Positive Alizarin Red Clumps in Milwaukee Shoulder Syndrome

To the Editor:

Milwaukee shoulder syndrome is a destructive, basic calcium phosphate crystalline arthropathy characterized by pain, large-joint effusion, and loss of function in the affected joint[1]. It classically affects those over 70 years of age, 90% of whom are female. The syndrome is often associated with rotator cuff defects, and the effusion is noninflammatory with numerous aggregates of calcium hydroxyapatite crystals in the synovial fluid. Identifying individual calcium hydroxyapatite crystals in synovial fluid can be elusive, since these crystals are not identified under plain and polarized microscopy, unlike monosodium urate (MSU) and calcium pyrophosphate dihydrate (CPPD) crystals. However, globular clumps of hydroxyapatite crystals may appear using plain light microscopy, but they are not birefringent. Such clumps have been described as "shiny coins," although often they either are nondescript or are not observed[2,3]. Other techniques including atomic force microscopy, electron microscopy, Fourier transform infrared microscopy, and radiographic diffraction have proven to be effective in identifying calcium hydroxyapatite crystals but are not practical in the clinical setting because of cost or limited availability[4]. A simple, rapid screening method using alizarin red stain and ordinary microscopy has been described[2], but is seldom utilized among practicing clinicians. When clumps of calcium hydroxyapatite crystals are stained with alizarin red they produce a characteristic "halo" of orange-red stain[2,3].

We describe an 82-year-old woman with recurrent shoulder effusion and clinical, laboratory, and radiologic findings consistent with Milwaukee shoulder syndrome. She was a retired nurse who exercised regularly with daily 2-mile walks and upper-extremity light weight-lifting. She initially presented to general medicine with right shoulder pain, limited range of motion, and a large joint effusion following a fall several weeks earlier. Plain radiographs of the shoulder showed no fracture or dislocation, but did reveal prominent narrowing of the right glenohumeral joint, sclerosis, and osteophytes of the humeral head. Given the large effusion, arthrocentesis of the shoulder was performed. Analysis of the synovial fluid exhibited a noninflammatory cell count with leukocytes of 831/mm^3. Gram stain and culture were negative. She was treated conservatively with nonsteroidal antiinflammatory agents and physical therapy. Months later she was referred to our clinic in rheumatology due to the recurrent expression of the effusion. Physical examination confirmed a monoarticular arthritis with a large anterior shoulder effusion, suggesting a crystalline arthropathy. Computer tomography of the affected shoulder revealed diffuse erosions of the humeral head and glenoid, large collar osteophytes, and areas of calcific tendinitis involving the supraspinatus and subscapularis tendons. Shoulder arthrocentesis was performed again (Figure 1); aspiration yielded over 50 ml of yellow synovial fluid. Analysis of the synovial fluid again exhibited a noninflammatory cell count with leukocytes 806/mm^3. Gram stain and culture were negative. Although plain and polarized microscopy was negative for MSU and CPPD crystals, poorly defined aggregates of crystals were seen that were not birefringent. When wet-drop preparation with alizarin red stain was applied, globular clumps of crystals surrounded by an orange-red halo were observed (Figure 2).

Figure 1. Shoulder arthrocentesis yielded > 50 ml of yellow synovial fluid, which exhibited a noninflammatory cell count, with leukocytes 806/mm^3.

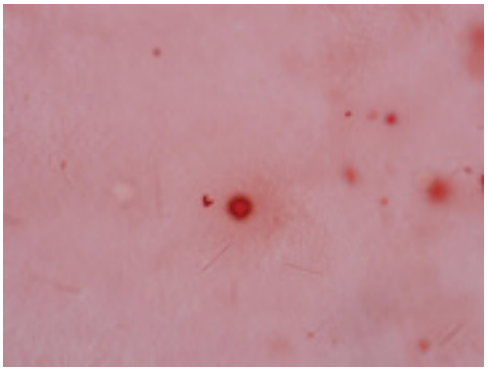

Figure 2. Wet-drop preparation with alizarin red stain revealed globular clumps of crystals surrounded by an orange-red halo (ordinary light, oil immersion, original magnification ×60).

Detection and identification of crystals in synovial fluid is critical for diagnosis and treatment of crystalline arthropathies. MSU and CPPD crystal analysis is done routinely in the clinic, but calcium hydroxyapatite crystals are seldom looked for. Wet-drop preparation with alizarin red stain is an easy, highly sensitive test to identify calcium hydroxyapatite crystals. In the appropriate clinical setting, alizarin red staining can help confirm Milwaukee shoulder syndrome.

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