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A Case of SARS-CoV-2 Vaccination-Induced Mesenteric Vasculitis Improved by Adalimumab in Ankylosing Spondylitis

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Abstract

Recently, SARS-CoV-2 vaccines have been reported to increase the incidence of immune-mediated diseases, including systemic vasculitis, in various rheumatic diseases. Herein, we report a case of severe mesenteric vasculitis following administration of an mRNA vaccine (Johnson and Johnson Ad26.COV2.S) in a patient with ankylosing spondylitis. A 49-year-old woman presented with massive hematochezia and multiple erythematous purpuric papules throughout her body after a single-dose inoculation with SARS-CoV-2 vaccine. Mesenteric vasculitis was diagnosed based on clinical investigation, abdominal computed tomography, colonoscopy, and skin biopsy. Her symptoms worsened after high-dose steroid therapy but dramatically responded to adalimumab treatment. The findings from this case suggest a causal relationship between the SARS-CoV-2 vaccine and mesenteric vasculitis, and the therapeutic advantage of TNF-α inhibitors for this severe complication.

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Introduction

Ankylosing Spondylitis (AS) is a chronic inflammatory disease affecting the spine and sacroiliac joints [1]. In general, the incidence of vasculitis in patients with AS is unusual. Although cutaneous vasculitis localized to the skin has been reported, systemic vasculitis is rare [2,3]. In particular, no cases of mesenteric vasculitis have been reported.

Recently, the incidence of vasculitis in the general population has been increasing owing to the SARS-CoV-2 vaccination. Although there are many cases of cutaneous vasculitis, severe cases, such as mesenteric vasculitis involving the gastrointestinal tract, are rare. In addition, most of the reported vasculitis cases were treated with glucocorticoids, and there have been no reported cases of improvement with adalimumab [4-7].

Herein, we report a case in which severe vasculitis that developed after SARS-CoV-2 vaccination in a patient with AS improved after administration of a TNF-α inhibitor.

Case Presentation

A 49 years old female was diagnosed with HLA-B27 positive Ankylosing Spondylitis (AS) in 2006. Stiffness and pain affected her pelvis and legs. Involvement of the thoracic spine and sacroiliac joints was confirmed by radiography. There was no bowel disease or psoriasis. The leg and back pain persisted after 3 months of treatment with Non-Steroidal Anti-Inflammatory Drugs (NSAIDs), including celecoxib, naxozol, and sulfasalazine. She received etanercept 50 mg weekly for three months. In 2009, at the age of 52 years, she started using adalimumab 40 mg biweekly, as she had worsened peripheral arthritis and inflammatory back pain. Subsequently, the AS activity remained low.

In June 2021, the patient presented with multiple erythematous purpuric papules with itching and pain in both legs. Two weeks prior, she was vaccinated with the Johnson and Johnson Ad26. COV2.S single dose, and adalimumab was discontinued for the vaccine. Allergic vasculitis after SARS-CoV-2 vaccination was suspected by a dermatologist and the symptoms improved after

Table 1: The published cases of systemic vasculitis after SARS-CoV-2 vaccination.

Patient No.	Age interval	Prior rheumatic disease	Vaccine/dose(s)	Interval (days)	Clinical diagnosis	Treatment	Ref.
1	90s	No	Moderna/2	10	IgA nephropathy	GC	[4]
2	40s	No	Moderna/1	19	IgA nephropathy	GC	[5]
3	50s	No	Moderna/2	4	ANCA-associated glomerulonephritis	GC plasma exchange, CYC, Rituximab	[20]
4	70s	No	Moderna/2	27	EGPA	GC	[6]
5	70s	No	Pfizer/2	14	ANCA-associated glomerulonephritis	GC, CYC	[21]
6	80s	No	Pfizer/2	14	ANCA-associated glomerulonephritis	GC	[7]
7	60s	No	Pfizer/1	28	Large vessel vasculitis	GC	[22]
8~17	61 (38~72)		7adeno/3 mRNA	19 (2~31)	6 ANCA 4 PAN	GC	[23]

GC: Glucocorticoid; CYC: Cyclophosphamide

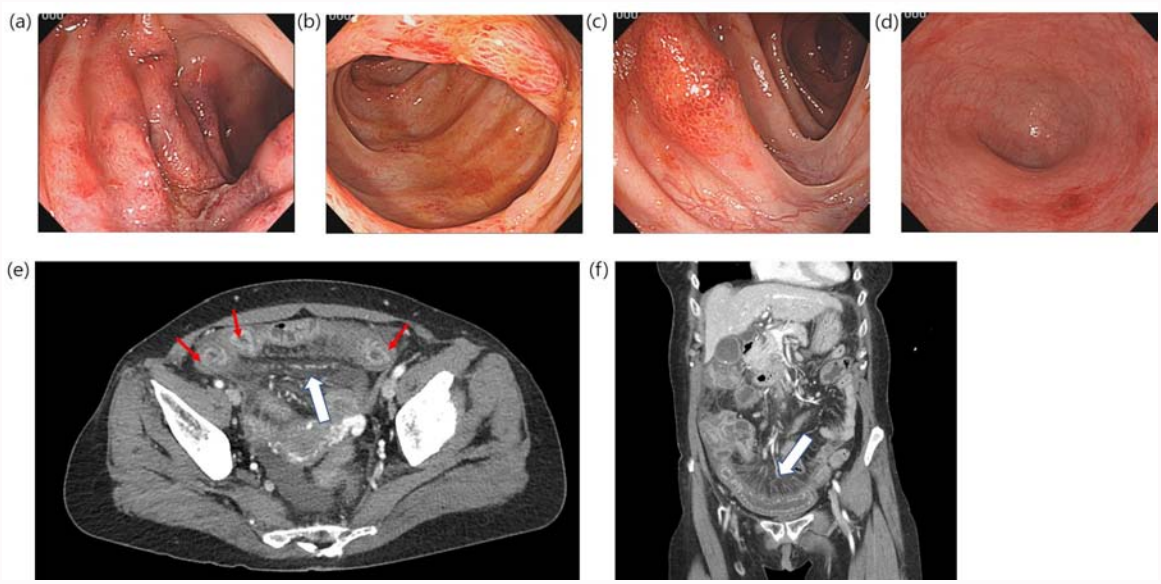

Figure 1: (a-d) Diffuse hyperemic edematous mucosa and intramucosal hemorrhagic spots and multiple ulceration lesions in colonoscopy. (a) ileocecal junction(b) splenic flexure (c) sigmoid-descending colon junction (d) rectum (e, f) double halo (target sign; arrow) and the prominent mesenteric vessels were pale (comb sign; bold arrow) in abdominal enhanced CT.

antihistamine administration.

One week later, she was admitted to the emergency room with massive hematochezia. The skin symptoms that earlier affected her legs recurred throughout the body. Blood tests depicted hemoglobin 10.1 g/dL, ESR 66 mm/h, CRP 102.3 mg/L, Cr 0.57 mg/dL, total protein 8.2 g/dL, and albumin 4.1 g/dL. Colonoscopy revealed diffuse hyperemic edematous mucosa and multiple ulcerative lesions from the rectum to the ileum. Abdominal enhanced CT illustrated intestinal wall thickening indicated by a double halo (target sign), and the prominent mesenteric vessels were pale (comb sign) (Figure 1). Viral and fungal infection tests, including HSV, CMV, AFB staining, and TB-PCR, were performed on colonic mucosal lesions, and all were negative. ASCA and p-ANCA levels were also negative. In the skin biopsy of the leg, perivascular infiltration was observed, and IgG, IgA, and M were all negative (Figure 2).

We suspected mesenteric and leukocytoclastic vasculitis. Administration of prednisolone (20 mg) gradually improved hematochezia and leg lesions. However, it's continued used led to recurrence of hematochezia and skin lesions. Adalimumab was restarted because there was no improvement in inflammation caused by prednisolone. Subsequently, mesenteric vasculitis and leukocytoclastic vasculitis in the legs completely recovered, and there was no recurrence (Figure 3).

Discussion

The incidence of vasculitis in patients with AS is unusual. There have been five reported cases of cutaneous vasculitis and 1 case of retinal vasculitis [2,3,8,9]. Severe cases of AS, such as mesenteric vasculitis, have not yet been reported. Vasculitis is usually idiopathic in nature. The known causes include infection, such as viral hepatitis, HIV, bacterial and fungal infections, or drugs, such as NSAIDs or antibiotics [2]. Additionally, vasculitis in AS may occur due to a paradoxical response to TNF-α inhibitors [10,11]. Most TNF inhibitor-induced vasculitis occurs within a short period of time after administration and is often limited to cutaneous vasculitis or worsening of existing symptoms. In addition, in many cases, the symptoms are mild enough to improve without the use of steroids or immunosuppressive agents. Our case is a case of severe vasculitis and since TNF-α inhibitors have been used for a long time, it is not considered to be vasculitis caused by a drug, infection, or TNF-α inhibitor, which are known probable causes [10].

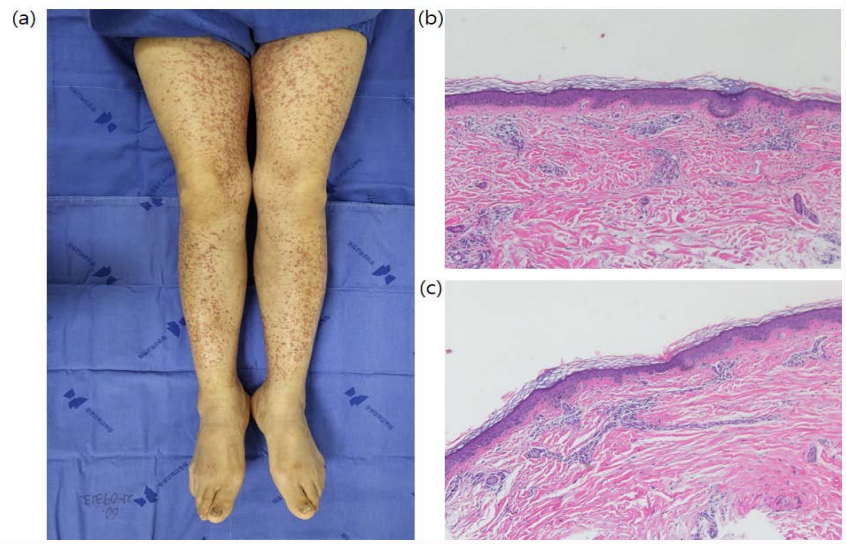

Figure 2: (a) Multiple erythematous purpuric papules on both lower legs. (b, c) Perivascular lymphocytic infiltration in upper dermis, histopathologically conforming to leukocytoclastic vasculitis (H&E stain).

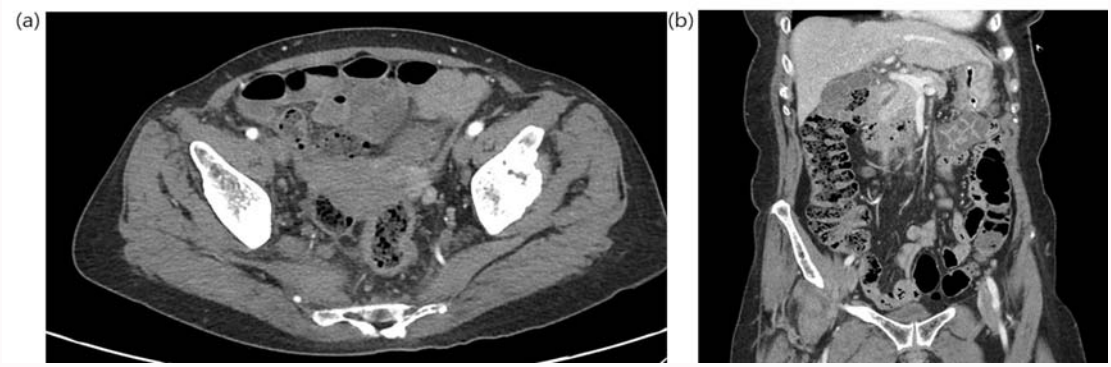

Figure 3: (a, b) CT illustrating improvement of target sign and comb sign after use of adalimumab.

Recently, the incidence of vasculitis has been increasing worldwide owing to COVID-19 and SARS-CoV-2 vaccination in the general population [12-14]. SARS-CoV-2 invades endothelial cells and induces a hyper inflammatory response, which can cause vasculitis by depositing immune complexes [15]. Since vaccines contain antigens of these infectious agents, these antigens can cause cross-reactivity and molecular mimicry, and adjuvants added to vaccines to enhance immunity can increase autoimmunity [16-18]. Additionally, vasculitis can be induced by a mechanism that increases autoimmunity. The reported SARS-CoV-2 vaccination-induced vasculitis is often skin-localized cutaneous vasculitis. In a patient with Rheumatic and Musculoskeletal Diseases (RMDs), one case of popular erythema and urticaria skin lesions was reported 10 days after AstraZeneca inoculation in a patient with psoriatic arthritis [19]. Severe vasculitis cases induced by SARS-CoV-2 vaccination reported to date are summarized in Table 1. This patient also developed mesenteric vasculitis and leukocytoclastic vasculitis 2 weeks after SARS-CoV-2 vaccination, and, hence, was considered to be SARS-CoV-2 vaccination-induced vasculitis.

Glucocorticoids (GCs) are used for treatment in most cases of vasculitis after SARS-CoV-2 vaccination. In some severe cases, plasma exchange, cyclophosphamide, and rituximab have been used in addition to GC. GC was also used in our patient; however, the symptoms recurred, and adalimumab, which was used for the patient's original disease and inflammatory bowel disease, was administered. Subsequently, the symptoms improved, and there was no recurrence.

Conclusion

In conclusion, mRNA vaccination in patients with AS can induce serious vasculitis such as mesenteric vasculitis. Vaccine side effects that do not respond to steroids may improve with TNF-α inhibitors.

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