Case Series

Post COVID-19 Vaccine-associated Complications

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The COVID-19 pandemic is being fought against worldwide; the major weapon against this pandemic has been the vaccine against it. There are reports of neurological complications and sequelae after COVID-19 vaccinations, some cases with ChAdOx1 nCov-19 is adenovirus vector-based vaccines. In India vaccination program against covid19 is using this vaccine by this vaccine. Reports of vaccine-associated side effects have emerged, which are rare but serious. This case series presents a few such cases reported in our hospitals:- RD Gardi Medical college (CR Gardi Hospital, Ujjain) and Charitable trust Hospital, Ujjain.

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Introduction

Case 1

Case of Vaccine-induced Thrombocytopenia and Thrombosis (VITT)

Background

Few reports of ChAdOx1 nCoV-19 adenoviral vector vaccine association with VIIT are reported in literature [1]. Here we describe a case presented in our hospital with, a presentation suggestive of acute onset cerebrovascular accident, with a history of recent administration of the COVID-19 vaccine (SII ChAdOx1 nCov-19). The patient was found to be a case of cerebral venous thrombosis with thrombosis of the right superior sagittal sinus, transverse sinus, and venous infarct.

As vaccination started, reports emerged of vaccine-associated thrombotic events that were later on recognized as "Vaccine Induced Thrombocytopenia and Thrombosis" (VITT). VITT is seen with vaccination by Adenovirus vector vaccine candidate, ChAdOx1 nCov-19 (AstraZeneca, through the University of Oxford and Serum Institute of India). Several hundred patients would develop this condition after the mass vaccination of millions of individuals through the exact incidence of VITT is unknown and appears rare.

First reported case in the literature, is described as a healthy 49 year old female healthcare worker who received her first dose of ChAdOx1 nCov-19 in mid-February 2021 and presented with acute onset pulmonary embolism and portal vain thrombosis which proved fatal.

Pathophysiology

VITT (Vaccine Induced Thrombocytopenia & Thrombosis) is caused by antibodies against platelet factor 4 (PF4, also called CXCL4) bound to platelets. This immunoglobulin G (IgG) activate platelets via low-affinity platelet FcγIIa receptors . These receptors are on the platelet surface and bind the Fc portion of IgG. They cause platlet activation and possibly other immunological activations and results in marked stimulation of the coagulation system and clinically significant thromboembolic complications., A similar syndrome of heparin-induced thrombocytopenia, with a similar mechanism, is known. Hence in VITT,

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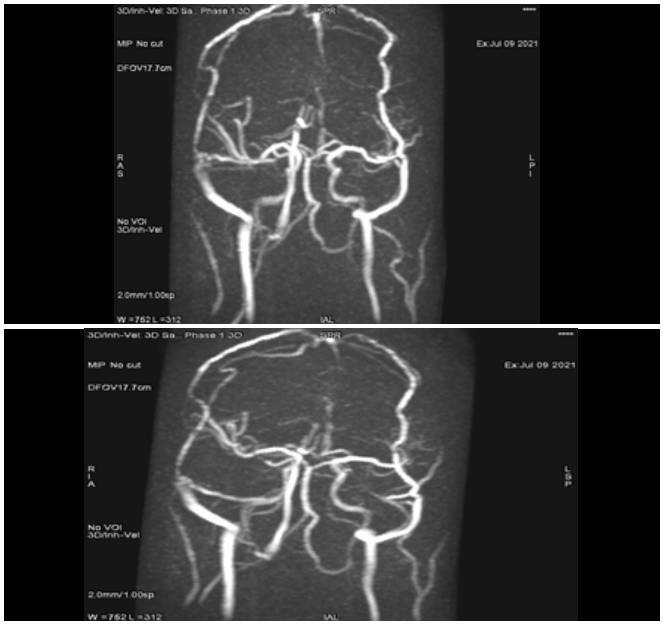

Figure 1: CT Head with MR venogram cuts showing Cerebral Venous sinus thrombosis

enzyme-linked immunosorbent assay (ELISA) PF4

Antibody assay is positive but there is no previous history of heparin exposure, this is

major diagnostic character in VITT along with a recent history of COVID-19 vaccination.

Platelet activation is caused by PF4 bound to platelets by PF4 antibodies, IgG class detectable in PF4/polyanion and PF4 ELISA.

Thrombosis of VITT can occur at typical sites of venous thromboembolism, such as deep vein thrombosis in leg and pulmonary embolism (PE) syndrome is characterized by thrombosis at abnormal sites, including splanchnic (splenic, portal vein, mesenteric) veins adrenal veins (risk of adrenal insufficiency), and brain and eye veins.

Autopsy studies of people who died of VITT show devastating venous thrombosis involving multiple vessels of varying sizes.

Case Presentation

A 60 year old male without any relevant past history presented in the emergency with complaints of persistent headache 2 days, right-sided weakness since 2 days. He had a history of COVID-19 vaccination Covidshield ChAdOx1 nCov-19 (AstraZeneca, University of Oxford, and Serum Institute of India), 1 week before.

On examination, he had right-sided weakness with a power 4/5 in right upper limb and lower limb and right plantar response was extensor, on sensory examination, there was impaired cortical sensation signs on the same side.

Investigations

We posted patient for CT head, suspecting CVA event. The radiology department suspected a Venous sinus thrombosis sign on CT; hence, MR Venogram cuts were additionally taken, which revealed Venous infract in right Parieto occipital region with superior sagittal sinus and transverse sinus thrombosis (Figure 1**).**

His laboratory investigation revealed, d-dimer elevated to 2012 ng/mL (Normal <500 ng/mL), platelet counts of 67000 and apTT of 40 sec against control of 35 seconds. PF4 heparin ELISA was not done in our settings.

Differential Diagnosis

- VITT (Vaccine-induced thrombocytopenia and thrombosis)
- HIT (Heparin-induced thrombocytopenia)

For diagnosis of VITT it is imperative to rule out prior Heparin administration in last 30 days , a positive history of vaccination 5–20 days, and INR, APTT, PT abnormalities to be ruled out for exclusion of DIC and ITP.

A scoring system for the diagnosis of HIT was developed by Lo *et al*., which was adopted due to similarity in pathophysiology. An absence of history of heparin exposure in the past and a presence of COVID-19 vaccination history with implicated vaccines gives diagnostic essentials. Thrombosis events were present in our case.

Scoring System for HIT

Adapted from Lo *et al*. day 0 was considered as the day heparin was started. HIT is defined as the day when platelet count begins to decrease.

A diagnosis of VITT was made and the patient was started on heparin.

Treatment

Therapeutic anticoagulation is one of the main treatments for VITT and is used unless contraindicated by extensive intracerebral hemorrhage. It is unclear whether heparin (unfractionated heparin or low molecular weight heparin [LMW]) is safe, effective or harmful in patients with VITT. Early reports of patients treated with heparin reported clinical deterioration, including death, and an early recommendation was to avoid heparin because VITT resembles HIT. However, with the growing understanding of the pathophysiology of VITT, it appears that heparin may be a reasonable choice for anticoagulation. In a series of 220 individuals with definite or probably VITT, the authors stated that "heparin did not appear to be harmful in patients who received it"; this included approximately one-fourth of individuals who received heparin at some point during their treatment.

Hence we started heparin infusion, at rate of initial: 80 units/kg bolus followed by a continuous infusion of 18 units/kg/hour.

Outcome

The patient was started on heparin infusion and within the next 5 days, the patient was clinically better with his headache resolved and with improvements in his sensory examinations findings. He was subsequently discharged uneventfully on antiplatlet medications and a follow-up is planned.

Discussion

VITT is a new syndrome associated with the COVID-19 vaccine candidate. Arterial adverse events, venous thromboembolism, and thrombocytopenia have been reported after Oxford-AstraZenexa ChAdOx1-S vaccination. Thrombocytopenia appears to be cardinal feature associated with it . . Consumption of platelets and their activation mechanism is similar to HIT syndrome. . Cases of this syndrome have increased worldwide due to millions of vaccinations done against COVID-19. As more and more world population shall be further vaccinated, more such cases are likely to be seen. Awareness about this new emerging syndrome and its management modality is hence desired for clinicians. The syndrome has proved to be fatal, with many deaths on record.

Learning Points

When to suspect

VITT may be suspected in persons who develop symptoms of thrombosis or thrombocytopenia within a reasonable period after administering any of the involved vaccines.

Which scoring system may help?

In classical HIT, the 4Ts score is used to estimate the pre-test probability of HIT and to determine the adequacy of HIT antibody testing. The same is adopted for VITT due to similar pathology. An absence of Heparin exposure history gives the diagnosis.

Case 2

Case of Post Vaccine Guillain Barre syndrome

Background

All viral infections are traditionally considered as a risk factor for GB syndrome due to molecular mimicry. Post-vaccination GB syndrome has been known with many vaccines. Post-COVID-19 vaccination GB syndrome is also reported in the literature, here we present a case with post-COVID-19 vaccine-induced GB syndrome.

Case Presentation

40 year old female, presented with complaint of back pain since and weakness developing around 20–25 days back with an ascending pattern i.e., bilateral lower limbs weakness was followed by weakness in upper limbs within 2 days. Further, in the next few days, the patient developed deviation of mouth to right side with drooling of saliva and right 7^{th} nerve lower motor neuron type of palsy. Patients had a history of COVID-19 vaccination Covidshield ChAdOx1 nCov-19 about 35 days back, followed by an episode of fever which resolved in 2 days with OTC treatment of antipyretics.

On examinations, her vitals were within normal limits, power was 4/5 in all 4 limbs, tone in lower limbs was reduced and bilateral plantars were absent. Knee reflex and ankle reflex were absent, while tone in upper limb was slightly reduced and with diminished DTR in the upper limbs.

There was no relevant past history and the patient was non-diabetic. No significant drug history.

Investigations

On routine investigations , ESR was 30 mm (1 hour), calcium 10.3 (Normal), RBS 159. The rest of the routine tests like CBC, LFT, KFT, electrolyte panels, FBS, ANA, TSH, were under normal limits. Based on ascending weakness, are flexia , with few sensory complaints, we suspected patient to be a case of GBS; hence, a CSF examination was done which showed albumino cytological dissociation, with high CSF protein and low cell counts.

Further, NCS study showed -- *Uncharacterizable Motor + sensory Polyneuropathy involving all four limbs.*

Treatment

Patient showed signs of recovery with supportive treatment and steroid was added to hasten recovery. In the next few days, the patient made an uneventful recovery with the resolution of weakness and sensory symptoms.

Discussion

Though a recent report on ; "Epidemiological and cohort study finds no association between COVID-19 and Guillain-Barre syndrome" [xix], but previous multiple reports [xx] linking GB syndrome and post-vaccine states are known and published in literature.

GBS is a heterogeneous condition characterized by progressive ascending bilateral symmetrical paresthesias and hyporeflexia or areflexia associated with moter weakness. Cranial neuropathy can also

occur. Complement activation, Molecular mimicry, and anti-ganglioside antibody production are all involved in GBS pathogenesis.

Back pain is also an important symptom and may be present before debilitating onset and may mislead clinicians in the early stages of diagnosis.

Few reports of GBS following COVID-19 vaccination are reported in relation of Johnson & Johnson trials.[3] and two other recent case reports related to the ChAdOx1-S/nCoV-19 vaccine in India and Britain.[4,5] As there was another case of GBS in the control group, the Jhonson and Jhonson case was not deemed to be secondary to vaccine group.[3] In other two case reports, cases were also temporally associated with COVID-19 vaccination, and presenting symptom was bilateral facial weakness notably. Therefore the association of GB syndrome and COVID-19 vaccination by Adenovirus Vector COVID-19 vaccines cannot be sufficiently ruled out.

Case 3

Case of Post Vaccine Acute Sensory Neuropathy

Background

Post COVID-19 vaccine, sensory neuropathy cases have been reported in literature. Here we present a case of post covid19 sensory neuropathy as presented to our institute.

Case Presentation

A 40 year old male presented with complaints of tingling & numbness in all 4 limbs since 4 days, mild fever and headache since 3 days. He had a history of COVID-19 vaccination 12 days back. His complaints first started in lower limbs then involved upper limbs. He subsequently had a sensation of insect crawling & tingling over lower and upper limbs.

There was no significant past history , and patient was non-diabetic and non-hypertensive.no significant drug history.

Investigations

On examination ,. there was no other significant finding. There was no neck rigidity or fever recorded during stay. On CSF examination, CSF glucose was 85 mg/dl and CSF protein was 206 mg/dl (significantly increased). CSF microscopy showed total 8 cells/hpf and all were lymphocytes. ANA was negative and

MRI brain was also done as workup and was normal, his Vit B12 levels were >1000pg/ml (Supra Normal Range) All other investigation like CBC, ESR, LFT, KFT, Electrolyte panels, FBS, ANA, TSH were in normal ranges.

His fundus examination was normal and no signs of papilledema or otherwise no any signs of Cushings triad were seen during stay.

Treatment

CSF showed high protein with normal glucose and there was no signs of any meningeal involvement. We concluded it to be immune mediated process, that can be a post vaccine immunological reaction; therefore, he was started on high dose glucocorticoid therapy, which was later tapered and stopped as patient recovered.

The patient showed complete recovery in a few days with steroid therapy , and he was discharged.

Discussion

Post COVID-19 vaccination, small fibre neuropathy [xxi] with similar complaints and symptoms is known, as reported NCS was normal but biopsy showed multilayer inflammation and involvement in small nerve fibers. A similar disease was seen in our case.

The SARS-CoV-2 antibody profile was consistent with the post-vaccination status but ruled out the possibility that previous asymptomatic COVID-19 exposure resulted in a strong immune response. The evolution of the patient's clinical picture immediately after vaccination and the exclusion of other known etiologies suggest a possible causal relationship.

Concerns about neurological complications of vaccination are not new and include the development of Guillain-Barré syndrome (GBS), but the associated risks are small. It is on the order of 1–2 GBS per million doses of influenza vaccine and is favorable for influenza vaccination recommendations. Although rare, a few case reports of small fibre neuropathy following various vaccinations have been described in the literature.

More study is required in this matter.

Conclusion

- The COVID-19 vaccine is safe and effective, and serious reactions after vaccination are rare.
- Millions of people have received COVID-19 vaccines till now, hence more & more cases are being reported.
- VITT is a new syndrome associated with COVID-19 vaccine candidates. Thrombocytopenia appears to be cardinal feature associated with it. The consumption of platelets and their activation mechanism is similar to HIT syndrome. As more and more world population shall be further vaccinated, more such cases are likely to be seen.
- The association of GB syndrome and COVID-19 vaccination by Adenovirus Vector covid19

vaccines cannot be sufficiently ruled out. GBS is a heterogeneous disease. It is typically characterized by rapidly progressive ascending bilateral paresthesias and decreased motor strength associated with hyporeflexia or areflexia. Cranial nerve damage can also occur.

- Post COVID-19 vaccination small fibre neuropathy is also being seen increasingly. The evolution of the patient's clinical picture immediately after vaccination and the exclusion of other known etiologies support the possibility of causality.

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