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Remitting Seronegative Symmetrical Synovitis with Pitting Edema (RS3PE) in the Setting of Renal Cell Carcinoma in a Native American/American Indian Patient

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ABSTRACT

Remitting seronegative symmetrical synovitis with pitting edema (RS3PE) is a rare inflammatory arthritis characterized by pitting edema and symmetric synovitis of hands and feet. The condition is typically treated by steroids, with an excellent clinical response. The relapsing and remitting nature of the disease, along with shared similarities with other rheumatic disorders often serve as a challenge to establishing a diagnosis. It is frequently categorized as a paraneoplastic syndrome due to the association of the condition with both hematologic malignancy and solid tumors. We present a case of an elderly Native American / American Indian male (NA/AI) with RS3PE diagnosed in the setting of renal cell carcinoma (RCC).

Keywords

RS3PE, Rheumatoid Arthritis, Renal Cell Carcinoma, Native American, American Indian.

Case Report

A 76-year-old NA/AI male presented to the rheumatology clinic to establish care for intermittent swelling in his wrists, hands, and fingers. The patient's medical history was significant for rheumatoid arthritis (RA) managed with hydroxychloroquine, RCC with recent nephrectomy, diabetes mellitus, and hypertension. The patient reported that he had been experiencing severe, intermittent swelling which was limited to his wrists, the palmar and dorsal surfaces of his hands, and his fingers. The patient remarked that this had resulted in significant limitations of his strength and range of motion in his wrists and hands. During the past several months the patient reported experiencing several such flares which had resolved with 5 mg daily prednisone for one to several weeks. Laboratory workup revealed a normal ESR and a C-reactive protein level. HLA-B27, ANA, dsDNA, Smith, SSA, SSB, RNP, centromere, SCL-70, RNA Pol III, Jo1 antibody, complement C3, C4 levels, and hepatitis B and C panel were negative. Rheumatoid factor was moderately positive. Notably, the patient had not experienced any additional episodes of swelling or pitting edema status post nephrectomy. The patient expressed the desire to discontinue hydroxychloroquine treatment as he did not believe he was benefitting from it. Additionally, the patient did not want to start another conventional synthetic, targeted synthetic or biologic disease modifying anti-rheumatic drug (DMARD) therapy.

Introduction

Remitting seronegative symmetrical synovitis with pitting edema (RS3PE) is a rare inflammatory arthritis with associated distal synovitis and pitting edema that was first described by McCarthy in a panel of 10 elderly patients, each experiencing edema of the hands and feet characterized by rapid onset and demonstrating a predictable response to treatment, as a subset

of seronegative rheumatoid arthritis with a unique condition that could be confused with polymyalgia rheumatica [1]. Typically, the disease is diagnosed through careful history and physical examination showing the classic 'boxer's glove' hands with supporting laboratory findings [2]. A negative rheumatoid factor favors the most common diagnosis of RS3PE and was previously a diagnostic criteria, however, some cases have been documented with a positive rheumatoid factor when RA was present before the onset of RS3PE, as in this case. This is consistent with other instances of RS3PE presenting as a paraneoplastic syndrome, leading to numerous episodes of edema with subsequent resolution of symptoms after successful treatment of underlying malignancy. The time to remission is variable with documented resolution between 2 to 300 days, but often resolving in a couple weeks to a couple months [2].

Discussion

RS3PE is a rare rheumatologic disease often seen in elderly patients with abrupt onset, marked pitting edema in hands and feet, and an excellent response to corticosteroids.

Although the link between RCC and RS3PE as a paraneoplastic syndrome is unclear, both disease processes are known to have elevated levels of vascular endothelial growth factor (VEGF) [2-4]. However, it is uncertain if VEGF can cause RS3PE or is produced in the same pathogenic process. VEGF inhibitors have been used successfully in the treatment of RCC, but the effect of these medications on RS3PE is yet to be studied [4]. Additionally, patients with RS3PE can have an increased Tumor Necrosis Factor-alpha (TNF-a) level, though it is unknown if TNF-a inhibitors would be beneficial in the treatment of recurrent RS3PE. Additionally, there is an unknown association between TNF-a inhibitors and their effect on renal cell carcinoma, with one study showing patients diagnosed with RA who were started on TNF-a inhibitors having the same rate of new diagnosis of renal cancer compared to the average population [5]. While RS3PE has been seen in diverse populations worldwide, most cases reported in the literature are from America and Europe. Additionally, there have been several cases reported out of Japan, with an estimated prevalence in 0.09% of all patients over the age of 50 seen in Japanese clinics [6,7]. While the exact etiology of RS3PE in our patient is unknown, we can genetically link it back to the shared ancestry between the NA/AI and the Northern Japanese via the ancestral people of northern Siberia [8].

Conclusion

To the best of our knowledge, this is the first observation of RS3PE presenting in a NA/AI patient with a background of RA and RCC. It should add to the fund of knowledge of this rather rare condition especially in the NA/AI population.

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