Paraneoplastic Remitting Seronegative Symmetrical Synovitis with Pitting Edema (RS3PE). An extensive review of 59 cases

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Background

RS3PE (Remitting Seronegative Symmetrical Synovitis with Pitting Edema) syndrome, a rare inflammatory arthritis, usually presents with acute onset pitting edema of hands. This frequently overlooked entity can also be a paraneoplastic manifestation of an underlying malignancy. We present, to the best of our knowledge, the most extensive review of the epidemiology, clinical findings and outcome of patients with paraneoplastic RS3PE.

Methods

A PubMed and OVID database search of the English language literature between January 1985 and July 2009 was performed using the keyword RS3PE in combination with neoplasia, etiology and management. All relevant English language articles were reviewed and references screened for additional articles. Data regarding patient age and gender, pathology, treatment, and outcome were recorded.

Results

We found 59 case reports of cancer in RS3PE since 1981 in a total of 224 patients with RS3PE, including two retrospective (n 12 and14) and one prospective study (n 10). The median age at time of diagnosis was 74 with M to F ratio of 2.8 to 1. The most common complaint at the time of presentation was bilateral pain and swelling of extremities. Approximately 50% of the patients had systemic complaints at the time of first visit. All patients (n 53) had pitting edema at the time of diagnosis with negative RF and no evidence of bony erosions on evaluation. In decreasing frequency, there were 28 solid tumors, including 11 prostate , 7 gastrointestinal, 3 lung and one each of male and female breast ,ovary, bladder, endometrium, hepatocellular and renal carcinomas. The 26 hematological disorders included 11 patients with non-Hodgkin's lymphoma, 6 with MDS, 2 with CLL, 3 with myeloma, 2 with amyloidosis and 1 each with ALL and AML. There were five cases with unknown primary. Overall, these data suggest that the malignancy rate associated with RS3PE is 29% (59 out of 224) with prevalence in clinical studies being 31% (11 out of 36). Malignancy may precede, coexist with, or be diagnosed after this syndrome (range 2 months to 14 years). Onset of RS3PE symptoms preceded the diagnosis of malignancy in 75% cases. Two of these cases revealed disease recurrence. 51% patients with paraneoplastic RS3PE (19/37) responded to steroids compared to >90% responses in patients without malignancy. Also, in a cohort of patients described by Paira et al, all patients who developed malignancies during the course of their life suffered a relapse of their symptoms with discontinuation of prednisone.

Conclusions

There is a need to heighten awareness of RS3PE among rheumatologists and oncologists, so that further work-up for malignancy is considered at the time of diagnosis. The presence of systemic complaints or non-response to steroids is particularly suspicious. However, we recommend that an underlying malignancy should be excluded in patients with RS3PE regardless. Also, the interval between onset of RS3PE syndrome and diagnosis of cancer can be fairly long, indicating that patients should be monitored for an extended period after diagnosis with RS3PE, making the role of primary care doctors absolutely crucial.