Immune Thrombocytopenia (ITP): Relapse Versus de novo After COVID-19 Vaccination

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COVID-19 vaccination, immune thrombocytopenia, coagulation

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Statements
Our institution does not require ethical approval for reporting individual cases or case series.

Verbal informed consent was obtained from the patient(s) for their anonymized information to be published in this article.

Supplemental materials: All data can be accessed directly from the corresponding author upon a formal request.

Letter to Editor
With the development of the new COVID-19 vaccines, recent case reports and series were published linking COVID-19 vaccines to immune thrombocytopenia (ITP) onset or relapse.1-3

We describe case series of ten patients with thrombocytopenia during the first 4 weeks after COVID-19 vaccination. Data was collected from first January to 31st July 2021. None of the patients described had SARS-CoV-2 infection at the time of ITP diagnosis or relapse. None of the patients reported with thrombocytopenia prior to COVID-19 vaccination.

A case-by-case description has been included in the supplement and a summary of results are found in Table 1. From January first - July 31st 2021 in Kuwait, 1,029,417 individuals had received the first dose only and 716,296 had received both doses of Pfizer vaccine, and 736,123 patients had received the first dose only and 289,592 had received both doses of AstraZeneca/Oxford vaccine. We describe 10 cases of ITP; three cases were de novo and 7 cases were ITP relapse after the vaccine which represents 1:1,750,000 of all patients who received both doses of Pfizer vaccine. All cases of ITP de novo were females, age range of 33 to 56 years, with time range between vaccine exposure and platelet count drop of 7 to 21 days and a platelet count range of 2 to 10 × 10^9/l. All patients required hospitalization and active treatment and two required second line therapy with thrombopoietin receptor agonists. Two patients had only partial response after 3 days and one had complete remission 10 days after the second admission.

Our cases varied in the timing of ITP onset ranging 4 to 21 days post vaccine, similar to a study by Lee et al. which showed that ITP relapse ranges 1 to 23 days post vaccine.2 However, this is in contrast to reported cases by Helms et al. that occurred one day post Moderna vaccine3 and by Tarawneh et al. that occurred three days post Pfizer vaccine.1

The cases presented here included different age groups (19-63 years) than those reported by others.1-3

The incidence of de novo ITP in Kuwait is very low (almost 1:1,000,000) of all vaccinated individuals in with difference in the incidence according to the type of vaccine (1: 368,000 for AstraZeneca/Oxford and 1:1.750,000 for Pfizer vaccine). Unfortunately, data on ITP prevalence in the population is

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| Case Number | Case 1 | Case 2 | Case 3 | Case 4 | Case 5 | Case 6 | Case 7 | Case 8 | Case 9 | Case 10 |
|-------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
| De novo ITP | No     | No     | No     | No     | No     | No     | No     | Yes    | Yes    | Yes    |
| Age         | 37Y    | 30Y    | 56Y    | 63Y    | 30Y    | 28Y    | 19Y    | 54     | 33     | 56     |
| Gender      | Female | Male   | Male   | Female | Female | Female | Female | Female | Female | Female |
| Base line treatment | Observation | Eltromobopag 25 mg/24h | Splenectomy in 2010 | Observation | Observation | Observation | Observation | Observation | Observation |
| Type of vaccine | Pfizer | Pfizer | AstraZeneca-oxford | Pfizer | AstraZeneca-oxford | Pfizer | AstraZeneca-oxford | AstraZeneca-oxford | Pfizer |
| first or second dose of vaccine | second dose | first dose | first dose | second dose | first dose | second dose | first dose | second dose |
| Time between vaccine and development of symptom | 10 days | 7 days | 14 days | 10 days | 7 days | 10 days | 4 days | 17 days | 21 days | 7 days |
| Platelet count | $2.5 \times 10^9/l$ Prednisolone 20 mg 2weeks | $1.1 \times 10^9/l$ IVIG 1gm Prednisolone 20 mg/24h for 1 week Eltromobopag increased to 25 mg/24h | $9 \times 10^9/l$ IVIG 1gm Romiplostim 250mcg | $3.5 \times 10^9/l$ None | $4.0 \times 10^9/l$ None | $3.0 \times 10^9/l$ Increase prednisolone to 40mg/24h, taper back to 5mg/24h over 3 weeks Romiplostim increased to 50mg/24h | $5 \times 10^9/l$ Methylprednisolone 1gm Prednisolone 20 mg Increase dose of eltromobopag to 75 mg/24h | $1.0 \times 10^9/l$ IVIG 1gm/kg Prednisolone 1 mg/kg for 8 weeks | $3.0 \times 10^9/l$ IVIG 1 gm/kg daily for 2 doses Prednisolone 1 mg/kg Romiplostim 3 mcg/kg once per week | $2.0 \times 10^9/l$ Pulse steroid IVIG 1g/kg for 2 days Prednisolone 1 mg/kg Eltromobopag 50 mg/24h |
| Response to treatment | Complete remission (platelet count 170 x 10^9/l) within 7 days | Complete remission (platelet count 300 x 10^9/l) within 8 days | Complete remission (platelet count 170 x 10^9/l) within 14 days | Spontaneous remission (platelet count 80 x 10^9/l) within 30 days | Spontaneous remission (platelet count 170 x 10^9/l) within 14 days | Platelet count back to baseline (70 x 10^9/l) after 5 days | Platelet count back to baseline (70 x 10^9/l) after 5 days | Partial remission (platelet count 50 x 10^9/l) within 3 days | Partial remission Platelet count was 50 x 10^9/l after 3 days during second admission | Complete remission Platelet count 226 x 10^9/l after 10 days of the second admission |
lacking in order to compare ITP incidence post vaccine to the general population.

**Significance Statement**

This paper is intended to raise awareness of the possibility of the occurrence of ITP relapse post COVID-19 vaccine like other vaccines previously reported. We presented ten cases, three of whom developed de novo ITP.

We do not advice against COVID-19 vaccination of such individuals but rather suggest performing CBC few days prior to and after vaccination aiming for an earlier discovery of ITP attack to provide a proper intervention as soon as possible, hence preventing undiagnosed severe thrombocytopenia, bleeding, and the need for aggressive therapy or hospital admission.

**Author’s contribution**

MA and MA initiated and coordinated the development of the paper, worked on data collection, analysis, and writing up the paper. MA, MA, NS, TR and LA analyzed and interpreted the results and helped in writing introduction. All authors read and approved the final manuscript.

**Declaration of Conflicting Interests**

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**Supplemental Material**

Supplemental material for this article is available online.

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