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Case report

Acute liver failure after vaccination against of COVID-19; a case report and review literature

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ABSTRACT

Background: Vaccination against COVID-19 remains as a main root of COVID-19 prevention. Few vaccines have been launched for this purpose recently with different side effects. Thrombotic events have been reported as a rare side effect after ChAdox1nCOV-19 vaccination that may cause death of recipient.

Case presentation: We report a case of hepatic artery occlusion after the first dose vaccination by ChAdOx1nCov-19. The patient was a health care worker, aged 34-year old. Past medical history was unremarkable and had not used heparin. Over the next couple of days after the vaccination, he reported headache, nausea, and dizziness as well as abdominal pain. His general status and the laboratories studies deteriorate quickly by increasing liver enzymes and severe coagulopathy. Clinically he had presented acute hepatic failure. He had been received blood products, prednisolone pulse along with broad antibiotics without benefit. He died on the sixth day.

Conclusions: Thrombotic events after vaccination is very rare but can develop in main arteries with lethal outcome. This event may mimic autoimmune thrombosis clinically.

1. Introduction

Coronavirus disease 2019 (COVID-19) is a worldwide health problem according to recent world health organization more than 121 million confirmed cases and more than 3 million death [1]. Actually vaccination against COVID-19 is considered as main root of protection of virus infection worldwide. In this setting several vaccines have been developed and their effectiveness for preventing virus infection have been proven. Therefore, according to their characteristics of each vaccine, different degrees of adverse events (AEs) are expected in recipients [2,3]. From February 2021 the COVID-19 vaccination was launched In Iran. Vaccination program initially performed among health care workers and patients with special conditions such as cancers or history of organ transplantation. For this purpose The minister of Health provides the vaccines from resources of Sputnik-V, Sinopharm and also ChAdOx1 nCov-19 (AstraZeneca). By introducing ChAdOx1 nCov-19 along with expected symptoms of vaccines such as pain, redness and swelling of injection site, local and general immune reaction, we observed unusual thrombotic events [4,5]. The WHO report thromboembolism can occur among receipt of ChAdOx1 nCov-19 and Johnson & Johnson (J&J) COVID-19 vaccines. Also according to European

Abbreviations: Coronavirus disease 2019, **COVID-19**; Adverse events, **AEs**; Intensive-care unit, **ICU**; Complete Blood count, **CBC**; Prothrombin time, **PT**; Partial thrombin time, **PTT**; Heparin-induced thrombocytopenia, **HIT**; Platelet factor 4, **PF4**; Trans membrane serine protease 2, **TMPRSS2**; Amino acid cleaving enzyme, **FURIN**; European Medicines Agency, **EMA**; UK Medicines and other Health products Regulatory Agency, **MHRA**.

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Medicines Agency (EMA) as well as UK Medicines and other Health products Regulatory Agency (MHRA) vaccine related thromboembolism event is a rare adverse effect of ChAdOx1 nCov-19 vaccine [6,7]. Here we explained a case with sever vaccine-induced thrombosis that cause acute liver failure and eventually death. According to our literature review regarding side effects of COVID vaccine, this case probably is the first case of hepatic artery occlusion post vaccination.

2. Case presentation

A 34-years-old healthy man in mid may2021 came to local hospital due to refractory headache and myalgia one day after received his first dose of ChAdOx1nCov-19. Over next couple of days he reported abdominal pain with nausea and dizziness. The abdominal pain was resisted to pantoprazole and acetaminophen.

His Past medical and familial history was unremarkable. As a health worker he checked regularly viral hepatitis as hepatitis Band C that were negative. He also had no history of regular medication or herbal medicines usage, alcoholic beverage of opium usage. Before vaccination COVID -19 was checked out by polymerase chain reaction (PCR) that was negative.

He had hospitalized in local health center (at the fourth day after vaccination) but due to degrading of his situation, he transferred to our center as tertiary center and liver transplantation center.

At admission (fifth day after vaccination) his blood pressure was 110/70 mmHg, cardiac Pulse rate was 110 beat per second, respiratory rate reached to 30 per minute and temperature was 37 °C with Spo2 94%.

The physical exam revealed moderate to severe abdominal pain on palpitation with the icteric sclera and petechial. The laboratory assessment at fifth day after vaccination in our center demonstrated the increasing of AST, ALT, bilirubin, D-dimer and elevated level of PT/INR (Table 1).

A nasopharyngeal swab sample for SARS-CoV-2 reverse transcriptase polymerase-chain-reaction (PCR) assay was negative. He underwent laboratory assessment for serology of other viral hepatitis such as hepatitis B and C, CMV, EBV also autoimmune hepatitis markers, ceruloplasmin level that all of them were negative.

Complete Blood count (CBC) with difference revealed significant elevation WBC level with low level platelet count, moreover prothrombin time (PT) and partial thrombin time (PTT) as well as C-reactive protein and D-dimer levels elevated (Table 1).

With suspicion of thromboembolic event He underwent imaging by color Doppler ultrasonography that illustrated massive emboli in portal-vein to the splenic with blockage of the hepatic artery by a thrombus. Due to his condition the medical team decided to admit him in intensive-care unit (ICU) in same day of hospitalization in our center.

During his hospitalization in ICU we observed deteriorate the general condition and gastrointestinal hemorrhage was reported, the platelet count remain low with the increasing trend of bilirubin level. Moreover D-dimer level and C-reactive protein increased significantly (Table 1). By diagnosis of disseminated intravascular coagulation (DIC) he received red cell, platelet and whole blood several times along with treatment by broad-spectrum antibiotic, prednisolone 1g/kg, IVIG (1g/kg). His condition worsened rapidly, and finally the patients pass away. The autopsy revealed liver massive infarction (Fig. 1).

Table 1
The characteristics of the patient.

Variables		
Age (year)	34	
Gender	male	
Duration from vaccination to first symptoms (day)	1	
Duration from vaccination to ICU admission in liver center (day)	5	
Duration of ICU hospitalization (day)	2	
	The lab result Just before ICU	The results during ICU admission
Liver tests		
ALT (U/L)	130	2215
AST (U/L)	60	532
ALP(U/L)	298	602
Total Bilirubin (mg/dl)	4.1	6.5
Direct Bilirubin (mg/dl)	2.1	3
INR	1.85	6.4
PTT (sec)	44.9	72
Troponin level (mg/dl)	0.01	0.03
D-dimer level (μg/ml)	15	22
Fibrinogen level (mg/dl)	77	80
CRP (mg/l)	70	122
WBC total	70000	20000
Neutrophil %	69	80
Lymphocyte%	20	20
Platelet count ($\times$ 1000/mm^3)	55	24
LDH	700	7550
Anticoagulant Treatment	No	No

ALT: Alanine Transaminase; AST: aspartate aminotransferase; The prothrombin time (PT), international normalized ratio (INR) partial thromboplastin time (PTT), WBC: White blood cells.

3. Discussion

We describe a case of sever hepatic artery thromboembolism presenting by acute liver failure associate with thrombocytopenia that occurred few days after ChAdOx1 nCov-19 vaccination for Covid-19 for the first time.

According to previous studies The unusual thrombocytopenia and thrombotic events develop about 1–2 weeks after vaccination against SARS-CoV-2 with ChAdOx1 nCov-19 predominantly among women [6,7]. Although present case was a young man that clinically thromboembolism event initiated aggressively during few days after vaccination, proposes a complication that clinically look like severe heparin-induced thrombocytopenia (HIT). This condition is defined as prothrombotic disorder initiated by platelet-activating antibodies that induce complexes between cationic PF4 and anionic heparine. In fact contrasting the usual presentation of HIT, patients with post –vaccination thrombotic event did not treated by heparin that can refer as vaccine-induced immune thrombotic thrombocytopenia (VITT)it also known as vaccine-induced prothrombotic immune thrombocytopenia (VIPIT) [8].

Furthermore it has been stated that other material or medications other than heparin including certain polyanionic drugs can cause a thrombotic disorder that be similar to HIT clinically and serologically. Moreover same event may be induces without history of exposure to any polyanionic medication, as observed after both viral and bacterial infections. In addition, almost all healthy adults have a reservoir of B cells specific for PF4–heparin complexes; production of "heparin-induced thrombocytopenia–like" antibodies by these B cells is kept in check by immune regulatory mechanisms [9].

The mechanism of vaccine induced thromboembolism has not well elucidated. The feature of post covid-vaccination thromboembolism indicates that the mechanism of it may same as autoimmune HIT. In this category, patient always was less sensitive to inhibition with high-dose heparin. It is proposed that the vaccine may induce an immune response causing to thrombocytopenia disorder. Hence, platelet-activating antibodies develop in the absence of heparin exposure. In autoimmune HIT, an endogenous polyanion triggers PF4 antibody formation. Hence it could be considered as an etiology of thrombosis event after vaccination. Patients In this condition compare to classic HIT, have severe thrombocytopenia, an increased frequency of disseminated intravascular coagulation and atypical thrombotic events [10,11]. In a case series by shults N. et al. indicated that an immune complexes comparable to those observed in the serum of patients with autoimmune heparin-induced thrombocytopenia can be detected in serum of these patients [10]. Also it is illustrated that almost all patients with vaccine induced thromboembolism thrombocytopenia syndrome has the antibody against PF4 without history of exposure to heparin. Activated platelets can be detected in serum of these patients [10,11]. According to clinical course of this patients we can offer an autoimmune reaction resemble of HIT after vaccination with ChAdOx1 nCoV-19 that induced massive vascular coagulation. Although in present case we had not evaluate the PF4 levels.

Previous reports almost reported the thrombosis in cerebral arteries as well as in abdominal veins as unusual presentation [7,10,12]. Considerably in our case hepatic artery occlusion, happened that induced massive liver infarction and eventually acute liver failure. In our opinion, regarding the patient's clinical course the hepatic artery occlusion was happened before and independently of DIC features in the end of his life.

The role of vaccines in which spike protein was used in liver of recipients is not clear. Furthermore, it is documented that adenovirus can bind to platelet and ultimately activated the platelet. This mechanism due to lack of enough copies of viruses may not work on the post vaccine thromboembolism thrombocytopenia [13]. Moreover, contraction between the virus spike protein with ACE protein in host cell may has a role in this manner as the virus spike protein binds ACE2 to gain cell entry [14]. Also other proteins such as trans membrane serine protease 2 (TMPRSS2) and paired basic amino acid cleaving enzyme (FURIN) are also important for infection [15].

There is few data regarding management of this event and it remain as a challenging issue. former studies illustrated the poor response to standard treatment of thrombosis but early treatment with intravenous immune globulin (IVIG), may provide good result against spontaneous heparin-induced thrombocytopenia ([16].

Our finding have some clinically implications that VITT is a non-well known phenomena that usually affected young healthy subject and needs more considerations. The physician must be aware regarding vein or atrial thrombosis events in different parts of body as abdominal or cerebral after ChAdOx1 nCov-19 vaccine, also requesting of platelet functional testing including PF4-polyanion antibodies, in patients who have unexpected symptoms after vaccination may be considered regularly. Rapid identification of this rare syndrome is important [5,17].

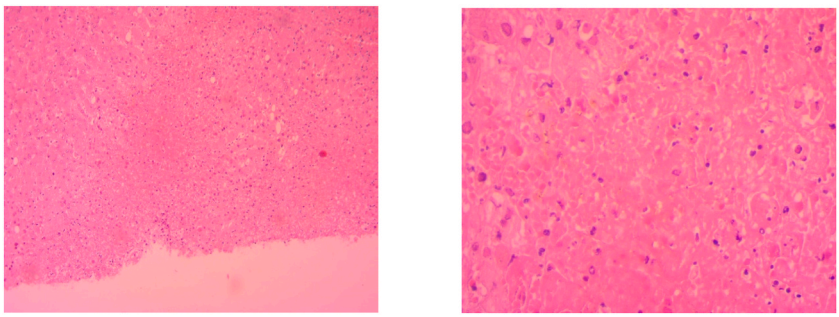

Fig. 1. Histopathology feature of massive liver infarct at autopsy.

Ethics approval and consent to participate

The study protocol was approved by the Board of Ethics of the GILDRC.

Consent for publication

The patient's next to kin has given their consent to publish for this study as the participant was already deceased. Written consent to publish this information was obtained.

Availability of data and material

All data and materials of this case is available.

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Authors' contributions

FZ and MS interpreted the patient data regarding the Liver disease and the transplant. MA analyzes and interpreted imaging studies. ESR and HZ collaboration patient's care and patient's follow up. All authors have read and approved the manuscript.

Declaration of competing interest

There is no conflict of interest in any circumstances.

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Not Applicable.

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