CLINICAL AND EXPERIMENTAL VACCINE RESEARCH

Henoch-Schönlein purpura following mRNA COVID-19 vaccination: a case report

Clin Exp Vaccine Res 2024;13:166-170
https://doi.org/10.7774/cevr.2024.13.2.166
pISSN 2287-3651 • eISSN 2287-366X

Mi-Ok Lee[1], Seok-Ju Yoo[2]
[1]Department of Infectious Disease Control, Ulsan Metropolitan City Hall, Ulsan; [2]Department of Preventive Medicine, Dongguk University College of Medicine, Gyeongju, Korea

Received: February 29, 2024
Revised: March 10, 2024
Accepted: March 20, 2024

Corresponding author: Seok-Ju Yoo, PhD
Department of Preventive Medicine, Dongguk University College of Medicine, 123 Dongdae-ro, Gyeongju 38066, Korea
Tel: +82-52-229-8325, Fax: +82-52-229-8319
E-mail: medhippo@dongguk.ac.kr

No potential conflict of interest relevant to this article was reported.

The coronavirus disease 2019 (COVID-19) vaccine was developed to provide immunity against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which was first reported in 2019. The vaccine has proven to be effective in reducing severity and mortality and preventing infection. Henoch-Schönlein purpura is an autoimmune vasculitis (immunoglobulin A vasculitis). Historically, vaccines have been administered primarily to children, and Henoch-Schönlein purpura has often been reported in children following vaccination. However, since the start of COVID-19 vaccination, an increasing number of cases have been reported in adults. Here, we report a case of a patient who developed hematuria and proteinuria after receiving the messenger RNA COVID-19 vaccine. A 22-year-old man presented to the hospital with a lower extremity rash, bilateral ankle pain, and abdominal pain 18 days after receiving the COVID-19 vaccine. The man had no significant medical history and was not taking any medications. Laboratory tests showed normal platelet counts but elevated white blood cell counts and C-reactive protein and fibrinogen levels. He was treated with the non-steroidal anti-inflammatory drugs, pheniramine and prednisolone. At 40 days after starting treatment, C-reactive protein levels were within normal limits, and no hematuria was observed. Treatment was terminated when the purpura disappeared. This report is intended to highlight the need for further research to be proactive and carefully monitor for conditions associated with the COVID-19 vaccine.

Keywords: COVID-19 vaccines, mRNA-1273 vaccine, mRNA vaccine, IgA vasculitis, Henoch-Schönlein purpura, Case reports

Introduction

Henoch-Schönlein purpura, now called immunoglobulin A (IgA) vasculitis, is an immune-mediated complex vasculitis. Henoch-Schönlein purpura affects capillary vessels and is characterized by the deposition of IgA on the walls of blood vessels [1]. Clinical manifestations mainly involve cutaneous purpura, abdominal pain, arthritis, and nephropathy [2]. This illness occurs primarily in childhood, and adult cases are less common. The etiology of Henoch-Schönlein purpura is not completely understood, but it was observed following upper respiratory tract infections, medications, vaccinations, and malignancies [3]. The onset of Henoch-Schönlein purpura following coronavirus disease 2019 (COVID-19) infections and COVID-19 vaccines has been consistently reported from 2020 to date. This case report aims to emphasize that Henoch-Schönlein purpura was highly likely caused by the administration of COVID-19

vaccines since Henoch-Schönlein purpura had a temporal association with the messenger RNA (mRNA)-1273 (Moderna Inc., Cambridge, MA, USA) administration, and there was no strong evidence for another cause.

Case Report

A 22-year-old man visited the Dongkang Hospital in Ulsan with a rash on the lower limbs, bilateral ankle pain, and abdominal pain. He was admitted to our hospital for spots on both feet and ankle pain, which started the day before visiting the hospital (Fig. 1). He had no remarkable medical history and was not on any medication. No signs of upper respiratory infection or COVID-19 infection were observed at admission. He had received the second dose of the mRNA COVID-19 vaccine mRNA-1273 (Moderna Inc.) 18 days before the visit. He did not have particular symptoms after receiving the first dose (mRNA-1273; Moderna Inc.).

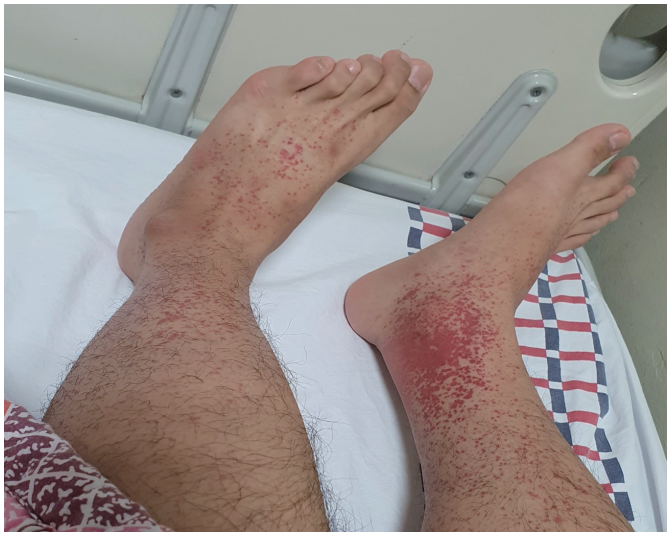

Fig. 1. Palpable purpura on lower limbs. Written informed consent for the publication of this image was obtained from the patient.

He developed a fever (37.9°C) after the admission. Laboratory findings indicated a normal platelet level, but a white blood cell count of 12.32 K/μL (normal range, 4.00–10.00 K/μL), a C-reactive protein (CRP) level of 1.03 mg/dL (normal range, 0–0.05 mg/dL), and a fibrinogen level of 479 mg/dL (normal range, 150–400 mg/dL). On the first day of admission, the level of D-dimer increased to 2.0 μg/mL (normal range, 0–1 μg/mL) but returned to normal afterward. The level of CH50 (50% hemolytic complement) increased to >60 U/mL (normal range, 32–58 U/mL). The serum IgA level was within normal limits; C3, C4, antinuclear antibody, and antineutrophil cytoplasmic antibody test results were negative. CRP levels increased to 2.86 mg/dL a day after admission but returned to normal limits 1 week later. Urinalysis findings showed hematuria (3+) and a urine red blood cell count of 20–29/HPF

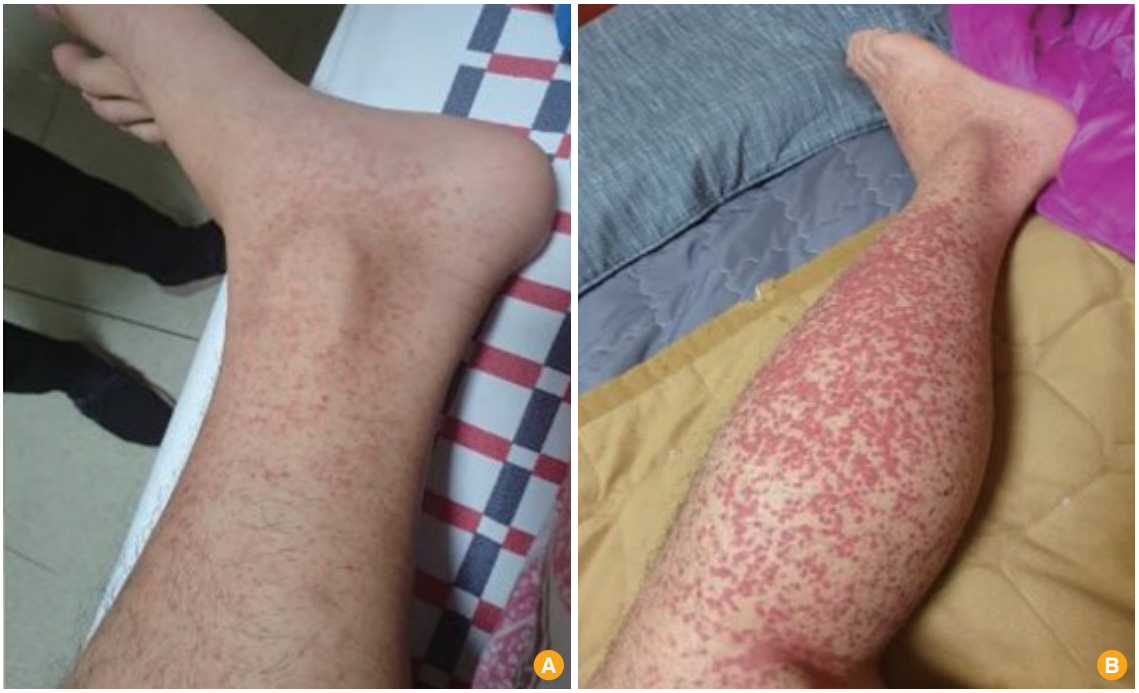

Fig. 2. **(A)** Day 1 of recurrence after improving symptoms and initiation of treatment with steroids. **(B)** Aggravated symptoms after discharge. Written informed consent for the publication of this image was obtained from the patient.

(high-power field) but did not show proteinuria. However, proteinuria (1+) was observed 10 days after the onset. On the fourth day of admission, he complained of severe abdominal pain. He had abdominal+pelvis computed tomography, but no bleeding was observed besides fatty liver.

On the first day of admission, the patient was prescribed pheniramine and a nonsteroidal anti-inflammatory drug and completely recovered on day 5. However, purpura recurred 2 days later, and the patient was prescribed prednisolone (PDS) 60 mg/day for 3 days and then discharged. The patient returned to the hospital the next day after discharge because purpura became severe, involving the thighs. Since the patient did not have other symptoms than purpura, and CRP, fibrinogen, and IgA levels gradually decreased, he was monitored while maintaining the previous dose of medication (Fig. 2). Once the symptom improved after 1 week, the dose of PDS was reduced to 30 mg/day, then gradually reduced to a low dose. On day 40 after the initiation of treatment, CRP level was within normal limits, and no hematuria was observed. Treatment was terminated as purpura disappeared. Since microalbuminuria was observed, a follow-up was conducted 3 months later. He has had a healthy life since; follow-up findings showed normal results and the absence of purpura.

The study was conducted by the Declaration of Helsinki, based on which patient information was anonymized. This study was conducted per the ethical criteria of the applicable field and approved by a Korean Public Institutional Review Board designated by Ministry of Health and Welfare (no., P01-202305-01-028). Prior consent was obtained from the patient to publish this report and images.

Discussion

Vaccination is the safest way to prevent crises from diseases. We have recognized the importance of vaccination and conducted a vaccination campaign when we face a crisis. The COVID-19 pandemic led to the rapid development of virus vector vaccines and mRNA vaccines and the conduct of campaigns for vaccination around the world. Fever, headache, myalgia, arthralgia, and pain at the injection site after the administration of vaccines are common adverse events that can occur after the administration of COVID-19 vaccines [4]. However, reports on autoimmune diseases among the adverse events of COVID-19 vaccines have increased, and the reported diseases include systemic lupus erythematosus, neuromyelitis optica, multiple sclerosis, and Henoch-Schönlein purpura [4-6]. Although Henoch-Schönlein purpura is uncommon in adults, Henoch-Schönlein purpura following COVID-19 vaccines has been frequently reported in adults. Therefore, we should closely monitor this [7,8]. Although most patients have a good prognosis, Henoch-Schönlein purpura represents the principal cause of morbidity to other serious diseases and mortality if gastrointestinal involvement and renal complications are presented in adults [1].

Although the exact etiology of Henoch-Schönlein purpura following COVID-19 vaccines is unknown, several hypotheses can be extracted by reviewing several studies.

(1) Some cytokines can regulate the immune system and cause inflammation by interfering with the regulation of the immune system. Inflammation, called a cytokine storm, can be caused [9,10].

(2) The increased anti-glycan antibodies elicited by the COVID-19 vaccines cross-react with galactose-deficient IgA1, which are the essential molecules in the multi-hit mechanism of the pathogenesis of Henoch-Schönlein purpura, and they form immune complexes and deposits in small vessels [11].

(3) Vaccine antigens may activate B- and T-cells and cause antibody formation with subsequent immune complex deposition in small-caliber vessels. Thus, immune complex and antibody deposition can be included on vessel walls [12].

The above hypotheses imply that COVID-19 vaccines can develop Henoch-Schönlein purpura by impacting the inherent autoimmune system in healthy persons or causing inflammatory responses in individuals with risk factors. Henoch-Schönlein purpura was confirmed based on the European League Against Rheumatism, the Paediatric Rheumatology International Trials Organization, and the Paediatric Rheumatology European Society (EULAR/PRINTO/PRES) classification criteria in the present case. The patient was diagnosed with Henoch-Schönlein purpura because he met four criteria: purpura without thrombocytopenia, renal involvement with hematuria, acute arthralgia, and abdominal pain (Table 1) [13].

In this case, a young, healthy man without a medical history of upper respiratory infection and COVID-19 infection had purpura 18 days after being administered the mRNA-1273 vaccine. We can predict that the COVID-19 vaccine directly or indirectly affected the patient and precipitated Henoch-Schönlein purpura.

The patient had hematuria on admission, but it was not detected after 7 days. Also, laboratory findings showed no proteinuria, but it was observed 10 days later. Afterward, micro-

 https://doi.org/10.7774/cevr.2024.13.2.166

Table 1. European League Against Rheumatism, the Paediatric Rheumatology International Trials Organization, and the Paediatric Rheumatology European Society (EULAR/PRINTO/PRES) 2008 classification criteria

Diagnostic criteria	Description
Mandatory criterion	Palpable purpura of the limb in the absence of thrombocytopenia
Minimum 1 out of 4 supportive criteria	(1) Acute abdominal pain
	(2) Acute arthralgia and arthritis
	(3) Renal involvement in the form of proteinuria or hematuria
	(4) Histopathological evidence of leukocytoclastic vasculitis or proliferative glomerulonephritis with predominant immunoglobulin A deposits

proteinuria was detected until discharge. Unfortunately, a skin biopsy of the purpura was not conducted. Accurate histopathological findings confirmed via skin biopsy can be an important objective rationale for making an accurate diagnosis and observing prognosis. According to a recent study by Ramdani et al. [14] published in March 2023, Henoch-Schönlein purpura reports have slightly increased in COVID-19 vaccines compared to all other drugs (information component, 0.22; 95% confidence interval [CI], 0.04 to 0.35). However, no difference was observed between COVID-19 vaccines and other vaccines (information component, 1.42; 95% CI, -1.60 to -1.28). A study demonstrated that COVID-19 vaccines did not differ from other vaccines as a factor that induces Henoch-Schönlein purpura [14]. However, since this study used data retrieved from VigiBase (Uppsala Monitoring Centre, Uppsala, Sweden) until June 1, 2022 and the event has been consistently reported, constant monitoring is needed. This study does not deny that vasculitis was caused by the COVID-19 vaccine. Thus, demonstrating an evident causal relationship with the vaccine remains challenging.

The possibility of Henoch-Schönlein purpura occurring after COVID-19 vaccination cannot be ruled out, so it is important to continue to study this condition and establish evidence of a causal relationship with the vaccine.

Accurate information about the safety of COVID-19 vaccines must be communicated to the public to ensure that COVID-19 vaccines become the foundation for national immunization in the future.

Public confidence in vaccination must be gained by providing accurate and correct information about the safety and efficacy of further developed COVID-19 vaccines, adverse events following COVID-19 vaccination, and actively communicating that vaccinees should seek appropriate medical care if they develop symptoms.

ORCID

Mi-Ok Lee *https://orcid.org/0009-0003-8748-4959*
Seok-Ju Yoo *https://orcid.org/0000-0001-9764-8097*

References

1. Nishimura N, Shiomichi Y, Takeuchi S, Akamine S, Yoneda R, Yoshizawa S. IgA vasculitis following COVID-19 vaccination. Mod Rheumatol Case Rep 2023;7:122-6.
2. Hahn D, Hodson EM, Willis NS, Craig JC. Interventions for preventing and treating kidney disease in Henoch-Schonlein purpura (HSP). Cochrane Database Syst Rev 2015;2015:CD005128.
3. Sirufo MM, Raggiunti M, Magnanimi LM, Ginaldi L, De Martinis M. Henoch-Schonlein purpura following the first dose of COVID-19 viral vector vaccine: a case report. Vaccines (Basel) 2021;9:1078.
4. Chen S, Fan XR, He S, Zhang JW, Li SJ. Watch out for neuromyelitis optica spectrum disorder after inactivated virus vaccination for COVID-19. Neurol Sci 2021;42:3537-9.
5. Kaur I, Zafar S, Capitle E, Khianey R. COVID-19 vaccination as a potential trigger for new-onset systemic lupus erythematosus. Cureus 2022;14:e21917.
6. Toljan K, Amin M, Kunchok A, Ontaneda D. New diagnosis of multiple sclerosis in the setting of mRNA COVID-19 vaccine exposure. J Neuroimmunol 2022;362:577785.
7. Hines AM, Murphy N, Mullin C, Barillas J, Barrientos JC. Henoch-Schonlein purpura presenting post COVID-19 vaccination. Vaccine 2021;39:4571-2.
8. Sugita K, Kaneko S, Hisada R, et al. Development of IgA vasculitis with severe glomerulonephritis after COVID-19 vaccination: a case report and literature review. CEN Case Rep 2022;11:436-41.
9. Najafi S, Rajaei E, Moallemian R, Nokhostin F. The poten-

tial similarities of COVID-19 and autoimmune disease pathogenesis and therapeutic options: new insights approach. Clin Rheumatol 2020;39:3223-35.
10. Delapierre A, Terrier B, Pillebout E, et al. Clinical phenotype and cytokine profile of adult IgA vasculitis with joint involvement. Clin Rheumatol 2022;41:1483-91.
11. Choi Y, Lee CH, Kim KM, Yoo WH. Sudden onset of IgA vasculitis affecting vital organs in adult patients following SARS-CoV-2 vaccines. Vaccines (Basel) 2022;10:923.
12. Corra A, Verdelli A, Mariotti EB, et al. Cutaneous vasculitis: lessons from COVID-19 and COVID-19 vaccination. Front Med (Lausanne) 2022;9:1013846.
13. Ozen S, Pistorio A, Iusan SM, et al. EULAR/PRINTO/PRES criteria for Henoch-Schonlein purpura, childhood polyarteritis nodosa, childhood Wegener granulomatosis and childhood Takayasu arteritis: Ankara 2008. Part II: final classification criteria. Ann Rheum Dis 2010;69:798-806.
14. Ramdani Y, Largeau B, Jonville-Bera AP, Maillot F, Audemard-Verger A. COVID-19 vaccination as a trigger of IgA vasculitis: a global pharmacovigilance study. J Rheumatol 2023;50:564-7.

 https://doi.org/10.7774/cevr.2024.13.2.166