

Pernicious Anemia Following COVID-19 Vaccination: A Report of Two Cases

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ABSTRACT

Since December 2019 and the global epidemic of COVID-19 different countries have focused on vaccines, and one of the inactivated produced vaccines was the Sinopharm COVID-19 vaccine. Some side effects of this vaccine were reported previously, including pain at the vaccination site, fatigue, lethargy, headache, and tenderness, which were more prevalent among individuals <49 years old.

Herein, we reported two patients aged 45 and 51 years old. Both patients have different signs and symptoms after receiving the second dose of the vaccine. None had a history of chronic disease. On examination and following labs and other diagnostic investigations, we found megaloblastic anemia due to atrophic gastritis and low intrinsic factor. These cases showed an autoimmune side effect of the Sinopharm COVID-19 vaccine that was previously reported with an exact mechanism but other features called Covid Arm, Guillain-Barré syndrome, and thrombocytopenia. The mechanism of this reaction is unclear yet.

Keywords: COVID-19; Vaccination; Pernicious anemia

INTRODUCTION

The widespread and progressive global respiratory distress syndrome epidemic caused by SARS-Cov-2 started in December 2019. Since then, different countries have focused on fighting the disease, and their main goal has been to focus on producing COVID-19 vaccines. The Sinopharm BIBP COVID-19 vaccine is one of two inactivated virus COVID-19 vaccines developed by Sinopharm's Beijing Institute of Biological Products¹. Effectiveness of Sinopharm' vaccine was consistent with phase III clinical trial findings². Peer-reviewed results published in *JAMA*

of Phase III trials in the United Arab Emirates and Bahrain showed that BBIBP-CorV was 78.1% effective against symptomatic cases and 100% against severe cases (21 points in the vaccinated group vs. 95 patients in the placebo group)³.

Sinopharm is the most commonly vaccine administered in Iran⁴. It is currently approved in 65 countries⁵. The side effects post-first dose of vaccine injection were site pain, fatigue, and headache, which were more common in individuals aged ≤49 years versus >49 years. Moreover, it found that hurt at the vaccination site, fatigue,

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lethargy, headache, and tenderness were the most common side effects post the first dose in both aged groups. All side effects for both doses were more prevalent among participants aged ≤ 49 years. The side effects were more common in females than males for both doses.

Case presentation

Case 1

A 51-year-old man underwent a home visit complaining of weakness and lethargy.

There was no evidence of systemic disease or any previous chronic disease in the patient's medical history. The patient had a history of receiving the second dose of the COVID-19 vaccine two weeks ago. In the first stage, all clinical examinations included blood pressure, cardiac test, and lung examination, and no abnormalities were observed except for the patient was pale and tachycardic. Therefore, the patient was referred for CBC to evaluate the possibility of anemia. The results were as follows: WBC: 3400 K/ μ l, HB: 7.1 gr/dl, PLT: 187000 $\times 10^3$ /ul, MCV: 108.9 fl. In additional tests, ESR: 34, D-DIMER: 3200, LDH: 3987, Fe: 134.2, TIBC: 311, and Ferritin: 235.91 was measured. According to the results of peripheral blood smear tests, the patient was asked to do a vitamin B12 level test, and the finding of this test was <150 pg/ml. Accordingly, complete examinations were performed: 1) ultrasonography of the abdominopelvic viscera and 2) a thoracic CT scan. No abnormal findings were found. The patient also underwent an endoscopy, followed by decreased gastric folds suggestive of atrophic gastritis with multiple target lesions. The pathologist also confirmed these findings, and the diagnosis of atrophic gastritis was made for the patient.

According to the bone marrow aspiration and endoscopy results, the patient underwent BMA/BMB and was diagnosed with megaloblastic anemia.

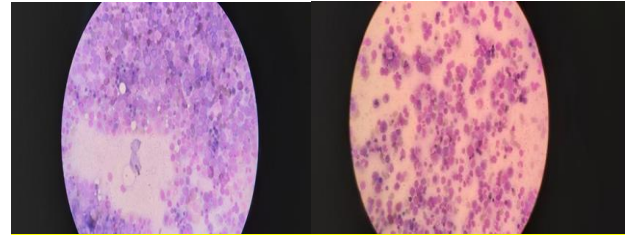


Figure 1: The bone marrow aspiration



Figure 2: The endoscopic result of patient

Case 2

A 45-year woman complaining of abdominal pain, nausea, and vomiting after receiving the second COVID-19 vaccine was referred to the emergency room. According to her initial history, the patient has been treated with losartan 25 mg twice daily and fluoxetine daily. No abnormal findings were found in the patient's clinical examination, including blood pressure and other cardiopulmonary reviews. Due to the mentioned symptoms and the lack of a positive point in the patient's studies and medical history, The patient requested laboratory tests. The results were as follows: WBC: 5200, HB: 5.2 gr/dl, PLT: 172000 $\times 10^3$ /ul, MCV: 121.2 fl, ESR: 114, LDH: 3078, and Ferritin: 312. According to laboratory findings and the lack of positive results in favor of malignant diseases: 1) in abdominopelvic sonography, 2) protein electrophoresis, and 3) the patient underwent a bone marrow aspiration and

biopsy. It was due to a high level of ESR, and she was diagnosed with megaloblastic anemia. The patient underwent an endoscopy due to anemia and intermittent epigastric pain, which it expected and without pathology. Given the possible diagnosis of megaloblastic/pernicious anemia, vitamin B12 was checked and reported its level was lower than usual. (<150 pg/ml) The patient was discharged after receiving a packed cell, vitamin B12, and folic acid.

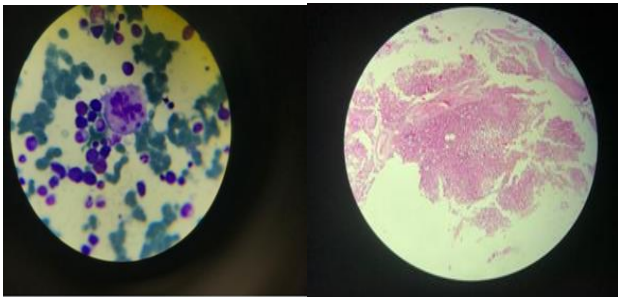


Figure 3. The bone marrow aspiration

DISCUSSION

Pernicious anemia results from a lack of vitamin B12⁶. It is characterized by anemia with pre-mylomegalocytosis, nervous system symptoms and gastrointestinal symptoms, including, loss of bladder or bowel control, mild diarrhea or constipation⁷. On the other hand, this disease is an autoimmune origin in which atrophy of the gastric mucosa decrease the number of parietal cells for producing the intrinsic factor which is necessary for vitamin B12 absorption⁸. Other causes of low vitamin B12 include insufficient dietary intake (which can be a risk in a vegan diet), celiac disease, or tapeworm infection.

Since the onset of the COVID-19 epidemic and the subsequent injection of various vaccines, various side effects such as Guillain-Barré syndrome and COVID Arm have been reported^{9,10}. In addition, thrombocytopenia was said many times^{11,12}. There are many adverse events after vaccination: vaccine product-related reaction, vaccine quality defect-related reaction, immunization error-related reaction, immunization anxiety-related reaction, and coincidental event¹³.

Pernicious anemia is a rare complication of the COVID-19 vaccine and has not been reported. The number of autoimmune disorders (ADs) affecting at least 5% of individuals vaccinated in childhood has increased significantly within the last 30 years worldwide^{14,15}. The question is whether vaccination should or should not be recommended for those with a personal or family AD history¹⁶. The etiology and trigger mechanisms of ADs are still unclear¹⁷. Nevertheless, several studies have suggested that vaccination and infection can lead to AD development in individuals with a genetic predisposition¹⁸. Hypotheses have been proposed that consider molecular mimicry¹⁹ or accidental activation of the host tissue self-antigens¹⁶ as the main pathogenic mechanisms.

According to the findings obtained from these two cases and the lack of intrinsic gastric factor in both cases (that was laboratory confirmed (81.52 in case one and 98.01 in case two)), the final diagnosis was pernicious anemia due to COVID-19 vaccination. The mechanism of this rare autoimmune reaction is still unclear.

Ethical Consideration

This study was approved by Ethics Committee of Shahid Sadoughi University of Medical Sciences (Ir.SSU.REC.1400.242).

CONFLICT OF INTEREST

The authors declare *they have no financial interests*.

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