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A Rare Adverse Effect of AstraZeneca VITT- Case Report

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Abstract

Introduction: COVID-19 pandemic presents an unprecedented global challenge on public health, vaccines remain our only hope.We are being vaccinated in large numbers with AstraZeneca ChAdOx1. Even though the adverse effects of vaccine reported ranges from mild allergic reaction to life threatening neurological manifestation; incidence of thrombotic side effects were very few and far between.Now there are a multitude of case reports regarding the thrombotic side effects of this vaccine and noteful among them is thrombosis with thrombocytopenia especially cortical venous sinus thrombosis.We report a case of a 23 year old lady who had CVT with thrombocytopenia following first dose of ChAdOx1 vaccine, along with its diagnostic and therapeutic challenges. She met the diagnostic criteria for Vaccine induced thrombotic thrombocytopenia -VITT as per the American society of hematology guidelines.

Conclusion:CVT with thrombocytopenia following AstraZeneca ChAdOx1 has very high mortality as per available literature. Prompt diagnosis and treatment is the key.

Keywords: COVID-19 ,Thrombocytopenia, Vaccine-induced thrombotic thrombocytopenia (VITT) , Cortical venous thrombosis , Covishield / Astrazeneca

INTRODUCTION

Novel coronavirus COVID-19 originated from Wuhan in late 2019 and India reported its first Covid-19 case in Kerala on January 27, 2020. World health organization declared it a pandemic by March11,2020 [1]. As of September 9,2021, there are 222,406,582 confirmed cases of Covid-19 with 4,592,934 deaths globally. Covid accounting 33,139,981 confirmed cases and 441,749 deaths in India. 5,352,927,296 vaccine doses have been administered globally as per WHO data on 5th September,2021. Despite, the fact that we have been battling Covid-19 since about 2 years, no drugs are validated to have significant efficacy in the clinical treatment of Covid-19. Only a safe and effective vaccine can play a pivotal role in eradicating Covid-19, given the high infectivity. Various vaccines platforms were under trial - vector mediated, mRNA, subunit and inactivated [2]. Several vaccines were approved under emergency use authorization (EUA) and vaccination drive is going on at quick pace in our country. As per ministry of health and family welfare data dated 10th September,2021, around 72.37 crore

vaccine doses have been given in India. India recorded its highest single day vaccination on Aug 16th - vaccinating around 88.13 lakh people in a day. It was estimated to take at least 65- 75% vaccine coverage to control COVID spread[3]. Vaccines that were thought as game changer, has its own demerits. We are in an era such that we are still tackling COVID and its complications, and now we are gearng up against the complications COVID vaccines. Lots of European studies have now published data on thrombotic potential of COVID vaccine especially ChAdOx1 vaccine [4,5,6]. In this report, we highlight how COVID vaccination history was the key to clinching the diagnosis.

CASE REPORT

Twenty-three-year-old lady presented to our hospital with headache, vomiting, numbness of head - 8 days post exposure to 1st dose of ChAdOx1. She was initially treated outside as case of migraine. On Day 12, She had one episode of seizure - GTCS followed by right sided monoparesis and referred to our hospital. MRI taken was suggestive of Superior sagittal sinus and right transverse sinus thrombosis (fig 1) and Hemorrhagic infarct in bilateral frontal and right parietal area (fig 2). She previously has no known comorbidities, no history of any drug / oral contraceptive intake, no family history related to bleeding or thrombotic manifestation, no history of recent infection. On admission, her GCS was E2V2M1, stuporous, with muscle power -0/5 right UL. She was intubated and mechanically ventilated in view of low GCS. Her lab reports revealed low platelets (44000 cells), high D dimer value (18.6 ug/ml) [7], COVID RT PCR was negative on admission.

Thrombocheck panel (Ana profile, anticardiolipin antibody, protein C&S, lupus anticoagulant) was sent which came out to be negative. In the background of COVID pandemic, COVID antibody was sent which came out to be positive. She was suspected to have Vaccine induced thrombotic thrombocytopenia (VITT) and Platelet factor PF4 antibody was sent [7,8](CLIA assay) which came as negative (sensitive test Elisa was unavailable)[9]. She was started on IVIG, steroid, Direct acting oral anticoagulant – Rivaroxaban, anti-epileptic. Patient showed dramatic improvement with treatment – GCS Improved to E4M6VT by day 3 and was extubated on day 4, lab parameter showed improvement in platelet count and limb power improved to 3/5 in right upper limb by day

She showed clinical improvement, follow up imaging showed resolution of CVT and was discharged on day 14 with newer oral anticoagulant (NOAC) and anti-epileptic.

DISCUSSION

Cortical venous thrombosis (CVT) is a neurological condition causing thrombosis with cortical infarct and serious venous hemorrhage [10]. Risk factors include pregnancy, postpartum, inherited clotting disorder - protein C, protein S deficiency, factor V mutation, antithrombin deficiency, inflammatory diseases' vasculitis, inflammatory bowel disease, oral contraceptive intake etc. [11]. Clinical presentation are headache, seizure, focal neurological deficit and encephalopathy. VITT with CVT is a serious adverse effect of ChAdOx1 with high mortality rate. Clinical manifestations and pathology were similar to Heparin induced thrombotic thrombocytopenia (HITT) [12]. Several mechanisms have been proposed for thrombotic thrombocytopenia. VITT onset 6-24 days after 1st dose of ChAdOx1, mostly suggesting immunogenic origin. Constituents of vaccine spike protein (endothelial damage and glycosaminoglycans shedding), polysorbate 80 were proposed as reason for production of PF4 antibodies. Adeno virus vector has also postulated to cause platelet aggregation by Von Willebrand P selectin mediated mechanism on animal studies. Diagnostic criteria for VITT as per American society of Hematology guidelines 1. Covid vaccination 4 to 42 days prior to symptom onset 2. Any arterial or venous thrombosis 3. Thrombocytopenia < 150 x 10^9 /L 4. Positive PF4 antibody 5. Markedly elevated D dimer & more than 4 times the upper limit of normal 7. PF4 antibody test is selectively sensitive only to ELISA 9. Mainstay of treatment for VITT are avoiding platelet transfusion, IVIG (reduces binding of antibody to platelet FcyRIIa) 1 g/ kg daily x 2 days, steroid, non-heparin anticoagulant- argatroban, bivalirudin, danaparoid, fondaparinux and directly acting oral anticoagulants for minimum three months.

CONCLUSION

Though the potential benefit of vaccination is beyond reproach, It is important that we acknowledge this

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rare but serious adverse effect of ChAdOx1 vaccine. Rapid diagnosis of VITT and prompt initiation of IVIG is the key. Though we couldn't demonstrate PF4 antibody positivity as ELISA test was unavailable [9], considering the clinical history and response to treatment, this is likely to be a case of VITT. Any further case reports regarding VITT following ChAdOx1 may force us to rethink concerning its use in high-risk group especially pregnant women and switch to mRNA vaccine like Moderna and Pfizer which has lesser incidence of VITT[13] .

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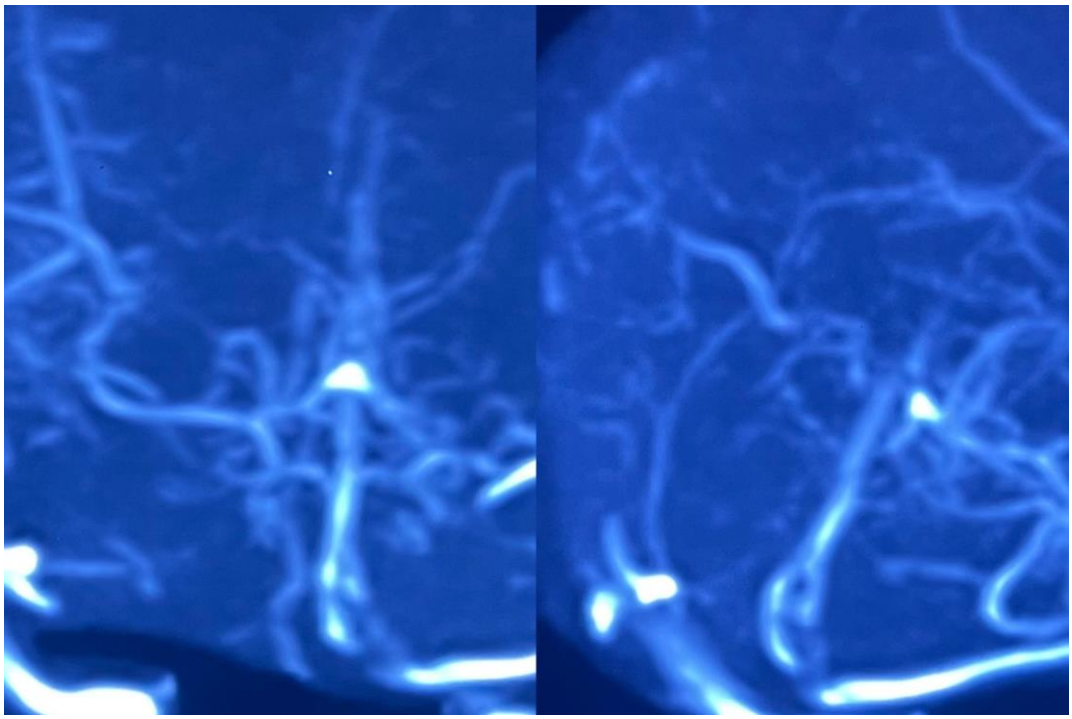

Fig 1: Superior saggital sinus and right transverse sinus thrombosis

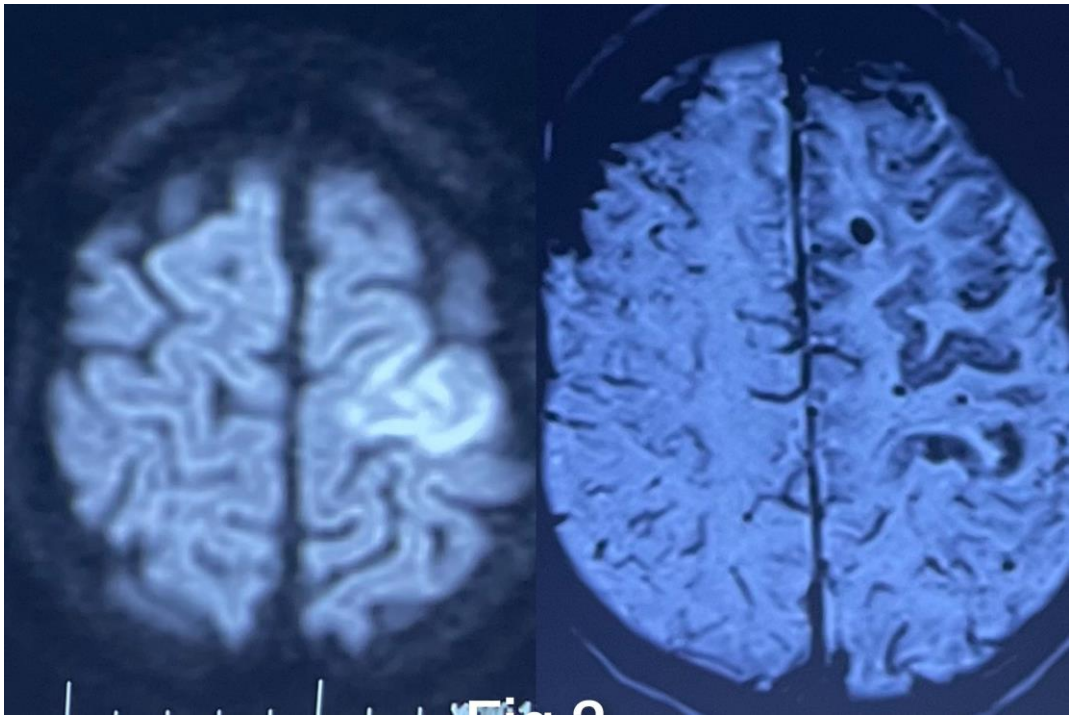

Fig 2: Hemorrhagic infarcts in frontal and parietal area

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