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Paraneoplastic remitting seronegative symmetrical synovitis with pitting edema (RS3PE), improved following surgical resection of prostatic carcinoma: A case report

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ABSTRACT

RS3PE syndrome is a rare condition that occurs in elderly individuals which can present alone or in association with various rheumatic or malignant diseases.

We present a case of a 77-year-old man who was diagnosed with adenocarcinoma of the prostate and initially under active surveillance. 2 months after the diagnosis, he presented with arthralgia in both shoulders and knees, pitting edema of the both hands and feet.

The patient underwent radical prostatectomy since the link between prostatic carcinoma and RS3PE was suspected. After 7 months from operation, the patient has no symptoms or signs of RS3PE.

Introduction

Remitting seronegative symmetrical synovitis with pitting edema (RS3PE) syndrome is a rare clinical condition which was first described by McCarty in 1985.[1] It has been reported as a paraneoplastic syndrome, frequently together with prostate, stomach, and colon cancers. This syndrome is characterized by acute onset symmetrical distal synovitis, pitting edema of the dorsum of the hands, and seronegativity of rheumatoid factor (RF). It generally responds well to low-dose corticosteroid treatment and remains in remission for a long time unless associated with malignancy.[2–4] We report a case of RS3PE syndrome associated with prostatic adenocarcinoma improved following after radical prostatectomy.

Case presentation

A 77-year-old man with no previous history of trauma, fever, weight loss or any other metabolic or rheumatologic disease presented with arthralgia in both shoulders and knees, pitting edema of the both hands and feet (Fig. 1).

The patient had been diagnosed with adenocarcinoma of the prostate with a Gleason score of 6 (3 + 3) and a clinical stage of cT2aN0M0, 2 months before the presentation of these symptoms. Prostate-specific antigen (PSA) was 6.14 ng/ml at that point of time, and he was under active surveillance.

Results of routine laboratory investigation are summarized in Table1

The levels of C reactive protein (CRP) increased to 25.61 (mg/dL). Besides, the levels of Matrix metalloproteinase-3 (MMP-3), which is known to be sensitive to RS3PE syndrome,[2] increased to normal upper limit (117.7ng/ml).

RF, antinuclear antibody (ANA) and anti-cyclic citrullinated peptide (anti-CCP) were negative.

Clinical diagnosis was RS3PE syndrome and prednisolone was

Abbreviations: ANA, (antinuclear antibody); Anti-CCP, (Anti-cyclic citrullinated peptide); CRP, (C reactive protein); Interleukin 6, (IL-6); MMP-3, Matrix metalloproteinase-3); PSA, (Prostate-specific antigen); Remitting seronegative symmetrical synovitis with pitting edema, (RS3PE); Rheumatoid factor, (RF); Tumor necrosis factor a, (TNF-a).

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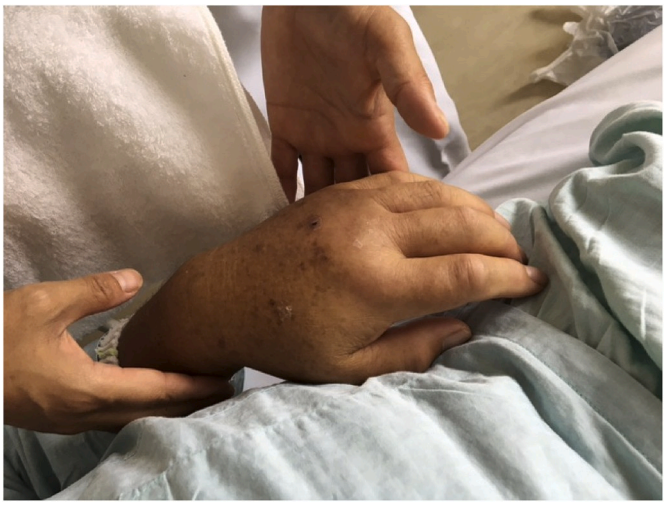

Fig. 1. The patient showed pitting edema of the both hands before the treatment of prednisolone in dose of 15mg daily.

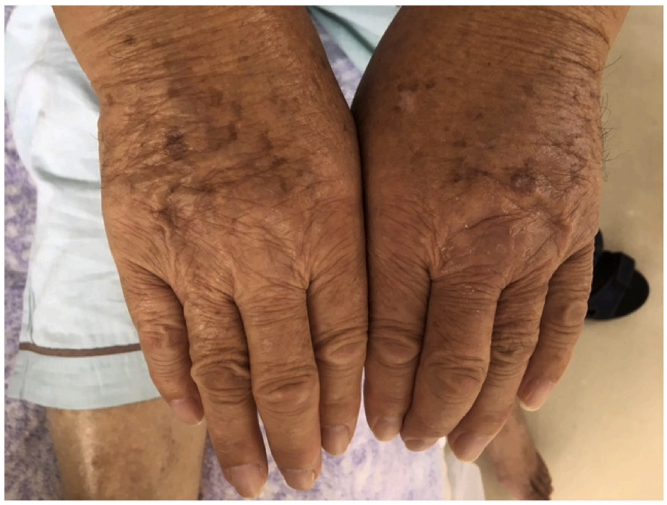

Fig. 2. His pitting edema of the both hands disappeared after treatment of prednisolone.

Table 1
Results of laboratory tests at diagnosis of RS3PE syndrome, and after 2 months from radical prostatectomy.

Laboratory test	at diagnosis of RS3PE syndrome	after 2 months from surgery
leukocytes	10000/μL	5500/μL
Hemoglobin	13.0 g/dL	14.1 g/dL
Mean cell volume	94 fL	96 fL
Albumin	2.8 g/dL	4.0 g/dL
Ferritin	715 ng/mL	212 ng/mL
CRP*	28.74 mg/dL	0.21 mg/dL
PSA*	6.14 ng/mL	< 0.01 ng/mL
Anti-CCP*	< 0.5 U/mL	< 0.5 U/mL
ANA*	< 40	< 40
MMP-3*	117.7 ng/mL	39.3 ng/mL
sIL-2R	1020 U/mL	540 U/mL

Abbreviations: CRP: C reactive protein; PSA: Prostate-specific antigen; Anti-CCP: Anti-cyclic citrullinated peptide; ANA: antinuclear antibody; MMP-3: Matrix metalloproteinase-3

started in dose of 15mg per day. One week later, the edema almost disappeared (Fig. 2) and CRP was markedly decreased to 5.38 (mg/dl).

Although his symptom and laboratory data had improved with PSL, the patient underwent robot-assisted radical prostatectomy 2 months after the diagnosis of RS3PE since the link between prostatic carcinoma and RS3PE syndrome was suspected.

Pathological examination of the prostate specimen demonstrated well differentiated adenocarcinoma, Gleason score of 7 (3 + 4). There was no evidence of involvement of the seminal vesicles, bladder or lymphovascular and the resection margin was negative. PSA immediately decreased to less than 0.1 ng/ml.

After 2 months from the operation, the prednisolone medication had been reduced in steps and ceased without any related adverse effects. At that point of time, the levels of CRP and MMP-3 decreased to 0.21 mg/dl and 39.3 ng/ml, respectively (Table1).

After 7 months from the operation, the patient has no symptoms or signs of RS3PE syndrome, without having any evidence of cancer recurrence, and his PSA level has remained undetectable (PSA <0.1 ng/ml).

Discussion

The etiology of the RS3PE syndrome is unknown. An infectious agent is presumed to be the triggering factor but none has been confirmed.[3] This syndrome has also been described in neoplastic conditions. Review of some literatures indicates that RS3PE syndrome may coexist with or precede a malignant state.[2–4] Recently, case of a patient who developed RS3PE related to immune checkpoint inhibitor therapy has been reported.[5]

Diagnosis of RS3PE syndrome is based on clinical features as follows: (1) bilateral pitting edema of the hands, feet or both, (2) sudden onset of polyarthritis, and (3) age over 50 years.[1]

Seronegativity for RF and dramatic response to low-dose corticosteroid treatment are also characteristics of the disease. The levels of MMP-3 and CRP are often raised.[2] There are some reports of a good response to low dose corticosteroids in RS3PE patients with associated neoplasia, similar to the idiopathic case.[2,3] On the other hand, poor response to corticosteroids is also reported in paraneoplastic RS3PE syndrome.[3,4] Particularly in such cases, the best management of paraneoplastic RS3PE syndrome is to treat the malignant process; most patients seem to respond after successful treatment of the underlying malignancy after surgical treatment of the tumor and/or chemotherapy or radiotherapy.[3,4]

Likewise, also in the RS3PE patients with associated neoplasma who respond well to low dose corticosteroids, such as shown in this report, we should consider radical treatment for malignancy. This is because of the following reasons: some reports suggest the underlying malignancy may have triggered RS3PE syndrome via an inflammatory process involving both interleukin 6 (IL-6) and tumor necrosis factor a (TNF-a),[3] and it is often difficult to withdraw steroids from the patients with paraneoplastic RS3PE.[2] In our report, improvement in symptoms of RS3PE syndrome may have been solely due to the steroid administration, but we inferred that radical prostatectomy have improved the cancer-related inflammatory microenvironment and resulted in steroid withdrawal.

In this report our patient was under active surveillance against prostate cancer initially.

Afterward, we performed radical prostatectomy since the link between prostatic carcinoma and RS3PE syndrome was suspected. In consequence, the symptoms of RS3PE syndrome disappeared completely and withdrawal of steroids without any related adverse effects were achieved.

To the best of our knowledge, there are several cases of prostatic carcinoma associated with RS3PE syndrome have been reported, but ours is the first documented case of improved RS3PE syndrome following surgical resection of prostatic carcinoma.

This case reminds the necessity of taking into account prostate cancer as a possible cause for RS3PE syndrome.

Conclusion

We reported the case of RS3PE syndrome improved following surgical resection of prostatic carcinoma. Patients diagnosed with RS3PE syndrome should be carefully investigated for a possible neoplasm.

Declaration of competing interest

None.

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