Pseudopodagra: A presenting manifestation of infective endocarditis

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ABSTRACT
Podagra is a term used to describe acute monoarthritis of the first metatarsophalangeal (1st MTP) joint. The most common diagnoses of arthritis in this joint are: crystal-induced synovitis, septic arthritis, traumatic conditions and reactive arthritis. When etiologies other than gout are involved this is frequently referred to as pseudopodagra. We report the case of a patient who presented with pain and swelling of the 1st MTP. The absence of intraarticular crystals and hyperuricemia encouraged further evaluation of the patient. A cardiac murmur was investigated by echocardiography, which revealed valvular vegetations and the diagnosis of infective endocarditis (IE) was established. This is the first reported case of a podagra-like presentation of IE. As in this case, the diagnosis of gout should rest on findings beyond the presence at 1st MTP arthritis, with evaluation of all extraarticular signs in order to rule out other possible diagnoses.

Introduction
Podagra is a term used to describe acute monoarthritis in the first metatarsophalangeal (1st MTP) joint. Because of the close association of podagra with gout, when other etiologies are diagnosed this manifestation is frequently referred to as pseudopodagra. In all cases, aspiration of synovial fluid from the affected joint, with its gross examination and laboratory analysis, is important for definitive diagnosis. We report pseudopodagra as a presenting manifestation of infective endocarditis (IE).

Case report
A 77-year-old man was admitted to the hospital via the emergency room in September 2003 with a history of fever and acute left foot pain and swelling (Fig. 1). The patient had been well until one week before admission when he received an influenza vaccination. Three days after the intervention he had two episodes of fever, 38.5°C, and was treated empirically with macrolide antibiotics.

The day before admission he suffered acute severe pain in his left foot with redness and swelling of the base of the large toe. He had a history of ischemic heart disease with a prior myocardial infarction and residual heart murmur and was under chronic therapy with low dose aspirin and angiotensin converting enzyme inhibitors. The patient did not smoke nor drink alcoholic beverages. He had not undergone dental or urogenital procedures in the previous six months. In the prior year he had suffered two bouts of presumed viral illness, with fever for several days in each episode.

Physical examination at admission revealed that the temperature was 36°C. The patient appeared generally well with unremarkable findings except for a grade 2/6 systolic murmur heard over the mitral valve and left 1st MTP redness, swelling and tenderness. No cutaneous lesions accompanied the arthritis. Blood studies revealed: hemoglobin 9.9 gr/dl (13.5-17.5), mean corpuscular volume 90 (77-93), hematocrit 29% (40-54), white blood cells 3,990/mm² (4,000-11,000) with a normal differential count and platelets 121,000/mm² (150,000-400,000). Renal studies, liver
enzymes and uric acid level were normal. Erythrocyte sedimentation rate was 84 mm/hr (0-20). C-reactive protein was 30 mg/dl (0-6). Rheumatoid factor (RF) was positive at a titer of 1:80 (not known to be positive in the past). Synovial fluid from the 1st MTP was colorless, clear, with no evidence of crystals under light microscopic examination. Gram stain and culture were negative. Due to the small quantity of synovial fluid, a cell count and chemistry studies were not performed. A 99m technetium bone scan demonstrated increased uptake at the 1st MTP (Fig. 2). The patient was treated with etodolac with a good clinical response at the 1st MTP after 48 hours. At this time, new, red, small nodular skin lesions appeared on the fingers of his right hand. Blood cultures were negative.

Because the patient had a history of several episodes of fever, an old heart murmur, new skin lesions, anemia and crystal negative arthritis, a transthoracic echocardiogram (TTE) was performed. It revealed severe mitral regurgitation (MR) with two valvular masses typical of endocardial vegetations (Fig. 3). Repeated blood cultures were negative.

The patient was treated with full doses of gentamicin and ampicillin for six weeks with resolution of the clinical picture. Follow-up uric acid levels were within normal limits.

At one year follow up, the patient felt well with no symptoms nor signs of arthritis. A repeat TTE was performed in another hospital after one year and reportedly revealed moderate MR, without vegetations.

Discussion

Infective endocarditis (IE) due to microbial infection of the heart valves may develop insidiously or abruptly and is associated with a high risk of extracardiac manifestations. As in the present case, in 5-15% of patients with IE blood cultures are negative, 1/3 to 1/2 of these because of prior antibiotic exposure, complicating diagnosis and treatment (1).

Rheumatic manifestations are frequent extracardiac expressions of IE, with a range of 25-41% patients thus involved in most series (2, 3). Patients may present with peripheral arthritis, sacroiliitis, spondylitis, cutaneous leukocytoclastic vasculitis or polymyalgia rheumatica and have a positive RF or low complement (C3, C4) levels at presentation (3, 4). Arthralgias and arthritis may be present for months before the onset of fever or other signs of IE (5). At times, the rheumatologic manifestation at presentation may divert attention away from the underlying IE, obscuring the full clinical picture and obfuscating the diagnosis.

In a recent retrospective study over a span of 12 years (3), rheumatic manifestations were present in 46 of 110 IE patients, with peripheral arthritis observed in 15 of these. Of 13 patients who underwent arthrocentesis two of the six patients with a negative culture had monosodium urate crystals present. Those with gout were men, both 61 years of age, with arthritis of the 1st MTP and ankle, respectively, which did not improve with antibiotics alone (3).

As the musculoskeletal or vasculitic manifestations of IE, at presentation, may mimic rheumatic problems, a high clinical awareness of the possibility of this underlying infectious etiology is essential for identification of this severe and long-lasting disease which requires rapid diagnosis and therapy. In a recent article (6) the following criteria were suggested as useful in suggesting a primary rheumatologic manifestation of the IE:

1. The absence of previous rheumatic disease or episodes of backache;
2. Intravenous drug abuse (7);
3. Acute synovitis in certain joints (single metacarpophalangeal joint,

Fig. 2. Increased uptake in 1st MTP (arrow) on 99m technetium methylene diphosphonate bone scan of our patient.

Fig. 3. Vegetation on the mitral valve (arrow) on the transthoracic echocardiogram of our patient.
sternoclavicular, acromioclavicular joints) that are not frequently involved alone in the more common forms of arthritis (8).
4. Atypical presentation of polyarthritides, especially with low grade fever, irrespective of the presence of RF or HLA B27 (6).
5. Prolonged flu-like illness with arthralgias and/or myalgias, especially when accompanied by a significantly elevated ESR and/or new anemia (3,6);
6. Backache with fever (3,9);
7. Unilateral sacroiliitis (5,10).

The most common diagnoses in acute 1st MTP monoarthritis, as in other cases of monoarthritis, are trauma, crystal-induced synovitis (gout and pseudo-gout), septic arthritis, or reactive arthritis (11). On the other hand this monoarticular arthritis is occasionally the first symptom of polyarticular disease, such as inflammatory bowel disease, psoriatic arthritis, osteoarthritis or rarely, rheumatoid arthritis (11). In this patient, the absence of intraarticular crystals in the presence of normouricemia promoted further evaluation and examination of all extraarticular signs in order to rule out other diagnoses. The accuracy of the clinical diagnosis of gout, without crystal confirmation, is uncertain. The aspiration of synovial fluid from the affected joint, gross examination and analysis of the fluid by Gram stain, culture, cell count, chemistry (glucose and protein levels) and polarized light microscopic examination is important for definitive diagnosis (12).

The presence of crystals does not exclude infection, however, especially since an antecedent joint disease such as gout is known to predispose to septic arthritis in an affected joint.

In conclusion, we report a case of IE with pseudopodagra as its initial manifestation. The case illustrates the importance of synovial fluid aspiration and full examination in all cases of acute monoarthritis, even when clinically crystal-induced arthritis is highly suspected. Both in the presence as well as absence of synovial fluid crystals, a full evaluation of all extraarticular signs present would mitigate against missing the proper diagnosis.

References