccine induced immune thrombotic thrombocytopenia' (VITT). However these kind of cases should undergo further test to formally label them as VITT.

CONCLUSION

Vaccination against COVID-19 is crucial in containing the spread of SARS-CoV-2 and controlling this pandemic. Despite of the reported vaccine related morbidity and mortality, the benefits of the vaccine outweigh its complications. The motive behind reporting these cases is to create an awareness amongst the policy-making bodies so that measures can be taken at the preventive level by standardising a treatment protocol in susceptible groups receiving vaccination; or by following a streamlined diagnostic approach in suspected cases.

DECLARATION OF PATIENT CONSENT

The authors clarify that they have obtained all appropriate patient consent forms, the particulars of which include sharing of their clinical and diagnostic information. The patients understand that their identity will not be disclosed, however anonymity cannot be guaranteed.

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Nil

CONFLICTS OF INTEREST

None

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