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Acquired thrombotic thrombocytopenic purpura: A rare disease associated with BNT162b2 vaccine: Reply to comment from Doyle et al.

To the Editor,

We thank Dr. Doyle and colleagues for sharing their national data on de novo/relapsed acquired thrombotic thrombocytopenic purpura (aTTP) in the UK from January to November 2021. According to their report, there was no increased number of aTTP presentations during the peak of the UK vaccination program, and the incidence of aTTP cases was within the expected range of England's population, with no increase in treatment demand for aTTP during 2021. In contrast, we have reported on a cluster of aTTP patients presenting on average 14 days after the BNT162b2 vaccine.[1] The 1-month occurrence

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of aTTP patients in the first quartile of 2021 was the average annual number of aTTP patients (two–three) in a tertiary Israeli hospital.

There are several possible explanations for the difference in these reports.

Doyle et al. report that 59/90 (64%) of treated aTTP patients in the time frame defined above had one or more COVID-19 vaccinations; 47% of those were ChAdOx1 and 52% were BNT162b2. In contrast, only the BNT162b2 vaccine was used in Israel until November 2021. While there are several additional reports on mRNA COVID-19 vaccine (BNT162b2 and mRNA-1273)–associated de novo/relapsed aTTP worldwide,[2–6] there are only two reports of ChAdOx1-associated aTTP.[7,8] A difference in the side effect profile associated with mRNA (Pfizer-BioNTech and Moderna) compared to adenoviral vector-based (AstraZeneca/ Johnson & Johnson) COVID-19 vaccines was recently demonstrated.

For example, myocarditis is associated with mRNA vaccines[9] and vaccine-induced immune thrombotic thrombocytopenia (VITT) in the AstraZeneca vaccine.[10]

One must also remember that there is worldwide under-report to national reporting systems of drugs' side effects in general and of COVID-19 vaccines specifically, and there may be more BNT162b2-associated aTTP cases than those reported in the literature so far.

Therefore, one can speculate that the low number of de novo/relapsed aTTP patients in the UK would have been double if only the BNT162b2 vaccine were used.

There is difference in the ethnic composition between Israel and the UK, and different genetic context could be another explanation for the difference in aTTP complication in response to the COVID-19 vaccines in different parts of the world.

There are reports on aTTP association with other vaccines (e.g., H1N1 vaccine, pneumococcal vaccine) as mentioned in our report,[1] so that COVID-19 vaccine–aTTP association is not different from previously described vaccine-associated aTTP.

Interestingly, the third BNT162b2 vaccine in Israel was associated with immune thrombocytopenic purpura (ITP) and not aTTP (data not reported yet), suggesting that there may be a dose-dependent immune modulation.

aTTP associated with BNT162b2 vaccine is rare; therefore, we strongly support the use of COVID-19 vaccines in the general population including aTTP patients. As discussed in our report, we suggest having protective measures before and after COVID-19 vaccination in aTTP patients.[1]

We strongly agree with the authors for the need of reporting aTTP presentations following COVID-19 vaccination to a national reporting system scheme.

CONFLICTS OF INTEREST

The authors declare no competing financial interests.

AUTHOR CONTRIBUTIONS

D. Blickstein wrote the manuscript. M. Koren-Michowitz provided input on the manuscript.

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