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Case Report

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A Case of COVID mRNA Vaccine Linked Antiphospholipid Syndrome

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Introduction: There have been several reports of thrombotic adverse events after administration of the mRNA Covid vaccine [1, 2]. The onset of autoimmune disease has also been reported following viral illness as well as following vaccination [3]. Antiphospholipid syndrome (APS) is an autoimmune hypercoagulable state that can result in thrombotic events such as deep venous thrombosis, pulmonary embolus, and stroke [4]. Antiphospholipid antibodies (aPLs) are associated with APS syndrome. However, not all individuals with aPLs will develop antiphospholipid syndrome as antiphospholipid antibodies are also present in up to 5% of the healthy population. Antiphospholipid antibodies have been reported after infections and vaccines. Antiphospholipid syndrome has also been reported following natural Covid infection [5]. Herein we present a case of antiphospholipid syndrome following Covid mRNA vaccination associated with life-threatening thrombosis, dyspnea, and hypoxia coupled with multiple adverse reactions affecting skin, respiratory, nervous, and vascular systems.

Case Presentation: A 22-year-old male in otherwise excellent health is recommended a Covid vaccination. Subsequent to his second dose, he suffers a large pulmonary embolus requiring hospitalization. He has no history of trauma, immobility, or medical risk factors for venous thrombosis. He is also on no culprit medications, has no history of drug use, and has no family history of hypercoagulability. The antiphospholipid antibody: anti-cardiolipin IgG, is found to be greater than ten times the upper limits of normal. The anticardiolipin antibody level being greater than 150 gpl, normal being less than 14 gpl. Per guidelines, these values are repeated and remain markedly elevated (greater than 150 gpl), thus confirming the "antiphospholipid syndrome." His anti-cardiolipin IgM antibodies are noted to also be elevated, supporting the recent development of these antiphospholipid antibodies. Notably, his repeated Covid PCR testing during hospitalization was negative for Covid infection and his Covid nucleocapsid antibodies in subsequent repeated tests were also negative for prior natural Covid infection or exposure [6].

Repeatedly positive antiphospholipid antibodies (at 12 weeks and greater) confirm the hypercoagulable syndrome. In fact, the patient had documentation of significantly raised triple positive aPLs (anti-cardiolipin, anti-beta 2 glycoprotein, and Lupus Anticoagulant (LAC)). The findings suggest the possibility of an autoimmune reaction to the Covid mRNA vaccine triggering the antiphospholipid syndrome.

He was treated with Apixiban and prednisone in the hospital. Later, after confirmation of APS, he was continued on Apixiban (10 mg daily) and treated with hydroxychloroquine (400mg daily) with a favorable clinical response. Prednisone was initially discontinued, and dexamethasone (6 mg) implemented as an anti-inflammatory. .His subsequent clinical course remains that of gradual improvement.

Discussion: Autoimmune and complement abnormalities have previously been reported after mRNA vaccination [7]. Others have noted that "Antiphospholipid antibodies may represent a risk factor for thrombotic events following COVID-19 vaccination and deserve further investigations." They also propose that in the case of "pre-existent aPLs, infections may trigger pro-inflammatory cascades able to promote development of a full-blown APS. It is possible that the same scenario can take place following parenteral inoculation of vaccines [8]." Although rare,, cases of hypercoagulability after Covid-19 vaccines have been recognized in the medical literature. Others have advised that late expression of adverse vaccine reactions should also be considered as well as "potential safety problems that may be identified only after widespread use" [9]. We are aware of known antigens used in the production of mRNA vaccines, including PEG or polyethylene glycol. "It has been reported that the interaction of the immune system with lipidic nanoparticle therapeutics could result in hypersensitivity reactions (HSRs) or

an infusion reaction, referred to as complement activation-related pseudo-allergy (CARPA)" [10]. Current studies show that interactions between the complement and coagulation pathways involved in hypercoagulability are closely related and it is thought that the complement system may induce a series of innate inflammatory responses that help to fight infection when activated [11]. In addition, "It is now appreciated that complement is a functional bridge between innate and adaptive immune responses that allows an integrated host defense to pathogenic challenges" [12]. Further, studies explain, "Expanding data indicates that complement may be activated in patients with aPL and function as a cofactor in the pathogenesis of aPL-associated clinical events" [13].

Recent studies have been published citing autoimmune reactions occurring after SARS-CoV-2 mRNA vaccination, including New-Onset Systemic Lupus Erythematosus (SLE) and Acquired hemophilia as well as a notable case of SLE and antiphospholipid syndrome after COVID-19 vaccination in which that patient, a 42-year old woman is described as having no previous medical history and as having inflammatory manifestation (arthralgias), dyspnea and hypoxia. These issues are similar to the multisystem symptoms that occurred in the case presented herein [14-16].

The production of respective antibodies are seen after vaccine in these reactions. Although mRNA vaccines do not contain adjuvants, this response is similar to the *Autoimmune/Inflammatory Syndrome Disease Induced by Adjuvants* (ASIA) or *Shoenfeld's Syndrome,* disease induced by adjuvants (ASIA) or Shoenfeld's syndrome, known to exhibit "constitutional symptoms, arthralgias, myalgias, myositis, neurological manifestations, and the appearance of autoantibodies"[13].

In this case study of antiphospholipid syndrome, markedly raised antiphospholipid antibodies (triple positive aPLs) were well documented as were significant thrombotic complications. Thus, although rare, the possibility of thrombotic complications and autoimmune events seen after mRNA covid vaccination may have implications for the many new medications currently being designed to be delivered by similar means.

Conclusion: This case discusses the potential induction of an autoimmune disorder that can result in thrombophilia and potential for thrombotic complications following exposure to mRNA therapies. We suggest that pre-screening for aPLs prior to undergoing mRNA vaccinations in autoimmune and other susceptible populations should be considered. Although this patient had no previous allergic reactions to prior vaccination, due to the known hypersensitivity reactions discussed in the medical literature in liposomal and lipid nanoparticle therapeutics studies pre-SarsCov-2 vaccines, we further suggest that individuals with a history of serious allergic reactions should be considered for assessment and possible pre-treatment prior to vaccination and monitoring post-vaccination.

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