



Remitting seronegative symmetrical synovitis with pitting edema syndrome postsecond COVID-19 vaccination: a case report

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Introduction and importance: Coronavirus disease 19 (COVID-19) has become the most serious public health crisis of our generation, and vaccines are effective in preventing its infection. Remitting seronegative symmetrical synovitis with pitting edema is an idiopathic rare benign syndrome, but it could be secondary to autoimmune diseases. Here, the authors reported the first case of this syndrome's development after COVID-19 vaccination.

Case presentation: A 52-year-old woman presented with hand edema, arthralgia, and morning stiffness, after receiving the second dose of mRNA COVID-19 vaccination. Examination revealed edema in the dorsum of both hands and symmetrical tenderness of the shoulders, elbows, wrists, knees, and ankles. Blood test results were normal except for elevated levels of C-reactive protein. The immune profile and the tuberculin test were also negative. A hand radiograph showed soft tissue edema. Ultrasonography of the extremities has shown tenosynovitis. Remitting seronegative symmetrical synovitis with pitting edema syndrome was diagnosed according to the diagnostic criteria. She was treated with 30 mg/day prednisolone, with a complete disappearance of edema and arthralgia after 10 days, and the C-reactive protein level was decreased.

Clinical discussion: Vaccines are still the most effective and protective method against COVID-19 infection, but it may trigger an immunological response. Remitting seronegative symmetrical synovitis with pitting edema (or sometimes RS 3 PE) is a rare nonunderstood syndrome identified by symmetric polyarthritis, synovitis, acute pitting edema of hands and/or feet, and a negative serum rheumatoid factor, with an excellent prognosis to treatment with steroid. Usually occurred in the old aged population, young patients' cases were mentioned. As the authors did not find any data about our subject, this is the first case of this syndrome development after the second dose of COVID-19 vaccination.

Conclusion: The occurrence of acute symmetrical seronegative polysynovitis with extremities edema, in the elderly, should guide toward the diagnosis of this syndrome.

Keywords: COVID-19 vaccination, COVID-19, extremities edema, RS3PE, synovitis

Introduction

Coronavirus disease 2019 (COVID-19) has changed people's lifestyles since 2020. It affects all organs and systems, including the musculoskeletal system^[1].

Vaccines are still the most effective and protective method against COVID-19 infection^[2]. As we know, no research has confirmed the mechanisms for vaccine-induced autoimmune disorders. In addition, some researchers are convinced that the vaccine does not trigger autoimmune diseases^[3].

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HIGHLIGHTS

- Many rheumatic manifestations have occurred post coronavirus disease 19 vaccination, and the mechanism of action is controversial.
- Remitting seronegative symmetrical synovitis with pitting edema is a rare benign rheumatologically condition, that could be associated with other conditions.
- It is the first case of this syndrome's development after coronavirus disease 19 vaccination.

Only a few rare cases were reported concerning Remitting seronegative symmetrical synovitis with pitting edema syndrome. It is presented by acute onset distal edema of both extremities^[4]. Here, we report a case of RS3PE's second COVID-19 vaccination.

Case presentation

A 52-year-old woman presented to our rheumatology clinic with hand edema, generally moderate to severe arthralgia, and morning stiffness lasting for an hour for the last 10 days.

She received the second dose of mRNA COVID-19 vaccination 2 weeks ago. She has no previous medical history or family history.

Physical examination revealed edema in the dorsum of both hands (Fig. 1) and symmetrical tenderness of shoulders, elbows,



Figure 1. Edema in the dorsum of both hands.

and wrists, in addition to the knees and ankles. The rest of the physical examination was unremarkable.

Blood test results were normal except for elevated levels of C-reactive protein (CRP; 23 mg/dl; normal: 0–6 mg/dl). The immune profile was negative, including the anticyclic citrullinated peptide antibody, the rheumatoid factor test, and the antinuclear antibody. HLA-27 was negative. The Tuberculin test was also negative.

Vascular endothelial growth factor and metalloproteinase level did not analyze, because they are unavailable in Syria.

A hand radiograph showed soft tissue edema. The chest radiograph was normal. Ultrasonography of the extremities has shown tenosynovitis.

Thoracic, abdominal, and pelvic computed tomography scans were normal. Papanicolaou's smear was normal.

Remitting seronegative symmetrical synovitis with pitting edema syndrome (RS3PE) was diagnosed according to the diagnostic criteria: age greater than or equal to 50 years, acute onset, pitting edema in the extremities with synovitis, and negative rheumatoid factor^[5]. She was treated with 30 mg/day prednisolone, with a complete disappearance of edema and arthralgia after 10 days, and the CRP level was decreased. The treatment on steroids was continued; with a 5 mg/week tapering dose. No relapse was observed in 6 weeks of follow-up. The patient was left on 5 mg/day prednisolone, and she was well done every 3 months of follow-up for 12 months.

The work has been reported in line with the Surgical Case Report (SCARE) criteria^[6].

Discussion

Vaccines are still the most effective and protective method against COVID-19 infection^[2]. It may trigger an immunological

response. Molecular mimicry is caused by genetic similarities of virus spike protein components to endogenous cross-reactive human antigens, and this generates autoreactive lymphocytes and antibodies. On the other hand, vaccine-induced immunity by the cell-mediated and humoral response. Neutralization antibodies and memory cells may influence the responses to vaccination in patients with immune diseases. As we know, no studies have confirmed the mechanisms by which vaccine-induced autoimmune disorders, meanwhile, some researchers are convinced that vaccine is not a trigger factor for autoimmune diseases^[7–9].

Remitting seronegative symmetrical synovitis with pitting edema syndrome (RS3PE) is characterized by symmetrical polyarthritides, with a sudden onset of pitting edema over the extremities, especially in older ages, and males, with elevated CRP, ESR, and negative rheumatoid factor, and an excellent prognosis to treatment with steroids^[4,5], as in our case.

Although the disease is more occurred in the old aged population, young patients' cases were mentioned^[10].

Until now, it is still a matter of debate, as to consider a syndrome or a disease^[5].

Its pathogenesis is not clear until now. Vascular endothelium-derived growth factor, which increases vascular permeability, may play a role as a major contributor to edema and synovitis, as well as IL-6, which is elevated in the synovial fluid of these patients, in addition to the HLA type, especially HLA B27, and infectious agents^[4,5,11,12].

The differential diagnoses include polymyalgia rheumatic and late-onset rheumatoid arthritis, and it coexists with cancer, and various rheumatic diseases, like Sjogren's syndrome, ankylosing spondylitis, sarcoidosis, and others^[5,10].

The diagnostic criteria suggested for this syndrome are age greater than or equal to 65 years, symmetrical synovitis, and edema over the extremities, morning stiffness, negative rheumatoid factor, and dramatic response to steroids^[4], and these were our diagnostic criteria.

The treatment of choice is prednisolone, besides nonsteroidal anti-inflammatory drugs and hydroxychloroquine^[4,5,13]. We gave our patient 30 mg/day of prednisone.

Rapid response to doses of maximum 30 mg prednisone was mentioned, as we had found.

This remission is usually well-sustained, as in our case, except if it is a paraneoplastic phenomenon, the improvement is only partial, with a higher rate of relapses^[14,15]. As we did not find any data about our subject, this is the first case of this syndrome's development after COVID-19 vaccination.

Conclusion

The occurrence of acute symmetrical seronegative polysynovitis with extremities edema, in the elderly, should guide toward the diagnosis of this syndrome.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the national research committee and with the Helsinki Declaration.

Declaration of patient consent

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. Institutional approval is not required for this case study.

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No fund.

Author contribution

Y.H. and A.H. conceived, designed and acquired data for the work and N.K. analyzed it. M.K., shared her expert opinion to support treatment decision and also revised it.

Conflicts of interest disclosure

The authors have no conflicts of interest to declare.

Research registration unique identifying number (UIN)

This case do not detail a new surgical technique or new equipment/technology, so it is not required.

Guarantor

Yara Hodifa.

Data availability statement

The case data is available.

Provenance and peer review

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