a complete remission for more than a year with administration of hydroxyurea alone. These authors conclude, as did we, that hydroxyurea appears to have a role in the management of eosinophilic leukemia.

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Severe Disabling Polyarthritis Associated with Bacterial Endocarditis

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THE DIAGNOSIS of infective endocarditis is often elusive, and atypical presentations may mislead the physician into considering other diseases.[1] We have recently seen a young woman wth endocarditis whose chief presentation was severe, disabling, bilaterally symmetrical polyarthritis. We report this unusual case with a brief review of the literature concerning the joint manifestations of infective endocarditis.

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Report of a Case

A 22-year-old woman was admitted to Harbor General Hospital in August 1974 because of severe joint pains. She had been in good health until ten days before admission, when she noted the gradual onset of intense pain, stiffness and pronounced swelling in both ankles. In the seven days before admission, similar symptoms developed in both knees, wrists and shoulders. About this time a nonpruritic rash developed on both feet. The joint pains and swelling were of such magnitude that the patient became totally bedridden for the week before admission. Chills and fever had been present during the ten days before admission to hospital. There was no history of syphilis or gonorrhea, and her last sexual contact had been four weeks before admission.

The patient indicated that there had been no abuse of drugs (either orally or intravenously). She was taking no medications and noted allergy to penicillin. There was no history of rheumatic fever. There were no recent dental, genitourinary or gynecological manipulations.

On physical examination, the patient's vital signs were temperature, 39.5°C (103.1°F); pulse, 100 per minute; respiratory rate, 16 per minute,

and blood pressure, 110/70 mm of mercury. There were no Roth's spots, petechial hemorrhages or clubbing. There was a nontender erythematous rash on the dorsum of both feet. The chest was clear to percussion and auscultation. There was no neck vein distension. On cardiac examination, a grade II/VI, soft, nonradiating systolic ejection murmur was noted at the lower left sternal border. There were no gallops or rubs. There was no hepatosplenomegaly or lymphadenopathy. On joint examination warmth and extensive swelling of the ankles, knees and shoulders was seen. There was also tenosynovitis of both wrists. There was extreme pain and pronounced limitation of motion of all involved joints. Results of pelvic and neurologic examinations were within normal limits.

At admission, laboratory values were hematocrit 36 percent, leukocyte count 3,600 per cu mm, with a normal differential, and a platelet count of 250,000 per cu mm. Intermediate purified protein derivative (PPD) and coccidioidin skin tests gave reactive readings. Serum urea nitrogen, creatinine, electrolytes, antistreptolysin O titer and C-reactive protein were within normal limits. Sickle cell preparation was negative. Serum albumin was slightly decreased at 2.8 grams per 100 ml (normal 3.0 to 5.0 grams per 100 ml), and serum gamma globulin was notably elevated at 4.6 grams per 100 ml (normal 0.4 to 1.5 grams per 100 ml). Results of a serum Venereal Disease Research Laboratories (VDRL) test were positive at a 1:2 dilution, and of a fluorescent treponemal antibody absorption test (FTA-ABS) were weakly positive. Studies for serum rheumatoid factor and antinuclear antibody gave negative findings. Serum complement levels were not obtained. Results of repeated urinalyses were within normal limits. Although the knees, ankles and shoulders were notably swollen, only 2 ml of fluid could be aspirated on multiple attempts. The fluid was turbid, yellow in appearance. The viscosity was grossly normal by "string test." No cells were seen on microscopic examination; Gram stain showed no organisms. No crystals were seen under polarized light. Cultures of the fluid on blood agar, eosin-methylene blue (EMB) agar and Thayer-Martin agar (under 5 percent carbon dioxide) were negative. Insufficient joint fluid prevented quantitation of glucose and protein content. Cultures of the rectum, pharynx and cervix on Thayer-Martin agar (under 5 percent carbon dioxide) yielded no organisms. Findings on electrocardiogram were within normal limits. No abnormalities were seen on an x-ray film of the chest or on films of all the involved joints.

Intravenous administration of erythromycin was begun, 1 gram every six hours, because of the suspicion of disseminated gonococcemia. There was no improvement in symptomatology over the next 48 hours. On echocardiography, normal excursion of the anterior leaflet of the mitral valve was noted; however, the tracing was interpreted as consistent with a left atrial myxoma. A right heart catheterization was done, but failed to show a myxoma.

Four sets of blood cultures, drawn on admission, were subsequently reported as positive for Group D enterococci (according to the criteria of R. R. Facklam[2]). Administration was started of vancomycin hydrochloride, 500 mg every six hours given intravenously, and streptomycin sulfate, 500 mg every 12 hours given intramuscularly. On the fourth day of therapy, skin testing for penicillin hypersensitivity was done. The patient did not react to either the major or minor determinants, and aqueous penicillin G, 12 million units per day given intravenously, was substituted for the vancomycin. All joint signs and symptoms abated by the fifth day of therapy and repeat blood cultures gave negative results at that point. The infection was cured with a four week course of parenteral penicillin and streptomycin, interrupted by two leaves of absence taken by the patient against medical advice. It is of interest that the enterococcal bacteremia and severe joint symptoms recurred during one of these interruptions. The serum complement (B_1 C) was 150 mg per 100 ml (normal 140 to 164 mg per 100 ml) at the time of clinical and bacteriologic relapse. Blood cultures at the termination of therapy were sterile and the patient has remained well since.

Discussion

Although joint complaints are often associated with bacterial endocarditis,[3] severe symmetrical polyarthralgia and polyarthritis as a presenting syndrome has not been emphasized in the literature. Horder, in 1909, reported joint pains, "indefinite both in situation and cause," in 66 of his 150 patients.[4] He noted modest joint swelling in 27 of these patients, but in a later paper[5] remarked on the decreasing frequency of joint effusions in cases of bacterial endocarditis. Lib-

man is noted as not having seen objective signs in the joints of patients with bacterial endocarditis.[5] Thayer's review noted little more than the presence of joint pains in most of his patients.[7] Kerr in his extensive monograph on endocarditis described the joint findings as arthralgias which were "fleeting" in nature.[6]

Most reviewers since Kerr's publication have also alluded to joint complaints in bacterial endocarditis, but not as the main presenting syndrome and rarely as severe and incapacitating as in the present case.[1,3,8,9] Arthralgias remain fairly common and very occasionally a minor effusion is noted in one or two joints. However, polyarthritis with significant swelling in multiple joints is extremely unusual.[1,3,8-10]

Suppurative arthritis is uncommonly associated with bacterial endocarditis. In two large recent series of patients with purulent arthritis, bacterial endocarditis was not found as the cause in any of the 120 cases recorded.[11,12] In 50 cases of endocarditis cited by Banks and co-workers,[13] just one patient presented with a septic arthritis. Similarly, Tompsett reviewed 76 patients with endocarditis; in only one was suppurative arthritis present.[14] In the latter two instances, the infection was monoarticular.

The many other diseases that might manifest in a similar fashion make a polyarthritic mode of presentation even more difficult to diagnose as infective endocarditis. As was shown in the present case, several other entities that often present with symmetric polyarthritis (such as disseminated gonococcemia, collagen vascular disease and atrial myxoma) were initially considered before bacterial endocarditis was eventually diagnosed.

Still to be elucidated are the possible mechanisms of the joint manifestations of infective endocarditis. Whether they are caused by immune complex deposition[10] or by bland or infectious emboli, remains to be answered. Unfortunately, we were not able to obtain enough joint fluid to do the necessary studies to define the exact mechanisms involved (that is, a search for antigen-antibody complexes, complement studies and nitroblue tetrazolium testing),[15] nor were we able to obtain joint tissue for immunofluorescent studies and electron microscopy. The finding of pronounced joint swelling with but only small quantities of sterile joint fluid obtainable by aspiration, suggests that the pathologic process may have been limited to the synovial lining, a situation not dissimilar from that suggested for the early polyarthritis of gonococcal sepsis, where an immune complex cause has been suspected.[16] Of note was the rapid reversal of the present patient's extensive polyarthritis when standard combination antibiotic therapy for enterococcal endocarditis was instituted.[8,17] Also of interest was the recurrence of the entire clinical syndrome shortly after a suboptimal course of antimicrobial therapy was given,[8] with blood cultures again being positive for Group D enterococci.

Summary

A patient with enterococcal endocarditis presented with severe, progressive, symmetric polyarthritis with sterile joint fluid. Appropriate antimicrobial therapy resulted in cessation of the bacteremia and a rapid resolution of the extensive polyarthritis. Clinicians should be aware of this unusual mode of presentation of infective endocarditis, a disease in which early recognition and proper therapy may be lifesaving.

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