

# Haemostatic Disarray Following COVID-19 Vaccine – a Case of Acquired Haemophilia A

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We read with interest Hafeez et al. discussion regarding concern about haemostatic adverse effects post vaccination.<sup>1</sup> Many haemostatic complications post COVID-19 vaccination have been reported including the syndrome of thrombocytopenia and thrombosis, as discussed by Hafeez et al.<sup>1</sup>

In 2019, a new pandemic of coronavirus arose from China and quickly spread across the world.<sup>2</sup> It became a public health emergency.<sup>2</sup> Covid-19 infection usually begin with flu like symptoms however, about 10% of the symptomatic subjects may experience more severe course of the disease.<sup>2</sup> Vaccination became the cornerstone strategy in disease control and prevention of new and more severe cases of COVID-19 infection.<sup>2</sup>

Here we would like to add to the haemostatic adverse events post vaccination reported by Hafeez et al. and report a case of Acquired Haemophilia A (AHA) one week following a Pfizer-BioNTech SARS-CoV-2 vaccine. AHA is a rare bleeding disorder (reported incidence; 1 per million/year) which results in spontaneous bleeding in people with no history of a bleeding disorder.<sup>3</sup> It is believed to be caused by autoantibodies directed against factor VIII (FVIII).<sup>3</sup> It most often seen in elderly patients and is often associated with autoimmune conditions or malignancies but many cases are idiopathic.<sup>3</sup> Here we discuss the rare occurrence of AHA post vaccination.

A 72-year-old gentleman developed forearm, arm and thigh bruising approximately one week after receiving the first dose of the Pfizer-BioNTech COVID-19 vaccine in April 2021. He attended his family doctor when the bruising extended, who referred him urgently to hospital. He had a history of successfully treated prostate carcinoma [prostate-specific antigen was 0.07 ng/ml (normal range = 0-4 ng/ml)], non-insulin dependent diabetes and hypertension. His physical examination was unremarkable other than tongue swelling and extensive bruising. Bloods showed anaemia (haemoglobin: 79 g/L), a normal platelet count ( $288 \times 10^9/L$ ), a prolonged activated partial thromboplastin time [APTT] of 71 s [normal range = 25.1-36.5 s] and a normal prothrombin time and fibrinogen. His lupus anticoagulant screen was negative. The Factor VIII level was reduced [0.01IU/ml [normal range = 0.50 to 1.49 IU/ml]] and Factor

VIII inhibitor quantification demonstrated an inhibitor of 70 B.U/ml, consistent with a diagnosis of acquired Haemophilia A. He was treated with one dose [4500 units] of FVIII inhibitor bypassing activity [FEIBA] to control the bleeding and prednisolone 60 mg once daily [reduced dose due to age and history of diabetes]. He experienced no further bleeding episodes. CT imaging showed no evidence of malignancy. He completed four weekly doses of rituximab 375 mg/m<sup>2</sup> and underwent a slow steroid taper. His FVIII level was normal and his inhibitor screen negative 6 weeks after diagnosis. Remission has persisted despite stopping all immunosuppression.

According to the European Centre for Disease Prevention and Control, 82.2% of adults have had at least one dose of a covid-19 vaccine and this rises to >94% in Ireland.<sup>4</sup> Pharmacovigilance is key when new medications or vaccines are introduced, especially to such a large proportion of the worlds' population as rare complications are likely to be seen.<sup>5</sup> Adverse Events Following Immunisation (AEFI) are reported in 53.7 per 100,000 COVID-19 vaccine doses administered.<sup>6</sup> The most common adverse events associated with the COVID-19 vaccine to date are allergic skin reactions and pain/redness/swelling at the injection site. Serious AEFI was reported in 2.8 per 100,000 doses of COVID-19 vaccine administered.<sup>6</sup> Four other cases of AHA following SARS-CoV-2 vaccination have been reported to date.<sup>7-10</sup> Education about pharmacovigilance and trust in the system is key to limit vaccine scepticism.<sup>5</sup>

The potential correlation between vaccinations and autoimmune disease has been postulated for a long time.<sup>4</sup> The pathogenic mechanism and aetiology of this is still unclear.<sup>5</sup> It has been suggested that the mechanism of autoimmune disease development post vaccination is by molecular mimicry, by which viral or bacterial agents trigger an immune response against

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autoantigens.<sup>5</sup> Another hypothesis is; bystander activation, which involves the activation of quiescent auto-reactive T and B cells.<sup>5</sup> However, it is suggested that some people are more susceptible to developing these reactions due to a genetic predisposition to autoimmune diseases.<sup>5</sup> This hypothesis may explain the pathogenesis of AHA post SARS-CoV-2 vaccine.

COVID-19 infection rates are rising worldwide.<sup>4</sup> Booster doses are being administered and the vaccination programme is being expanded to children.<sup>4</sup> More haemostatic adverse events post vaccination are likely to be seen. Therefore, ongoing pharmacovigilance is required.

### Author Contributions

E. O'Shea, O. Daly, C. Duggan and M. Crowley contributed in the acquisition and interpretation of data as well as to the patient's clinical care. E. O'Shea and M. Crowley drafted the article and all authors revised it critically for important intellectual content. All authors approved the version to be published.

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

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### Trial Registration

Trial registration was not required.

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