

## Lower Limb Oedema Revealing Symmetrical Seronegative Remittent Synovitis after SARS-COV-2 Vaccination

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### Abstract

### Case Report

**Introduction:** Remitting seronegative symmetrical synovitis with pitting edema (RS3PE) is a rare clinical entity characterized by “remitting,” “seronegative,” and “symmetrical” synovitis with pitting edema on the dorsum of the hands and feet. Although rheumatic or malignant diseases are diseases that are known to coexist with RS3PE, other factors such as medication, infection, and vaccination have been reported to be associated with RS3PE. **Objectif:** To report the case of an 81-year-old man without rheumatic ATCD who had an RS3PE resulting from vaccination against Covid 19, based on an mRNA vaccine (BNT162b2 mRNA) and supported in our training in January 2022. **Case report:** An 81-year-old man, with cardiovascular risk factors such as type 2 diabetes on metformin, well-balanced hypertension, and a history of hiatal hernia complicated by iron deficiency anemia, was followed up for moderate IM valve disease under treatment. The patient presented to the emergency room with lower limb oedema, and inflammatory arthritis that had been evolving for 2 months. Three days after receiving the third dose of Pfizer's covid 19 (BNT162b2 mRNA) vaccine, the patient presented with bilateral inflammatory polyarthritis and symmetric large joints. The joint involvement was associated with swelling of the hands and feet. The hemogram showed lymphopenia at 900elements/mm<sup>3</sup> and CRP at 140mg/L, SV at 76mm and D-dimer at 3000ng/ml. Having first ruled out a cardiac, hepatic or renal origin, we then ruled out inflammatory rheumatism, connectivitis or small vessel vasculitis. In search of the origin of this picture, the thoraco-abdomino-pelvic scanner was in favor of an inhalation pneumonia and a hiatal hernia. He ruled out a probable solid neoplastic origin. The PSA was normal. We retained the diagnosis of RS3PE secondary to vaccination as the only triggering factor for this syndrome. The patient was put on oral corticosteroid therapy with rapid degression and adjuvant treatment. The evolution was favorable without relapse. **Discussion and conclusion:** RS3PE is a rare rheumatic syndrome affecting elderly males and it is characterised by acute onset of symmetrical pitting oedema and small joint synovitis involving mainly the hands and, less often, the feet. The pathogenesis of RS3PE remains largely unknown. Elevated serum levels of VEGF facilitate increased capillary permeability and synovial angiogenesis, leading to subcutaneous oedema and tenosynovitis, may be an important pathogenic mechanism in RS3PE. It is important for clinicians to keep in mind the possibility that rare phenomena may occur after vaccination.

**Keywords:** RS3PE, oedema, inflammatory arthritis, vaccination, Covid 19, corticosteroid therapy.

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## INTRODUCTION

Remitting seronegative symmetrical synovitis with pitting edema (RS3PE) is a rare clinical entity characterized by “remitting,” “seronegative,” and “symmetrical” synovitis with pitting edema on the dorsum of the hands and feet. Although rheumatic or malignant diseases are diseases that are known to coexist with RS3PE, other factors such as medication,

infection, and vaccination have been reported to be associated with RS3PE.

We report the case of an 81-year-old man without rheumatic ATCD who had an RS3PE resulting from vaccination against Covid 19, based on an mRNA vaccine (BNT162b2 mRNA) and supported in our training in January 2022.

## CASE REPORT

An 81-year-old Caucasian man with cardiovascular risk factors, type 2 diabetes on metformin, well-balanced hypertension, and a history of hiatal hernia complicated by iron-deficiency anemia, was followed for moderate MI valve disease on treatment. The patient presented to the emergency room with low limb oedema, and inflammatory arthritis that had been evolving for 2 months.

Three days after receiving the third dose of Pfizer's covid 19 (BNT162b2 mRNA) vaccine, the patient presented with bilateral inflammatory polyarthritis and symmetric large joints. The joint involvement was associated with swelling of the hands (in boxing gloves) Figure 1 and feet (in socks) Figure 2, which were soft, taking the bucket for clinical examination.

The hemogram showed lymphopenia at 900elements/mm<sup>3</sup> and CRP at 140mg/L, SV at 76mm and D-dimer at 3000ng/ml. Having first ruled out a cardiac origin, the ECG was in regular sinus rhythm with an electrical LVH associated with significant repolarization disorders, a complement by ETT was performed, showing a non-dilated non-hypertrophied LV with preserved systolic function, moderate MI, non-elevated LVP, a non-dilated compliant IVC.

The hepatic and renal origin of the edema was ruled out, we then eliminated an inflammatory rheumatism, a connectivitis or a small vessel vasculitis.

In search of the origin of this picture, the thoraco-abdomino-pelvic scanner was in favor of an inhalation pneumonia and a hiatal hernia. He ruled out a probable solid neoplastic origin. The PSA was normal.

We retained the diagnosis of RS3PE secondary to vaccination as the only triggering factor for this syndrome.



**Figure 1: Hand oedema in boxing gloves**



**Figure 2: Edema of the foot in socks**

The differential diagnosis included:

- Rheumatoid arthritis: ruled out due to the negativity of anti CCP antibodies
- Gout: discarded due to chronic symptoms and normal uric acid
- Connectivity or vasculitis: negative immunological assessment

The patient was put on oral corticosteroid therapy with rapid degression and adjuvant treatment. Pneumopathy was put on antibiotics. The evolution was favorable without relapse.

## DISCUSSION

Vaccination against SARS-CoV-2 infection is increasing worldwide due to the pandemic. BNT162b2 (Pfizer), mRNA-1273 (Moderna), and ChAdOx1 nCoV-19 (AstraZeneca) vaccines are available. Their efficacy in preventing severe respiratory conditions has been established. However, as the number of vaccinated people increased, it became evident that various adverse reactions such as fever, myalgia, general fatigue, skin lesions, thrombosis, and deterioration of preexisting rheumatic disease could occur as a result of vaccination [1].

Individualized in 1985 by Mc Carty, the RS3PE syndrome (or benign acute edematous arthritis of the elderly) carries out a table of polysynovitis with distal edema. Affecting with preference the man of more than 65 years, its evolution is usually favorable under corticosteroids at low dose [2].

RS3PE is a rare rheumatic syndrome affecting elderly males and it is characterised by acute onset of symmetrical pitting oedema and small joint synovitis involving mainly the hands and, less often, the feet [3].

A cross-sectional study among healthcare professionals indicated that BNT162b2 mRNA COVID-19 was associated with vaccination-induced arthritis/ arthralgia in 17% of the population studied [3]. Rarely vaccines can trigger a new-onset rheumatic disease; however, data regarding the SARS-CoV-2 vaccines are lacking.

The pathogenesis of RS3PE remains largely unknown. Elevated serum levels of VEGF facilitate increased capillary permeability and synovial angiogenesis, leading to subcutaneous oedema and tenosynovitis, may be an important pathogenic mechanism in RS3PE [4].

Although most cases are idiopathic, RS3PE has been associated with other rheumatic conditions, malignancies, parvovirus infection, installation of the intravesical BCG and more recently with immunotherapies [5].

Proposed diagnostic criteria include the following: bilateral pitting oedema of both hands, sudden onset of polyarthritis, age over 50 years and seronegative for rheumatoid factor [6]. Further, dramatic response to low dose glucocorticoids, and attainment of remission in most patients, support the diagnosis of RS3PE.

In our case, the patient met the criteria mentioned above and the kinetics of the onset of symptoms 3 days after the 3rd dose of the vaccine) strongly suggests that RS3PE was triggered by vaccination.

A previous case study described an 80-year-old man who developed RS3PE 2 days after the 2nd dose of Covid 19 vaccine (BNT162b2 mRNA). The course under corticosteroids was favorable [7].

The differential diagnosis included crystal-induced arthritis, such as gout or calcium pyrophosphate deposition disease, but the absence of chondrocalcinosis and the persistent nature of the patient's symptoms. An additional consideration was late-onset rheumatoid arthritis; however, the autoantibodies were negative, and the dorsal hand pitting oedema is not a classic manifestation of rheumatoid arthritis [8].

## CONCLUSION

RS3PE is a rare rheumatic syndrome affecting elderly males and it is characterised by acute onset of

symmetrical pitting oedema and small joint synovitis involving mainly the hands and, less often, the feet. The pathogenesis of RS3PE remains largely unknown. Elevated serum levels of VEGF facilitate increased capillary permeability and synovial angiogenesis, leading to subcutaneous oedema and tenosynovitis, may be an important pathogenic mechanism in RS3PE. It is important for clinicians to keep in mind the possibility that rare phenomena may occur after vaccination.

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