Case report

Remitting seronegative symmetrical synovitis with pitting edema (RS3PE) as the presenting manifestation of colorectal cancer: A case report

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ABSTRACT

Introduction: Remitting Seronegative Symmetrical Synovitis with Pitting Edema (RS3PE) is a rare syndrome which was first reported by McCarty et al. in 1985. The association between RS3PE and both benign tumors and cancers has been reported in the literature.

Case Presentation: We hereby report a case of RS3PE associated with an early-stage colorectal cancer. A 67-year-old male patient not known to have any medical illness presented to the rheumatology clinic complaining of bilateral joint pain in both ankles for 5 weeks associated with symmetrical feet edema. Laboratory findings showed negative rheumatoid factor (RF), anti-nuclear antibody (ANA), and anti-cyclic citrullinated peptide (anti-CCP). Inflammatory markers (C-reactive protein and erythrocyte sedimentation rate) were high. Ultrasound showed grade II synovitis in both ankles without erosions. The symptoms rapidly resolved with short-term low-dose corticosteroid. Fecal occult blood was requested, and it returned positive. Colonoscopy was done and showed polyploid lesions in transverse colon. The histopathological analysis revealed adenocarcinoma of the large bowel.

Conclusion: In conclusion, RS3PE patients should be screened for concomitant malignancy in order to intervene immediately and treat cancer at an early and curable stage. Further studies on screening methods of malignancy in such patients are essential and critical to prevent the devastating complications.

Keyword: RS3PE; Colorectal, Paraneoplastic syndrome, Adenocarcinoma, Seronegative.

Introduction

Remitting Seronegative Symmetrical Synovitis with Pitting Edema (RS3PE) is a rare syndrome which was first reported by McCarty et al. in 1985. Ten patients (8 elderly men and 2 elderly women) presented with symmetrical acute onset of polysynovitis associated with edematous dorsa of the hands. Rheumatoid factor was negative in all patients, and no bone erosions were noticed on imaging. The clinical and laboratory signs Of inflammation remitted gradually, thus given the name "Remitting seronegative symmetrical synovitis with pitting edema" by the authors [1]. The prevalence of RS3PE is still unknown in the literature; however, there is a study conducted in Japan reported an incidence of 0.09% estimated from 3,347 patients [2]. The association between RS3PE and both benign tumors and cancers has been reported in the literature. The malignancies associated with this syndrome

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Include both hematological and solid tumors representing an average rate of 20% of all cases [3]. We hereby report a case of RS3PE associated with an early-stage colorectal cancer.

Case Report

A 67-year-old male patient not known to have any medical illness presented to the rheumatology clinic complaining of bilateral joint pain in both ankles for 5 weeks associated with bilateral feet swelling.

Family history was unremarkable.

On examination, the patient was afebrile. There was bilateral pitting edema in both feet extending up to the ankle joint with marked tenderness and restricted range of motion. Other systems were unremarkable. Laboratory findings showed negative rheumatoid factor (RF), anti-nuclear antibody (ANA), and anti-cyclic citrullinated peptide (anti-CCP). Inflammatory markers (C-reactive protein and erythrocyte sedimentation rate) were high. Ultrasound showed grade II synovitis in both ankles without erosions. The diagnosis of RS3PE was established given the clinical picture as well as the negativity of rheumatoid factor, and the elevated inflammatory markers. The symptoms rapidly resolved with short-term low-dose corticosteroid. During follow-up, the patient reported bowel habit changes on further questioning; fecal occult blood was requested, and it returned positive. Colonoscopy was done and showed polyploid lesions in transverse colon. The histopathological analysis revealed adenocarcinoma of the large bowel; however, metastatic work-up was negative. The patient was referred to general surgery for further management of his colorectal cancer.

Discussion

RS3PE was first described by McCarty et al. in 1985. [1] It is a rare rheumatological syndrome which was previously considered as a subset of rheumatoid arthritis (RA) in elderly patients; however, it is now recognized as a distinct syndrome for its unique clinical picture which differs from any other condition. This syndrome is characterized by an acute onset of symmetrical polyarthritis involving the hands and/or feet with associated pitting edema and negative RF [4]. It usually affects elderly above 60 years with a male-to-female ratio of nearly 2:1 [5]. The laboratory findings include elevated inflammatory markers such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR), anemia of chronic disease, negative RF, and rarely positive ANA. Serum matrix metalloproteinase-3 (MMP-3) level may be higher in patients with paraneoplastic RS3PE [6]. X-ray is usually non-specific, and bone erosions are classically absent. MRI is best used to detect small amounts of effusion. Color Doppler ultrasonography is the imaging modality of choice for RS3PE, and it is regarded superior to other imaging modalities [7]. The pathogenesis is not fully understood; nevertheless, it is believed that vascular endothelial growth factor (VEGF) contributes to its mechanism by increasing vascular permeability leading to polysynovitis and pitting edema of the extremities. Higher levels of VEGF were found in RS3PE patients compared to RA and other connective tissue diseases [4]. RS3PE can mimic multiple conditions such as polymyalgia rheumatica, elderly-onset rheumatoid arthritis, systemic lupus erythematous (SLE), systemic sclerosis, and mixed connective tissue disease [8]. However, Olivé et al. proposed diagnostic criteria in 1997 to distinguish RS3PE, which include: (1) Age > 50 years, (2) bilateral pitting edema of the hands, (3) sudden onset of polyarthritis, (4) seronegative RF, and (5) absence of radiological evidence of joint destruction [9]. This syndrome usually responds to low-dose corticosteroid and remains in remission for a long period unless accompanied with cancer; in which it tends to respond poorly to steroid therapy. [4] Interestingly, our patient responded to the drug, and all symptoms remitted dramatically. RS3PE can represent a paraneoplastic condition; it may coexist with or even precede a wide range of hematological and solid organ malignancies [5]. The hematological malignancies include Hodgkin's lymphoma, leukemia, myelodysplastic syndrome, and angioimmunoblastic T cell leukemia. While solid tumors include prostate, gastrointestinal, lung, breast, ovary, bladder, and endometrium. There are also reported cases of malignancies with unknown origin [3]. There is no a specific test that can be used to detect malignancy in such patients. However, a recent study reported that serum levels of basic fibroblast growth factor (bFGF) might be used as a useful predictor biomarker for malignancy in RS3PE patients with a suggested optimal cut-off value of 10 ng/mL [10]. The high index of clinical suspicion and the awareness of such correlations between rheumatological symptoms and malignant pathologies remain the cornerstone in identifying paraneoplastic rheumatological conditions. This in-hand valuable tool can guide clinicians to clinically investigate the patient thoroughly for an underlying malignant entity [6]. In

our patient, the colon cancer was detected in its very early stage and managed accordingly.

Conclusion

RS3PE patients should be screened for concomitant malignancy in order to intervene immediately and treat cancer at an early and curable stage. Such screening guidelines are lacking; therefore, further studies are needed to establish accessible, reliable, and cost-effective screening methods for these patients.

Conflict of Interest

None

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None

References

1. McCarty DJ, O'Duffy JD, Pearson L, Hunter JB. Remitting Seronegative Symmetrical Synovitis With Pitting Edema: RS3PE Syndrome. JAMA [Internet]. 1985 Nov 15;254(19):7-2763. Available from: https://doi.org/10.1001/jama.1985.03360190069027

2. Okumura T, Tanno S, Ohhira M, Nozu T. The rate of polymyalgia rheumatica (PMR) and remitting seronegative symmetrical synovitis with pitting edema (RS3PE) syndrome in a clinic where primary care physicians are working in Japan. Rheumatol Int [Internet]. 2012;32(6):9-1695. Available from: https://doi.org/10.1007/s00296-011-1849-3

3. Li H, Altman RD, Yao Q. RS3PE: Clinical and Research Development. Curr Rheumatol Rep [Internet]. 2015;17(8):49. Available from: https://doi.org/10.1007/s11926-015-0525-0

4. Yao Q, Su X, Altman RD. Is Remitting Seronegative Symmetrical Synovitis with Pitting Edema (RS3PE) a Subset of Rheumatoid Arthritis. Semin Arthritis Rheum. 2010 Aug 1;40(1):89–94.

5. Joseph ADD, Kumanan T, Aravinthan N, Suganthan N. An unusual case of remitting seronegative symmetrical synovitis with pitting edema: Case report and literature review. SAGE Open Med Case Reports [Internet]. 2020 Jan 1;8:2050313X20910920. Available from: https://doi.org/10.1177/2050313X20910920

6. Lakhmalla M, Dahiya DS, Kichloo A, Fatima T, Edigin E, Wani F. Remitting seronegative symmetrical synovitis with pitting edema: a review. J Investig Med [Internet]. 2021 Jan 1;69(1):86 LP – 90. Available from: http://jim.bmj.com/content/69/1/86.abstract

7. Klauser A, Frauscher F, Halpern EJ, Mur E, Springer P, Judmaier W, et al. Remitting seronegative symmetrical synovitis with pitting edema of the hands: Ultrasound, color doppler ultrasound, and magnetic resonance imaging findings. Arthritis Care Res (Hoboken) [Internet]. 2005 Apr 15;53(2):33-226. Available from: https://doi.org/10.1002/art.21067

8. Chen YM, Chen LK, Hwang SJ, Chen DY, Arai H. Remitting seronegative symmetrical synovitis with pitting edema (RS3PE) syndrome: A case report. J Clin Gerontol Geriatr. 2011 Mar 1;2(1):9-27.

9. Olivé A, del Blanco J, Pons M, Vaquero M, Tena X. The clinical spectrum of remitting seronegative symmetrical synovitis with pitting edema. The Catalán Group for the Study of RS3PE. J Rheumatol [Internet]. 1997;24(2):6-333. Available from: http://europepmc.org/abstract/MED/9034993

10. Gan Y, Sun Y, Jin J, Wang Y, Chen J, Chung Y, et al. bFGF could be a biomarker of malignancy in RS3PE syndrome: an ambispective single-center cohort analysis of 51 patients. Arthritis Res Ther [Internet]. 2021;23(1):261. Available from: https://doi.org/10.1186/s13075-021-02638-0