



Case Report

Autoimmune Events after the COVID-19 Vaccination: Case Reports and Review

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Abstract

Pandemics, infectious diseases were important factors in people life from the time as they first appear on the world, changed their life style and even the geographical habitation. Recently COVID-19 pandemics also damaged our life deeply, caused havoc difficult to fix. It was urgent to come up with a solution for the humanity, so all around the World many scientist focused on investigation of vaccination on COVID-19 infection and they were able to present to the market a successful vaccines, but earlier than it should be. Even though safety of the vaccines were proven with the phase III trials, long term side effects still unknown. There are many reports about developing autoimmune diseases (i.e. Systemic Lupus Erythematosus) especially following mRNA vaccination. Based on these information's we reported three cases here who developed autoimmune diseases in two weeks following vaccination. So it has been recommended that in patients who have autoimmune background should not be vaccinated with mRNA based vaccines.

Introduction

SARS-COVID 19 infection was a big threat all around world during the last three years. This virus is a beta-coronavirus (β -Cov), classified in the zoonotic virus family. It was first detected in human in 2003 with severe acute respiratory syndrome coronavirus (SARS-CoV), afterword it breaks out in 2012 as Middle East Respiratory Syndrome coronavirus (MERS-CoV) [1]. Recently β -CoVs infection named SARS-CoV-2 or SARS-COVID 19 was appeared in Wuhan city of China in 2019 and spread around the World in a very short period, effecting more than 80 million people. Mortality rate was estimated as 2,2% because of bilateral interstitial pneumonia and acute respiratory distress syndrome (ARDS). It has been demonstrated that COVID 19 destroys normal antiviral protective effect especially in older patient with comorbidities [1]. Genetic backgrounds also accused for the severity of cases; leading to lymphopenia, reduction of regulatory T cells, overproduction of proinflammatory cytokines

[1-4]. In these circumstances, it was urgent to come up with a safe and effective vaccination for the humanity. In the first year of pandemic 200 research centres in different countries bypassed many procedures to rush to explore an effective vaccine against this dreadful virus. But only ten of them managed to come up to Phase 3 clinical trial for human [5]. Unfortunately, it was always difficult to be certain about the safety of vaccines. There were upsetting examples in the history in point of this matter. For example, in 1955 during the poliovirus vaccination, 51 cases had permanent paralysis and five of them died. Likewise, in 1976 in the United States during the influenza A (H1N1) vaccination 450 paralytic Guillain- Barre syndrome cases were reported; it was statistically significant if you compare to normal population [5]. Because it was emergency, vaccines were presented to the market earlier than it should be without investigation of the probable long-term side effects in details [5-8]. After the observation of these vaccinated patients, some argument came out about vaccines triggering of Systemic Lupus Erythematosus (SLE) and other autoimmune

diseases in a patients with genetic backgrounds [5-9]. Supporting the genetic background, HLA Class II, HLA- DR3 or HLA-DR4 found more sensitive developing T1DM following viral infection [4]. Even though there has been no proven relationship, found between COVID-19 vaccination and autoimmunity, case reports keep coming about it. On the other hand there are some evidence that the viral infections itself also SARS-CoV-2 may lead to autoimmune diseases [2-4,9-14]. So it is difficult to say whether infections or vaccination is responsible for autoimmune diseases. For the investigation of this debate in this paper, three cases were presented who developed autoimmune diseases following mRNA COVID 19 vaccination.

Case Reports

Case 1: 33 years old female came to our clinic with severe weakness and pain in her arms and legs. She is being treated with insulin for her Type 1 Diabetes Mellitus (T1DM) for 11 years. 2 weeks ago, she had her third shot of Covid-19 vaccine (Pfizer BioNTech) and had covid-19 SARS disease. In her blood tests urea and creatinine values were mildly elevated and moderate normochromic normocytic anemia was detected. Her laboratory tests were shown on Table 1. Her other results are ANA (+) 1/100 titer, DFS-70 pattern, Anti-ds DNA (ELIZA):581 positive, Covid-19 PCR negative (Table 1). Her kidney biopsi showed ClassIV lupus nephritis. She was treated for Systemic Lupus Erythematosus (SLE) Class IV Lupus Nephritis (LN) with corticosteroid 1mg/kg, Mycophenolat Mophetyl 500X3 and Hydroxychloroquine 200mg. She was responded well to this treatment, symptoms and proteinuria disappeared, serum creatinin level dropped to normal level.

Case 2: 67 years old male patient was applied to our clinic with severe dyspnea. 20 days ago, he had had his fifth shot of Covid 19 SARS Pfizer BioNTech vaccine. His blood tests showed severe anemia, and his direct and Indirect Coombs tests are 3 positives

(+++). He was treated for autoimmune haemolytic anemia and recovered well (Table 2).

Case 3: 31 years old female patient came to our clinic with numbness on her hands and feet. She had her second dose of Covid 19 SARS Pfizer BioNTech vaccine one week ago. In the laboratory, examination hypocalcemia (6,5mg/dl) and serum PTH level (0,6pg/mL) were found extremely low. Due to there were no other reason to explain hypoparathyroidism she was diagnosed as autoimmune hypoparathyroidism after the vaccination (Figure 1).

	Fist day	Day 5	Day 10
ESR mm/h	91	92	17
WBC 10e3/mme3	3,54	9,89	10,5
Hb g/dl	8,3	7,8	10,6
BUN mg/dl	34,9	39	17
Creatinine mg/dl	1,88	1,7	0,89
CrtCl* ml/dak		45,5	
Albumin g/dl	3,52	3,49	4,02
LDH U/L	254	205	
HbA1c	6,34		
Ferritin ng/mL	233,8	335	
D-dimer ng/ml	4190	1002	355
CRP mg/dl	1,55	0,84	<0,20
Procalcitonin ng/L		0,12	
C3 g/L	54		83
C4 mg/dl	9,3		16,1
Proteinuria(spot)	-	++	
Microalb/Creat mg/g	904	5168	204
Proteinuria total mg/day	ND	3155	ND

Table 1: Laboratory examination of Case1.

	Day 1	Day 2	Day 3	Day 4	Week later
Hb g/dl	0,7	8,97	9,13		
Hct%	27,3	27,6	28,1		
LDH U/L		976		794	
ESR mm/h		102		85	
Ferritin ng/ml		510		541	
WBC 10 ³ /mm ³	14,75	18,07	19,78	21	
Procalsitonin ng/ml	0,14	0,07			
CRP	12,38	6,5		2,76	
Bilirubin, Ind mg/dl		1,36		1,58	
Bilirubin, Total mg/dl		3,61		2,81	
D.Cooms		4+			
I Cooms		2+			
PLT 10 ³ /uL	303,4	289,5	308,7		
p-ANCA					+
Haptoglobin					<8
Reticulocyte %					4,2
Fibrinogen mg/dl					364

Table 2: Laboratory findings of Case 2.

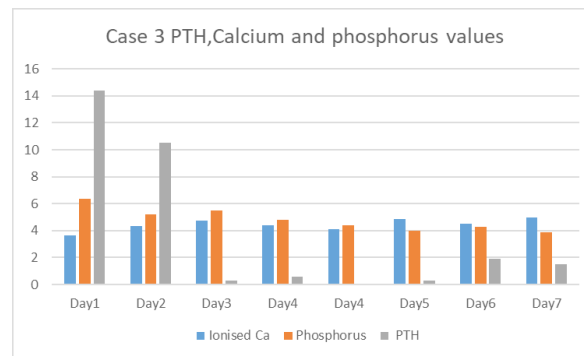


Figure 1: Graphic showing Parathormone, Calcium, Phosphorus levels of case 3.

Discussion

People who are genetically predisposed to autoimmunity are easily triggered by environmental factors to develop autoimmune diseases. Among these environmental factors, viral infections and vaccines are considered priority [1-4]. Even though it was not documented clearly how the viruses trigger autoimmunity, it was explained that some of the virus proteins mimic human proteins and stimulated B and T cells; furthermore organism develop autoanticores against these proteins and leading to autoimmune diseases (Molecular mimicry) [4,12]. This mechanism especially have taken place in Herpes Simplex related stromal keratitis, Enterovirus and Type 1 Diabetes and coxacki virus and autoimmune

myocarditis [3,4]. Pathogenesis of Systemic Lupus Erythematosus also was explained by virus exposure, for examples; Epstein Barr (EBV), Cytomegalovirus (CMV), Human Endogen Retrovirus (HERVs) [15]. Since viruses and autoimmunity was thought very much related to each other, recently question came up about COVID-19 infection and autoimmunity. Thus recently Favalli et al took attention COVID-19 infection related Rheumatoid Arthritis [14]. Thus, during the COVID-19 pandemic it was observed that T1DM increased tremendously, this is a good evidence to support the idea about the relationship between COVID-19 infection and autoimmunity and T1DM [16]. COVID-19 infection stimulates immune system extensively so it has been claimed that in the person

with genetic predisposition might be elicited the autoimmune diseases [14].

In case No:1, presented above, since she had been suffering T1DM for 11 years so she was considered very much predisposed to autoimmunity. Unfortunately, she was vaccinated with the Pfizer BioNTech without knowing that she was suffering with COVID-19 infection. Thus, two weeks later she developed Systemic Lupus Erythematosus (SLE) and Lupus Nephritis (LN), and luckily taken under control easily. This case found worthy to be reported since there were several similar cases in the literature to support this observation [6,7,16,17].

Under these circumstances since it was in such a short period to present vaccine into the market, it was very difficult to conclude about especially long term side effects of COVID 19 vaccination. Among these long term side effects, possibility of triggering the autoimmunity is most noteworthy [5,17]. If infection itself might trigger the autoimmunity, so it is most likely that vaccination also may cause to wake the autoimmunity. Even though, there are several case reports, which claim the association between vaccination and autoimmunity; there are no certain evidence to prove this relationship [18-24].

Second case developed autoimmune haemolytic anaemia (AIHA) 20 days later following the vaccination with Pfizer BioNTech. There has been reasonable amount of publications about developing complement mediated AHA induced by COVID-19 vaccinations [24-27]. Fattizzo et al reported a case series and review with Paroxysmal Nocturnal Haemoglobinuria (PNH), AIHA, Cold Agglutinin disease, and Haemolytic Uremic syndrome, developed or exacerbation after the infection or vaccination [24]. They have an interesting observation that the ones their condition flared after the vaccinations, their clinical courses were more mild than the cases developed after the COVID-19 infection [25]. In these series, all patients were needed transfusions, treatment with complement inhibitors and immunosuppresses.

Our third case developed hypoparathyroidism following vaccination; this observation is very rare in the literature but we could not find any other reason to explain this other than autoimmune hypoparathyroidism [28,29]. Moreover there are many evidences and case reports in the literature to support the relationship and autoimmunity and COVID-19 vaccinations for examples; Immune thrombocytopenia, autoimmune hepatitis [30-32].

Nevertheless, vaccination of patient with autoimmune diseases especially with rheumatoid arthritis is something that we should approach consciously. Patients with autoimmunity and rheumatic diseases; under the cytotoxic therapy are more prone to develop severe infectious diseases, so advantage of vaccination is more predominant than some unexpected uncertain complications.

It is recommended that patient with rheumatic disease and under the treatment of glucocorticosteroids, cytotoxic agents; are not recommended to be the vaccinated with the live attenuated viruses [22].

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