



Short Communication

Acquired Hemophilia A: A possibly fatal complication of SARS-COV-2 infection

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Acquired Hemophilia A (AHA), also known as Acquired Factor VIII deficiency, is a bleeding disorder caused by autoantibody generation against coagulation Factor VIII (FVIII), leading to inhibition of its pro-coagulative effects and causing severe bleeding [1,2]. AHA is a rare disorder, having an incidence rate of 1.5 in 1 million per annum [3]. Previous data regarding AHA have suggested half of AHA cases to be idiopathic, however the other half has been associated with a plethora of factors; including infections, auto-immune diseases, pregnancy, malignant diseases and certain cancers [1,4]. AHA usually manifests with mucocutaneous and soft tissue bleeds, resulting in hematomas, epistaxis, ecchymosis and gross hematuria [5]. With multiple incidences of AHA being reported following severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) or after coronavirus disease 2019 (COVID-19) vaccination [4,6,7] - and a four-fold increase in AHA incidence compared to the historical rate - it becomes important to contemplate upon an association between COVID-19 and AHA [8].

In the recent past, multiple studies have presented cases of AHA after COVID-19 infection. Guerra et al. reported a case of 74-year-old women who presented with gross hematuria, due to right ureteral orifice bleed, four weeks after recovering from COVID-19 infection [9]. A similar case was reported Nardella et al. of spontaneous developments of ecchymosis bilaterally in the deltoid region, which was followed by further subcutaneous hematomas in the lower limbs. These hematomas also developed few weeks after resolution of Covid-19 symptoms [10]. This association was further emphasized by Wang et al., whom reported hematomas and diminished sensations in the right upper limb, with further bleeds from intravenous catheters in an asymptomatic Covid-19 patient [6]. Moreover, a delayed case of AHA was reported in a 73-year old man by Hafzah et al., who developed a large ecchymosis on his left thigh, four months after getting infected with the Covid-19 virus [7]. An interesting case of AHA re-exposure was also reported of a 66-year-old man, who developed severe cutaneous and muscle bleeds following Covid-19 infection. The patient was initially diagnosed with AHA about

a decade ago, and had been successfully treated, however the Covid infection triggered the re-appearance of AHA [4].

Moving further, a possible co-relation between AHA and mRNA corona-virus vaccines have also been observed lately. Leone et al. reported four incidences of AHA in the Italian population after administration of Pfizer-BioNTech mRNA Covid-19 vaccine [11]. Al Hennawi et al. also reported cutaneous hematomas on multiple sites in a 75-year old male after the administration of the second dose of the same vaccine [12]. A similar case was also reported by Radwi et al., with presentation of hematomas after both doses of Pfizer-BioNTech Covid vaccine in a 69-year old male [13]. Adding on, multiple cases of AHA have also been reported after inoculation with the Moderna Covid-19 mRNA vaccine. Cittone et al. reported three cases of AHA in the Swiss population [8]. Moreover, Fu et al. also presented a case of a 77-year-old male with multiple ecchymoses bilaterally on the forearms and legs, with further papules and hemorrhagic blisters on the patient's back and hands three weeks after the second dose of the Moderna vaccine [14].

SARS-COV-2 infection has been associated with several hematological issues - including development of lupus anti-coagulants and auto-immune hemolytic anemia - with AHA being one of the disorders. The exact etiology for this association remains vague, however it has been postulated that specific patients in the convalescent phase of the Covid-19 infection might develop an antibody response that cross reacts with the pre-existing antigenic determinants of coagulation factors and/or the red blood cell membrane [15]. Adding on, AHA presentation following Covid-19 vaccination might be due to a couple of factors. It is hypothesized that the vaccine might produce a non-specific activation of autoreactive B and T cells, leading to AHA [13]. Furthermore, antigenic mimicry might also result in the association [13]. Therefore, the aforementioned mechanisms could be the possible pathophysiology of AHA in Covid-19 patients.

In conclusion, although SARS-COV-2 mostly affects the respiratory tract, clinicians must also be aware of other less reported outcomes

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involving other organs. Here we have highlighted the possible association of AHA, a possible fatal complication, in COVID-19 patients. Because of AHA's life threatening nature, it should always be considered in differential diagnosis in COVID-19 patients with normal platelet levels presenting with bleeding. Moving forward, studies need to be conducted to better understand the causative relationship between SARS-CoV-2 and the potentially fatal disease AHA.

Ethical approval

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Author contribution

Hasan Fareed Siddiqui: Conception of the study, drafting of the study, agreeing to accuracy of the work,

Taymmia Ejaz: Conception of the study, final review of the study, agreeing to accuracy of the work,

Aisha Fareed Siddiqui: Conception of the study, drafting of the study, agreeing to accuracy of the work,

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Trial registry number

1. Name of the registry:
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Guarantor

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Consent

Consent is not required to be taken for this article.

Declaration of competing interest

There were no conflict of interest.

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