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Case Report

Drug-Induced Lupus Following mRNA COVID-19 Vaccination and Monoclonal Antibody Infusion for Treatment of COVID-19 Infection

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INTRODUCTION

Drug-induced lupus (DIL) is an autoimmune condition that presents with clinical symptoms similar to Systemic Lupus Erythematosus (SLE) following exposure to a certain medication. DIL is unique because it typically resolves once the offending drug is discontinued, whereas SLE is a chronic condition. Over 100 medications have been linked to DIL, although it is less commonly linked to immunizations.[1,2] The literature highlights cases of DIL in connection with Hepatitis B, Human Papilloma Virus (HPV), and meningococcal vaccines, indicating their immunogenicity and their potential to initiate autoimmune processes.[3-6] With the recent rollout of the COVID-19 vaccines, the rare potential for DIL has been a concern, but current evidence suggests that the risk of DIL from the COVID-19 vaccines remains low and the benefits of vaccination tremendously outweigh any potential risks.[7] Furthermore, this case report highlights the difficulty of diagnosing DIL and how its diagnostic criteria differs from SLE. SLE has clear diagnostic criteria, such as the EULAR/ACR 2019 guidelines established by the American College of Rheumatology.[8] These guidelines utilize a designated scoring system based on symptoms and biological markers to help guide diagnosis.[8] DIL does not have specific guidelines and therefore makes it difficult for clinicians to recognize and diagnose patients with this disorder. In this manuscript, we present a case of DIL following vaccination with the Moderna mRNA COVID-19 vaccine and monoclonal antibody infusion. Our aim is to elucidate the diagnostic steps for DIL.

CASE REPORT

A 74-year-old male with a history of hypertension, post-traumatic stress disorder, and Ulcerative Colitis, who underwent a total proctocolectomy with end ileostomy 40 years ago, presented with chest pressure, abdominal pain, a non-painful, non-pruritic diffuse rash, and malaise. The patient reported that these symptoms started five weeks ago when he tested positive for COVID-19 and experienced mild constitutional symptoms, including headache and fatigue.

Two days after the initial positive test, the patient received a monoclonal antibody infusion. Two weeks following the immunotherapy infusion, he received his fourth COVID-19 vaccine. Over the next three weeks, he developed presenting symptoms, including anorexia and a 15-pound weight loss, with no associated nausea, vomiting, and dysphagia. The patient's home medications included amlodipine and citalopram. Upon admission, he presented with a fever (103.3°F), tachycardia, and tachypnea. On physical examination, he appeared cachectic, with elevated jugular venous distension, bilateral diminished breath sounds, and diffuse abdominal tenderness. Skin examination revealed numerous red, non-blanchable papules and plaques scattered throughout his body (Figures 1 and 2).

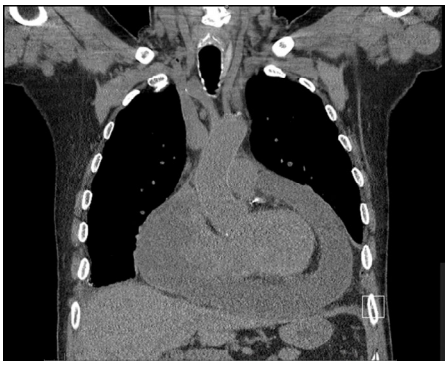

Figure 1. Coronal CT chest showing large pericardial effusion.

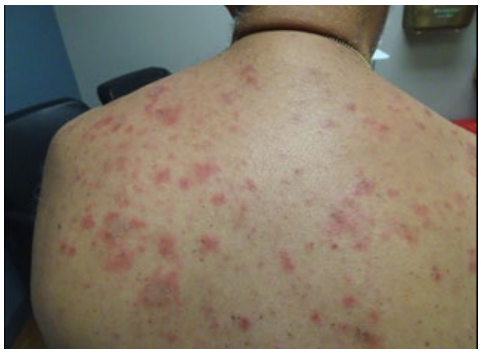

Figure 2. Eruption of papules and plaques on patient's back.

Relevant laboratory results revealed a WBC of 7.60/μL, creatinine 2.35 mg/dL (baseline of 1.12 mg/dL), CRP 16.9 mg/dL, ESR 50 mm/hr, Lipase 23, ALT 160 U/L, AST 139 U/L, ALP 498 U/L, Total Bilirubin 1.9, and albumin 3.1 g/dL (Table 1). A chest x-ray displayed pulmonary infiltrates, and a chest CT revealed a large pericardial effusion (Figure 1). Viral hepatitis serologies returned negative. Magnetic resonance cholangiopancreatography exhibited a normal appearance of intra and extrahepatic bile ducts without obstruction. Due to concerns about progressive hemodynamic changes, a pericardial window was performed. Cytology from the pericardial fluid indicated white blood cells with neutrophilic predominance, and pathology of the pericardium showed fibroadipose tissue, suggesting a mixed acute and chronic inflammatory process. Dermatology evaluation suggested a probable COVID-19 vaccine-related eruption of papules and plaques, clinically resembling pityriasis rosea (Figure 2). Blood cultures remained negative.

The unexplained, systemic processes raised concerns about a systemic autoimmune etiology. Rheumatological testing revealed a positive ANA of 1:1280 with a homogenous pattern, Anti-Histones 9.4 U, and Anti-RNP antibodies 1.7 (Table 2). However, results for anti-CCP antibody, C3 and C4 complement, ANCA (IBD, PR-3, MPO), Smith-antibody antibody, dsDNA antibody, chromatin antibody, anti-SSA, and Anti-SSB antibody were all negative (Table 2). Further chart review of lab findings from years prior showed that he had a negative

ANA during the evaluation of his inflammatory bowel disease. Given these findings, concerns for an autoimmune process emerged, leading to the initiation of IV methylprednisolone at 250 mg every six hours.

Table 1. Key laboratory values on admission versus three-month follow-up.

Relevant Laboratory Tests	On Admission	Three Months Post Discharge	Normal Ranges
Crt	2.35 mg/dL	1.27 mg/dL	0.7-1.3 mg/dL
ALT	160 U/L	23 U/L	8-40 U/L
AST	139 U/L	14 U/L	5-34 U/L
ALP	498 U/L	114 U/L	40-150 U/L
Serum Albumin	3.1 g/dL		3.4-5 g/dL
CRP	16.9 mg/dL	1.7 mg/dL	0-0.5 mg/dL
ESR	70 mm/hr	3 mm/hr	0-20 mm/hr

Table 2. Results of rheumatological/immunological testing and biomarkers.

Rheumatological Testing		
Description	**Result**	**Normal Ranges**
ANA IFA	Positive	Negative
ANA Pattern	Nuclear, homogenous	
ANA Titer	>=1:1280	Negative: <1:40 Low Ab level: 1:40-1:80 Elevated Ab level: >1:80
Histone Ab	9.4	Negative: <1.0 Weak Positive: 1.0-1.5 Moderate Positive: 1.6-2.5 Strong Positive: >2.5
dsDNA-Ab	6 IU/mL	Negative: </=4 IU/mL Indeterminate: 5-9 IU/mL Positive: >/=10 IU/mL
SM (Smith) Ab	<1.0	Negative: <1.0
Chromatin Ab	>8.0	Negative: <1.0
Anti-CCP Ab	<16	Negative: < 20 Weak Positive: 20-39 Moderate Positive: 40-59 Strong Positive >59
C4 complement	21 mg/dL	15-53 mg/dL
C3 Complement	135 mg/dL	82-185 mg/dL
ANCA (IBD)	Negative	Negative
ANCA (PR-3)	<1.0	</=1.0
ANCA (MPO)	<1.0	</=1.0
RNP Ab	1.7	
SM/RNP Ab	<1.0	Negative: <1.0
SS-A Ab	<1.0	Negative: <1.0
SS-B Ab	<1.0	Negative: <1.0

After ruling out infectious and malignant etiologies, the diagnosis of DIL became our top differential. The patient was discharged with an oral prednisone taper, commencing at 20 mg for six weeks, with a subsequent plan to reduce the dosage by 5 mg each week. A three-month follow-up revealed complete resolution of symptoms: cutaneous papules and plaques had entirely disappeared, liver enzymes returned to normal limits, cardiac function normalized with no recurrent pericardial effusion, and anti-Histones antibodies were negative.

DISCUSSION

DIL is an autoimmune disorder resembling idiopathic SLE, influenced by various factors including genetics, drug metabolism, and reactive metabolite formation.[9] DIL has been associated with over 100 drugs, and an example is minocycline-induced DIL, which is more prevalent in women and often presents with distinctive skin manifestations, hepatic involvement, and occasional association with anti-histone antibodies.[1,2] Symptoms of DIL can vary in severity, encompassing arthralgia, myalgia, and fever.[2] Despite sharing general lupus symptoms, there are no universally accepted diagnostic criteria for DIL. Consequently, diagnosing DIL can be challenging, as it may not always align with the American College of Rheumatology criteria for SLE.[9]

In DIL, laboratory findings commonly include mild cytopenia, elevated erythrocyte sedimentation rate, and the presence of ANA with a homogenous pattern.[2] While anti-histone antibodies are frequently associated with DIL, they can also appear in other autoimmune diseases.[10] Specifically, these antibodies are present in over 75% of DIL cases induced by hydralazine and procainamide. Additionally, anti-histone antibodies, often indicated by a homogeneous pattern, can occur in up to 50% of SLE patients. The sensitivity of anti-histone antibodies for DIL is 67%, with a specificity of 95%.[10]

In DIL, it is crucial to assess complement levels (C3 and C4) during DIL evaluations, as complement levels tend to be within the reference range in DIL patients, unlike SLE, where a reduction in complement levels is a common finding.[11] The diagnosis of DIL is suggested by the presence of lupus-like symptoms that resolve after discontinuing the drug and the exclusion of other autoimmune disorders.[2] The patient in our case displayed full resolution of cutaneous, cardiac, and liver functions as verified through laboratory and echocardiographic examination.

The CDC recommends delaying administration of the COVID-19 vaccine to individuals who have tested positive for the virus.[12] The guideline suggests waiting a minimum of three months after the onset of symptoms or a positive test for those who either developed symptoms or tested positive without symptoms. This delay allows the immune system to recover from the acute phase of the illness, as the vaccine may not be as effective in individuals still infected with the virus.[13] CDC also reports no need for delaying vaccination if a patient was given monoclonal antibodies or convalescent plasma during the illness period.[12] Our patient's case is a rare adverse event and further studies are required to investigate proper recommendations on how long between COVID-19 infection, monoclonal antibody infusion, and vaccination is appropriate to prevent such a significant event. This case emphasizes the importance of being aware of possible adverse reactions to the COVID-19 vaccine and treatment. The full spectrum of the mRNA COVID-19

vaccine side-effects is not yet fully understood so it is crucial to be cognizant of the possibility of DIL in cases like these after vaccination and treatment to make proper recommendations and diagnosis.

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Keywords: drug induced lupus, COVID-19, monoclonal antibody infusion, autoimmune, anti-histone antibody

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