



Letter

Onset of psoriatic arthritis associated with multiple wasp stings

Hymenoptera stings have been incriminated as a cause of beekeeper's arthritis, a form of arthritis closely mimicking osteoarthritis. Inflammatory mediators in Hymenoptera venom, such as mastoparan, may activate phospholipase A₂ (PLA₂), which could contribute to the development of psoriatic arthritis (PsA). However, there are no documented cases of Hymenoptera stings associated with the onset of PsA. We present a case of multiple wasp stings temporally associated with the onset of PsA in a 46-year-old man. A theoretical mechanism explaining this association is discussed.

A 46-year-old man with a history of psoriasis and no previous history of PsA presents with warmth, swelling, and asymmetric pain in multiple joints occurring 10 to 12 days after 6 to 8 wasp stings. Wasps were believed to be the stinging insect based on the man's description of the insect and the nest. Symptoms did not improve with acetaminophen, meloxicam, or tramadol, and the joint pain eventually caused him to become wheelchair bound. Medical history, social history, family history, and symptoms were unremarkable or noncontributory. Physical examination revealed a well-developed, well-nourished cooperative male oriented to time, place, and person who appeared to be in some distress. Vital signs were as follows: blood pressure, 128/72 mm Hg; pulse, 90/min; respiratory rate, 20/min; and oral temperature, 37.2°C. Physical examination findings were normal except for bilateral shoulder, left knee, and right wrist swelling with associated warmth, erythema, and tenderness to palpation. No nail pitting or psoriatic skin lesions were present.

Laboratory data were as follows: erythrocyte sedimentation rate, 74 mm/h (reference range, <17 mm/h in males); C-reactive protein, 24 mg/L (reference range, <1 mg/L); and rheumatoid factor, 15 IU/mL (reference range, <15 IU/mL). The results of testing for antinuclear antibody, anti-double-stranded DNA, HLA-B27, anti-cyclic citrullinated peptide, complete blood cell count, metabolic panel, and serum protein electrophoresis were negative. Aspiration of fluid was unsuccessfully attempted from all the affected joints, and the results of radiography of these joints were normal.

The patient was prescribed oral prednisone, 40 mg once daily, and after 3 to 4 doses had considerable relief of his joint pain. Methotrexate, 10 mg weekly, was added to this treatment program and up-titrated to 25 mg weekly. However, the dose of oral prednisone could not be decreased to below 20 mg/d.

The patient's onset of PsA was temporally associated with multiple wasp stings. Other forms of migratory arthritis were excluded. The pattern of joint involvement in PsA can be asymmetric, as in this patient, or symmetric. The subject's radiographs did not reveal typical PsA changes, such as pencil in cup deformities of the fingers, joint erosions, ankylosis or spondylitis of the spine, or metatarsal soft tissue swelling attributable to dactylitis. However, the absence of these findings is not uncommon in early PsA. Magnetic resonance imaging or ultrasonography may be required

to detect early changes not seen on radiographs, but these tests were not performed in this patient.¹

Although rare, arthritis after beestings or wasp stings has been described in the medical literature for several decades.² Cuende et al² published a case series of 34 beekeepers who developed arthritis of the fingers of the hands during the honey-collecting season. This beekeeper arthropathy resembles osteoarthritis in that the patients develop swelling, stiffness, tenderness, and nodules of the proximal interphalangeal joints and distal interphalangeal joints. Twenty-six percent of the patients in the study by Cuende et al² were younger than 30 years, and their symptoms occurred and recurred during August, during the honey-collecting season. These features, as reported in this study, are atypical for osteoarthritis because symptoms associated with OA are not seasonal and usually affect those 65 years or older. The explanation in the study by Cuende et al is that *Apis mellifera* venom contains PLA₂, an inflammatory mediator that leads to mast cell degranulation and is also found in the synovial fluid of patients with rheumatoid arthritis, osteoarthritis, and PsA.² Vadas and colleagues³ added credence to this theory when they found that rats that underwent intra-articular injections of PLA₂ from cobra venom or human rheumatoid arthritis synovial fluid developed rheumatoid arthritis-like arthritides. Bee venom contains the highest concentration of PLA₂ during the summer months, which may explain why the beekeepers' arthritis symptoms usually occur during August.² Wasp venom contains PLA₁, not PLA₂, but contains mastoparan, a peptide toxin that leads to endogenous PLA₂ activation and thus also could be implicated in inflammatory arthritis.^{4,5} There have been anecdotal reports of bee stings leading to improvement in osteoarthritis symptoms, and there is a form of alternative medicine termed *apitherapy* that uses beestings or venom for treatment of many conditions, including arthritis.⁶ However, aside from a few rat studies with promising results, these effects have not been replicated in human studies.⁷

The theory implicating PLA₂ with wasp stings and PsA is further supported by the following information. PLA₂ is elevated in inflammatory arthritides, including PsA.^{3,8} PLA₂ is also implicated in psoriasis because several articles have documented elevated PLA₂ in the serum and epidermis of patients with psoriasis. It is postulated that these high serum and epidermal levels of PLA₂ are responsible for immune cell activation in patients with psoriasis.⁹ This theory is supported by an article by Tang et al,¹⁰ who found that PLA₂ activates and upregulates cytotoxicity of natural killer (NK) cells, which are integral to the pathogenesis of PsA.¹⁰ These authors also found that interleukin 15, which is present in high concentrations of PsA synovial fluid and serum from patients with psoriasis, further activates PLA₂ and primes NK cells for enhanced cytotoxic killing.¹¹

In summary, this is a case of PsA temporally associated with multiple wasp stings. Mastoparan is a wasp venom-derived peptide toxin with multiple proinflammatory properties, including

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induction of PLA₂. Promotion of PLA₂ activity through interleukin 15 and resultant activation of NK cells has been implicated in the pathogenesis of PsA. Further investigation of the PLA₂ pathway in PsA may lead to novel therapeutic targets for the treatment of this debilitating arthropathy.

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