

A Case of Adverse Reaction to Booster Dose of COVID-19 Vaccination: Could D-Dimer Elevation Suggest Increased Clotting Risk?

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Abstract

We report the clinical case of a 40-year-old Italian woman, who soon after her booster vaccination with mRNA-1273 after the two previous vaccinations with BNT162b2, developed severe headache, high fever, and Musculo-skeletal pain. She went to the emergency department, where computerized tomography (CT) scans of chest and brain were performed, resulting in both negative for pathologic findings. On the contrary, white blood count was strongly lowered and D-dimer severely elevated. She improved after treatment with enoxaparin and the blood analyses returned in the normal range after ten days. This case supports the hypothesis that COVID-19 vaccines could increase blood clotting in some predisposed subjects. Therefore, we believe that robust and well-designed clinical trials, considering the evaluation of D-dimer levels, should be performed to eliminate any doubts on this issue.

Keywords

Adverse Reaction, COVID-19, Vaccination, Blood Clotting

1. Introduction

Since the beginning of the COVID-19 vaccinations, doubts have arisen about the risk of inducing a thrombotic profile in some subjects via the administration of the vaccine, just as it occurs in COVID-19 patients. The mechanisms by which these vaccines could interfere with coagulation are not yet completely understood. It has been documented that SARS-COV-2 infection can provoke in-

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creased blood clotting [1]. Critically ill COVID-19 patients presented elevated D-dimer levels about 60% of the time [2]. D-dimer is a biomarker of fibrin formation and degradation, and its elevation is a definitive confirmation of an abnormal blood clotting somewhere in the body [3]. A significant elevation of D-dimer was also reported in all patients with vaccine-induced immune thrombotic thrombocytopenia (VITT) and, as a result, this was included among the tests for suspected COVID-19 VITT [4].

2. Case Report

Written informed consent was obtained from the patient to publish this report in accordance with the journal's consent policy. A 40-year-old healthy Italian woman received her booster third dose of COVID-19 vaccination with Spikevax (mRNA-1273) on December 12, 2021. The previous two doses had been administered on February 2, 2021, and March 1, 2021, respectively, with Comirnaty (BNT162b2). After two days from the injection of the third dose, on December 14, 2021, the woman suddenly developed a severe headache, very high fever (39.5°C), and vomiting. For this reason, scared, she decided to go to the Emergency Department of the closest hospital, where, after the visit, CT scans of the brain and chest, and blood tests were performed. The physical examination of the patient was completely negative, the CT scans of the brain and the chest were also negative, whereas her blood tests showed marked leucopenia (WBC 1810 uL, 16.6% of Lymphocytes), modest decrease of platelets (192,000 uL) although still in the normal range, and a very high D-dimer (21,054 ng/ml, v.n. < 500) (**Figure 1**). A previous complete blood count, performed on August 4, 2021, showed that all the values were in the normal range. Following the emergency blood tests, physicians suggested hospitalization, however, because of the lack of available beds in the internal medicine department, the patient returned home. She was prescribed therapy with clarithromycin 500 mg twice a day per os, enoxaparin sodium 4000 U. I. fl once a day subcutaneously, paracetamol 1000 mg per os as needed. In quality of senior member of the Scientific Committee of "Terapia domiciliare C-19" (an Italian group of volunteers, founded by the lawyer Erich Grimaldi, engaged in contrasting the COVID-19 pandemic and in helping people with adverse reactions to COVID-19 vaccinations) I was asked to revise the clinical case of this woman. The therapy was immediately started, and blood tests were repeated the next days at a private laboratory. On December 15, 2021, WBC was 1870 uL with 50% of Lymphocytes, platelets were 171,000 uL, and D-dimer was 4490 ng/ml. On December 16, 2021, the headache had improved but severe pain and a sense of weight in the legs had emerged. An echo-color Doppler of the lower limbs did not show any pathologic findings. However, although slightly improved, WBC, platelets and D-dimer were still abnormal (WBC 2200 uL with 45% of Lymphocytes, platelets 192,000 uL, and D-dimer 2450 ng/ml). The suspected vaccine adverse reaction was reported to the VigiFarmaco site of the Italian Medicine Agency (AIFA). In the following days the patient's symptoms progressively reduced, while blood tests slowly and improved returned to

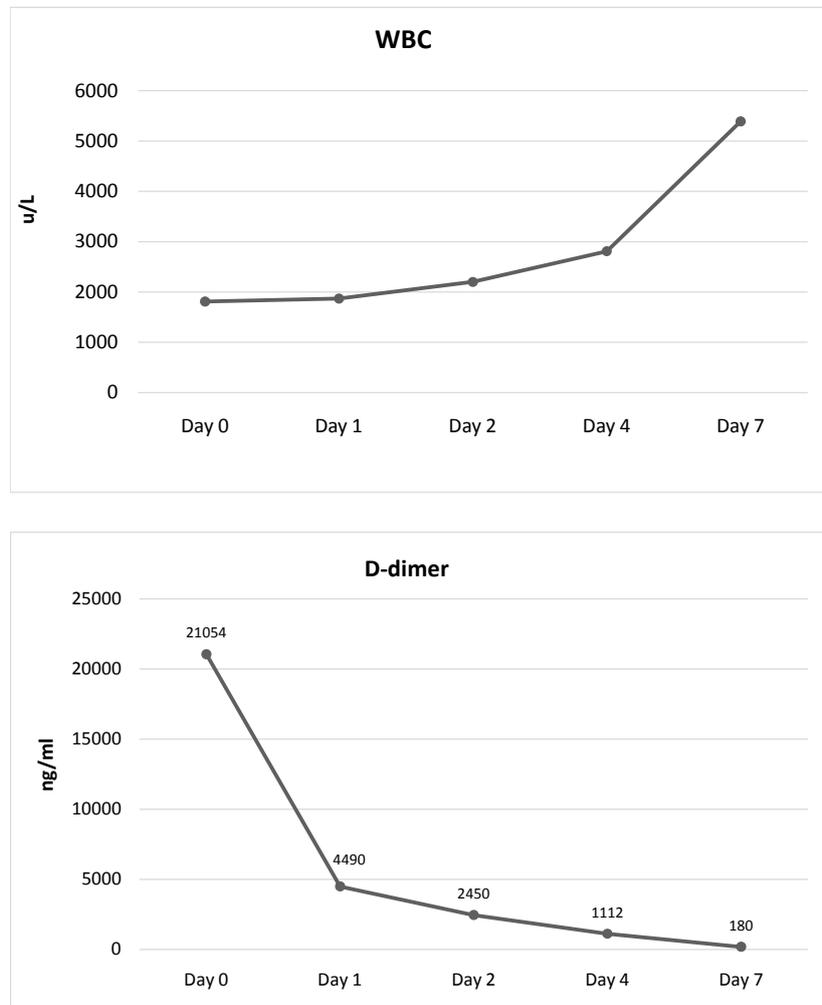


Figure 1. The figure shows the trends of white blood count (WBC) and D-dimer values from December 14 (Day 0) to December 21 (Day7).

normal on December 21, 2021 (WBC 5390 uL with 35.8% of Lymphocytes, Platelets 328,000 uL, and D-dimer 180 ng/ml).

3. Comment

The case of this 40-year-old woman is a clear example that further studies and surveillance on the effects of COVID-19 vaccines are needed. In fact, some doubts have been raised that also mRNA vaccines could determine micro and macro thrombosis, because a significant elevation of D-dimer was found in a certain percentage of subjects who were vaccinated for COVID-19 with any type of vaccine, and this was also reported to the VigiFarmaco site for reporting adverse drug reaction of AIFA. A recent article has reported that coagulation profiles could change significantly after vaccination, in the 7 days following the first injection, coagulation profiles were leaning toward shorter Prothrombin Time (PT), whereas, after 28 and 42 days, the effect was toward activated partial thromboplastin time and PT prolongation. By day 90, the coagulation profiles returned to

those before vaccination [5]. Considering the above, we believe that a D-dimer test must be considered in any coagulation study regarding COVID-19 vaccines [6].

In addition to the autoimmune mechanisms induced by adenovirus vaccines, it has been hypothesized that the spike protein itself could directly damage the endothelial cells and can bind to platelet angiotensin converting enzyme-2 (ACE-2) receptor enhancing platelets aggregation and thrombosis [7]. No scientific evidence is available supporting the fact that the spike proteins, synthesized after COVID vaccinations, could be toxic and damaging to our organs. However, no scientific evidence on this topic has been produced, by pharmaceutical companies producing vaccines, to eliminate any doubt either. On April 5th, 2021, the Association of American Physicians and Surgeons released an important declaration: “blood clotting needs to be watched with all COVID vaccines” [8].

In conclusion, as discussed above, the case of this Italian woman supports the idea that some clotting after COVID-19 vaccination can happen. Therefore, this important topic should be clarified as soon as possible to remove all doubt on the issue. We believe that robust and well-designed studies, always considering a D-dimer test, are needed to completely exclude that COVID-19 vaccines may promote thrombosis, particularly in some predisposed subjects, these are lacking at present.

Authors' Contribution

Serafino Fazio has made a substantial contribution to conception and writing of manuscript.

Manila Vaccariello was involved in revising the manuscript critically for important intellectual content.

Flora Affuso has been involved in acquisition of data, drafting and revising the manuscript.

Ethical Statement

This study does not need ethical approval. Written informed consent was obtained from the patient to publish this report in accordance with the journal's consent policy.

There were no funds to declare, and the authors do not have any conflict of interest to declare.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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