Remitting seronegative symmetrical synovitis with pitting oedema following BNT162b2 mRNA COVID-19 vaccination

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SUMMARY

Remitting seronegative symmetrical synovitis with pitting oedema (RS3PE) is a rare inflammatory condition that occurs in older adults. Here, we report a case of an 80-year-old man with no history of rheumatic disease who presented with acute onset of bilateral hand pain, pitting oedema and synovitis after the second dose of the BNT162b2 mRNA COVID-19 vaccine. Laboratory workup revealed elevated inflammatory markers and negative autoantibodies. Significant improvement was noted with prednisolone. This is the first reported case of RS3PE in an elderly patient with no previous rheumatic disease following mRNA COVID-19 vaccination.

BACKGROUND

Since the onset of the COVID-19 pandemic, more than 3 million people have lost their lives. The most effective approach against COVID-19 includes the development and administration of safe vaccines.[1] 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.[2] Rarely vaccines can trigger a new-onset rheumatic disease; however, data regarding the SARS-CoV-2 vaccines are lacking. In the present study, we report the first case of remitting seronegative symmetrical synovitis with pitting oedema (RS3PE) induced by BNT162b2 mRNA COVID-19 vaccination in a patient with no history of rheumatic disease. Healthcare providers need to be aware of this condition induced by COVID-19 vaccine and appropriately treat it.

CASE PRESENTATION

An 80-year-old Caucasian man presented with a 2-week history of acute onset of bilateral hand swelling and pain, which was worse in the left hand and was associated with paresthesia. The symptoms began 2 days following the second dose of the BNT162b2 mRNA COVID-19 vaccine. The patient's medical history included hypertension, hyperlipidaemia, atrial fibrillation, ischaemic cardiomyopathy, aortic valve stenosis, COPD, sleep apnoea and without any previous history of any rheumatic disorder. Physical examination revealed symmetrical pitting oedema in the dorsum of both hands and synovitis (figure 1).

INVESTIGATIONS

Laboratory investigations revealed an elevated erythrocyte sedimentation rate of 55 mm/hour (normal <20) and C reactive protein level of 120 mg/L (normal <5), with negative antinuclear antibodies rheumatoid factor and anticyclic citrullinated peptide antibodies (table 1). The full blood count, renal and liver function tests were normal. Hepatitis B and C antibodies, parvovirus B_{19} were negative. The hand radiographs did not show any evidence of erosion or chondrocalcinosis. Chest radiograph was normal.

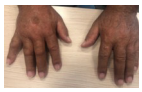

Figure 1 Clinical features of the patient bilateral pitting oedema of the dorsum of the hands, worse in the left hand.

DIFFERENTIAL DIAGNOSIS

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.

Given the abrupt onset of symptoms, the puffy oedematous hands and significant response to glucocorticoids, the patient was diagnosed with RS3PE.

TREATMENT

The patient took paracetamol without symptom relief. He was prescribed prednisolone 15 mg daily and had a remarkable improvement in his symptoms (figure 2). In addition, the patient also underwent physical therapy and used topical NSAIDs.

OUTCOME AND FOLLOW-UP

Three months following the onset of his symptoms, a trial to wean off prednisolone was unsuccessful, and the patient stills require prednisolone 5 mg daily. The repeated erythrocyte sedimentation rate

Figure 2 Clinical features following treatment with low-dose glucocorticoids. Significant improvement was noted with glucocorticoids, with less swelling.

Table 1 Laboratory studies

Laboratory studies	Results	Reference range
White cell count	8.8	4–10.0 x 10^9/L
Haemoglobin	13.1	12–16 g/L
Platelet	230	150–350x 10^9/µL
Sedimentation rare	55	<20 mm/hour
C reactive protein	120	<5 mg/L
Creatinine	0.9	0.6–1.2 mg/dL
Alanine aminotransferase	32	7–55 U/L
Aspartate aminotransferase	27	8–48 U/L
Alkaline phosphatase	79	45–115 U/L
Hepatitis C antibody	Negative	Negative
Parvovirus B_{19} IgM	Negative	Negative
Parvovirus B_{19} IgG	Negative	Negative
Antinuclear antibodies	Negative	Negative
Rheumatoid factor	10	<14 IU/mL
Cyclic citrullinated peptide antibodies	6	<20 U/mL

was 36 mm/hour (normal <20) and C reactive protein level of 3 mg/L (normal <5). We discussed the option to add a disease modifying antirheumatic drug, such as methotrexate, but the patient was reluctant to take the medication.

DISCUSSION

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] 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 5] 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.[5–8]

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.[7] Further, dramatic response to low dose glucocorticoids, and attainment of remission in most patients, support the diagnosis of RS3PE.

In our case, the patient fulfilled the criteria mentioned above and the kinetics of symptom onset (2 days after the second dose of the vaccine) strongly suggests that the RS3PE was triggered by the vaccination. A previous case series study described an 83-year-old patient with history of polymyalgia rheumatica who developed RS3PE, 7 days after the first dose of the BNT162b2 mRNA vaccine.[9] The patient had a prompt response to treatment and resolution of his symptoms.

Patient's perspective

'I am a farmer, and the joint pain deeply affected my quality of life and it impacted my ability to drive my tractor. The steroid is a miracle drug'.

Learning points

- This case underlines that RS3PE can be induced by vaccinations such as the BNT162b2 mRNA COVID-19 vaccine.
- The administration of low dose of glucocorticoid led to a rapid and excellent symptom response.

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