New Onset Systemic Lupus Erythematosus with Unusual Presentation and Multi-Organ Involvement after Covid-19 Vaccination in a Pediatric Patient: A Case Report

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Since the beginning of the COVID-19 pandemic, vaccination has been crucial in reducing deaths and hospitalizations. However, vaccination may trigger autoimmune responses. We present the first case of new-onset systemic lupus erythematosus in a 12-year-old girl, three weeks after receiving the first dose of Sinopharm BIBP COVID-19 vaccine. Complications of COVID-19 vaccines are typically mild. There have been reports of a potential association between the vaccines and autoimmune disorders. However, severe events are rare. Vaccination for COVID-19 is recommended even for those with a genetic predisposition to autoimmune disease, as the advantages of preventing COVID-19 outweigh the potential risks of acquiring autoimmune diseases.

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Case Report

INTRODUCTION

Immune system dysregulation is a potential complication of SARS-CoV-2 infection.[1,2] There is increasing evidence that COVID-19 is associated with the development of autoimmune responses.[1-3] COVID-19 vaccination reduces mortality and hospitalization rates.[3] Studies report a possible relation between COVID-19 vaccines and autoimmune disorders, including Guillain-Barre syndrome, thrombotic thrombocytopenia, IgA nephropathy, autoimmune hepatitis, and Systemic lupus erythematosus (SLE).[3,4] Several cases of new-onset SLE have been reported in adults after COVID-19.[3-5] Immune responses to viral antigens may trigger autoimmune disorders. There is growing evidence that infection with severe acute respiratory syndrome coronavirus 2 (SARS-COV-2) is associated with the development of autoimmune responses and occurrence of autoantibodies. The mechanism of autoimmune manifestations develop after COVID-19 is unknown.[2]

We report the first case of pediatric new-onset SLE in a 12-year-old girl after receiving the first dose of an inactivated COVID-19 vaccine, with multi-organ involvement This study aims to highlight the need for physicians to be aware of the clinical features of autoimmune disorders after the COVID-19 vaccination.

CASE REPORT

A 12-year-old girl presented to Akbar Children's Hospital in Mashhad, Iran, with fever, pancytopenia, and hepatosplenomegaly three weeks after receiving the first dose of the COVID-19 vaccine in February 2022. An informed written consent was obtained from the patient and her parents. There was no evidence of any previous illness. The bone marrow test revealed normal findings. In addition, she experienced severe pain in the upper abdomen. After analyzing the laboratory findings, physicians determined that she had acute pancreatitis (Amylase 182 U/L and Lipase 85 U/L) (Tables 1 and 2). The patient was managed with intravenous fluids, fasting and analgesics as well as treatment of the underlying disease (As

Table 1. Laboratory characteristics of the patient after the first dose of COVID-19 vaccination

Laboratory characteristics	The Third week	The Forth week	The Fifth week	The Seventh week	The eighth week	Reference range
White Blood Cells ×1000/ml	3.8	4.73	8.37		6.9	3.9-11.5
Neutrophil %	85.0	66.8	80.4		64	40-80
Lymphocyte %	12.5	29.2	16.4		36	20-40
Hemoglobin gr/dL	10	11	10.2		10.5	12.8-16
Platelets ×1000/µL	112	208	176		381	150-450
Urea Mg/dl	48				39	15-36
Creatinine mg/dl	0.7				0.5	0.6-1.3
ESR mm/hr	98	71		69	27	Up to 10
CRP Mg/dl	1.6	0.7		1.6	2	Up to 10
AST U/l	60		230		32	<31
ALT U/l	56			90	41	<31
Alb gr/dL	2.6		2.8		3.6	3.5-5.2
CPK U/l			1586			24-170
Aldolase U/l			10.4			Up to 7.6
Uric acid Mg/dl	3.5			7.2	4.5	Male:3.5-7.2 Female:2.6-6 Child:2-5.5
Amylase U/l		182	407.2			<100
Lipase U/l		85	126			<60
U/A:						
PH			6		5	
SG			1020		1030	
WBC /hpf			3-4		6-8	
RBC /hpf			Many		+++	
Protein			++		+	
Urine protein 24hr Mg/24hr			355		145	24-141
Urine creatinine 24hr Mg/24hr			242		309	16-326
Urine volume 24hr ML			700		1200	600-1600
urine protein to creatinine ratio Mg/Mg			1.12		0.27	<0.2
Anti-nuclear antibody (ANA) Index			Positive (>250)			Negative: <40 Borderline:40-55 Positive:>55
Anti-dsDNA antibody IU/ml			Positive (>100)			Negative: <25 Borderline:25-4- Positive:>40
Anti-beta2 glycoprotein IgG U/ml			Positive (27.1)			Negative: <10 Positive>10
Anti-beta2 glycoprotein IgM U/ml			Positive (16.7)			Negative: <10 Positive>10
Anti-cardiolipin IgM U/ml			Positive (11.2)			Negative: <12 Positive≥12
Anti-cardiolipin IgG GPL unit			Negative (8.4)			Negative: <12 Positive≥12
Anti-phospholipid IgG U/ml			4.2			Negative: <10 Positive>10
Anti-phospholipid IgM U/ml			11.2			Negative: <10 Positive>10
C3 Mg/dl			2.8		90	89-187
C4 Mg/dl			1.3		21	10-40
P-ANCA (MPO-ANCA) U/ml			10			Negative: <12 Borderline:12-18 Positive:>18
C-ANCA (PR-3-ANCA) IU/ml			11			Negative: <12 Borderline:12-18 Positive:>18

ESR: Erythrocyte Sedimentation Rate, CRP: C - reactive protein, AST: Aspartate Transaminase, ALT: Alanine Transaminase. Alb: Albumin. CPK: Creatine phosphokinase/A: Urine Analysis, SG: Specific Gravity, WBC: White Blood Cells, RBC: Red Blood Cell Anti-dsDNA: Anti-double-stranded-DNA, IgM: Immunoglobulin M, IgG: Immunoglobulin G, P-ANCA: Perinuclear anti-neutrophilic cytoplasmic antibodies, MPO-ANCA: Myeloperoxidase–Antineutrophil Cytoplasmic Antibody, C-ANCA: diffuse cytoplasmic Antineutrophil cytoplasmic antibodies.

Table 2. Clinical features and para-clinical findings of the patient after first dose COVID 19 vaccination

variable	The Third week	The Forth week	The Fifth week	The Seventh week	The eighth week
clinical features	Fever Rash	Fever Cough dyspnea Abdominal pain	Abdominal pain	Weakness	
physical examination	Hepatosplenomegaly	Respiratory distress abdominal tenderness	Abdominal tenderness edema of lower extremities	Tremor Proximal muscle weakness Impaired gait	Improvement in muscle weakness
Other para-clinical findings					
Chest X ray		left sided pleural effusion			
Abdominal ultrasonography		A bulge and heterogeneous pancreas in the tail area with collection of fluid around it. Stranding and inflammatory changes were seen.			
Chest ultrasonography		mild pleural effusion with a depth of 3 mm with atelectasis at the base of the left lung			
Bone marrow aspiration	Cellular hematopoietic marrow				
Echocardiography		mild to moderate MR and pericardial effusion			
EMG/NCV				Subacute polyneuropathy irritable myopathy	
kidney biopsy					Diffuse Proliferative Glomerulonephritis Consistent with Diffuse Lupus Nephritis, ISN/RPS class IV-G*
Treatment		Methylprednisolone IV (2mg/kg/day) The first dose of IVIG	3 days methylprednisolone pulses Hydroxychloroquine Mycophenolate mofetil Aspirin	2 days methylprednisolone pulses The second dose of IVIG	

EMG/NCV: Electromyography nerve conduction velocity, MR: mitral regurgitation, IVIG: Intravenous Immunoglobulin, IV: intravenous.
*International Society of Nephrology/Renal Pathology Society (ISN/RPS) 2003 classification of Lupus Nephritis, Diffuse global lupus nephritis: ≥50% of the involved glomeruli have global lesions.

will be explained below). Chest X-ray showed pleural effusion and echocardiography reported pericardial effusion. Lab results showed positive anti-nuclear antibody (ANA) > 250 and anti-double stranded DNA (Anti-ds DNA) test (> 100 IU/mL), proteinuria, elevated muscle enzymes (CPK 1586 U/L and Aldolase 10.4 U/L), and the presence of IgG and IgM anti-cardiolipin antibody levels)8.4 and 11.2 U/ml respectively). She was diagnosed with a Multisystem Inflammatory Syndrome in Children (MIS-C) and treated with intravenous immune globulin (IVIG) 1 gr / kg for two consecutive days and corticosteroids (2mg/kg/day). In the fifth week, she developed muscle weakness and edema in the lower extremities. (Table 1). On electromyography and nerve conducting velocity (EMG-NCS), there were signs of subacute polyneuropathy and irritable myopathy. She exhibited signs of systemic lupus erythematosus (SLE), including peripheral polyneuropathy, proximal myopathy, glomerulonephritis, and serositis (Table 2). She met the classification criteria of SLE, according to the EULAR/ACR-2019 and SLICC criteria.[6,7] The patient received methylprednisolone pulses (30mg /kg) for three consecutive days, hydroxychloroquine (5mg/kg/day), mycophenolate mofetil (500mg/m2/dose) and Aspirin (5mg/kg/day). The patient's symptoms, including reduced muscle strength, significantly improved. Kidney biopsy was performed which revealed diffuse proliferative glomerulonephritis (involving > 50% glomeruli) and endocapillary hypercellularity, consistent with diffuse proliferative lupus nephritis (ISN/RPS class IV), according to ISN/RPS 2018 approach (Figure 1). After three months of treatment, she resumed normal activities and the proteinuria resolved. The patient had regular follow up visits, every three months, to check the treatment process, laboratory tests, and restore her medications. During this period, her clinical symptoms resolved, she did not have proteinuria, and pancreatic enzymes were within normal limits. At the 9-month follow-up, significant improvement was observed and she maintained remission without any flare.

DISCUSSION

Viral antigens can cause immune responses by molecular mimicry, epitope spreading and B cell immortalization.[6,7] Activation of B cells by the virus and production of interferons have a significant role in SLE presentation following COVID-19. The production of interferon type I can release pro-inflammatory cytokines.[7,8] Other viral vaccines, such as influenza, measles, and HPV, were also reported to cause new-onset SLE.[9-11] The COVID-19 vaccines are designed to trigger immune responses by producing SARS-CoV-2 neutralizing antibodies.[10,11] A few cases of MIS-C have been

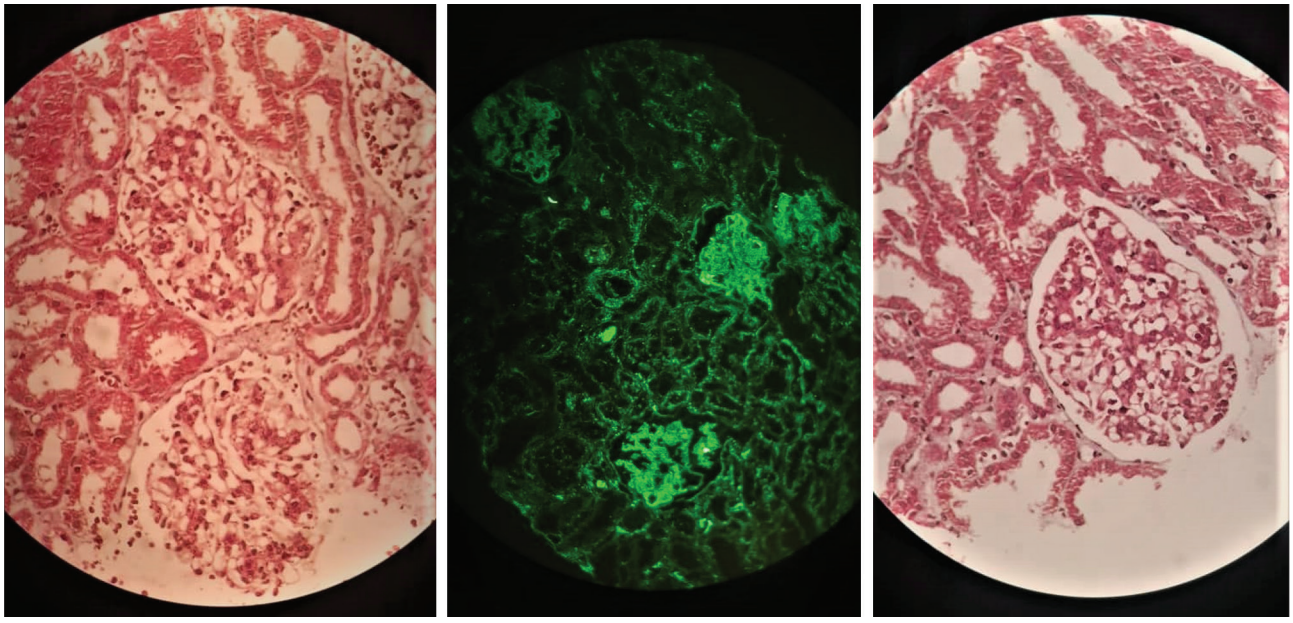

Figure. 1. Diffuse Proliferative Glomerulonephritis Consistent with Diffuse Lupus Nephritis, ISN/RPS class IV-G, and endocapillary hypercellularity according to ISN/RPS 2018 approach (A). Granular and linear capillary and mesangial immune reaction of antibodies in a full house pattern.

reported in children following the COVID-19 vaccination. There are few cases of new-onset SLE after COVID-19 vaccination in adults.[4,8] Alrashdi Mousa *et al.* reported a 22-year-old female who presented with acute pancreatitis as an uncommon manifestation of SLE, after COVID-19 vaccination.[12]

We presented a 12-year-old girl who developed symptoms of SLE, three weeks after receiving the first dose of the Sinopharm COVID-19 vaccine. While there has been one reported case of SLE after administration of the COVID-19 mRNA vaccine (Pfizer) with symptoms including a butterfly rash, pleuritis, joint involvement,[13] to the best of our knowledge this is the first case of Childhood-onset SLE (C-SLE) reported after receiving the inactivated COVID-19 vaccine). Our patient developed life-threatening SLE symptoms after COVID-19 vaccination. Unusual and severe manifestations included acute pancreatitis, polyneuropathy, and class IV lupus nephritis. Pancreatitis and polyneuropathy are uncommon complications of C-SLE.[14]

The benefits of getting vaccinated outweigh the rare events such as autoimmune disorders. COVID-19 can trigger the development of immune-mediated disease.[2,3] COVID-19 vaccination is recommended for people with genetic susceptibility to rheumatic disorders.[3]

CONCLUSION

There is not a clear relationship between the presentation of SLE and COVID-19 vaccination, but new-onset SLE may be triggered by COVID-19 vaccine.

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DECLARATIONS

Consent for publication: Informed written consent was obtained from the patient and her parents and We received a code of ethics (IR.MUMS.MEDICAL.REC.1402.123) from the Faculty of Medicine of Mashhad University to conduct the study.

Availability of data and materials: All data in this case report is available.

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AUTHORS' CONTRIBUTIONS

Vahedi and Pourbadakhshan participated in the design of

The study. All authors contributed to the interpretation of the results. All authors

Contributed to the drafting of the manuscript. All authors also contributed to the

critical revision of the manuscript for important intellectual content approved by the

final version, and are accountable for the integrity of its content

LIST OF ABBREVIATIONS:

SLE: systemic lupus erythematosus
COVID-19: coronavirus disease of 2019
ESR: Erythrocyte Sedimentation Rate
CRP: C - reactive protein
AST: Aspartate Transaminase
ALT: Alanine Transaminase
Alb: Albumin
CPK: Creatine phosphokinase
U/A: Urine Analysis
SG: Specific Gravity
WBC: White Blood Cells
RBC: Red Blood Cell
Anti-dsDNA: Anti-double stranded-DNA
IgM: Immunoglobulin M
IgG: Immunoglobulin G
P-ANCA: Perinuclear anti-neutrophilic cytoplasmic antibodies
MPO-ANCA: Myeloperoxidase–Antineutrophil Cytoplasmic Antibody
C-ANCA: diffuse cytoplasmic Antineutrophil cytoplasmic antibodies
EMG/NCV: Electromyography nerve conduction velocity
MR: mitral regurgitation
IVIG: Intravenous Immunoglobulin
IV: intravenous

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