

ARTHRITIS DUE TO WILSON DISEASE. PENICILLAMINE, PSORIASIS OR HEPATOCELLULAR CARCINOMA? BLURRED FOCUS, SHARP BOUNDARIES

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To the Editor,

A 50-year-old woman was seen due to pain and stiffness in the finger and knee joints for the last four months. She had morning stiffness of one hour. Her complaints were also present at night but worse during the day. She declared that the knee pain preceded her hand complaints but that it became worse in the last four months. Previously, she received physical therapy for her hands and knees in another center but it was not beneficial. Visco-supplementation and steroid injections had also proven to be ineffective. Her past medical history comprised Wilson disease (on remission with D-penicillamine for 20 years) and psoriasis for two years treated with topical drugs. Her two siblings also had Wilson disease and one of them had died due to liver failure.

Physical examination revealed psoriatic skin lesions in the frontal and occipital regions of her scalp and right elbow. She had bilateral acromioclavicular joint tenderness. Both wrists and small joints of the hands (predominantly the proximal interphalangeal joints) were swollen and warm, their motions were painful and limited. Knee and ankle joint motions were painful and limited on both sides, the right knee was warm to the touch. Laboratory evaluations were normal except for ALP: 143 U/L (35-129), GGT: 105 U/L (5-36), erythrocyte sedimentation rate: 64 mm/h (0-20) and rheumatoid factor: 24 IU/ml (0-20). Radiographs of the knee joints were consistent with grade 4 osteoarthritis; hand x-rays were unremarkable. Serological markers including ANA and anti-CCP were negative. The patient was also consulted to her hepatologist and a combination of methotrexate 7.5 mg/week, prednisolone 5 mg/day and a nonsteroi-

dal antiinflammatory drug has been started. On the 3rd month of therapy, she was found to have improved (decreased morning stiffness and arthritic joint findings). Prednisolone was stopped thereafter according to the suggestion of the hepatologist. On the 6th month control, she was in remission. On the 9th month control, as the morning stiffness was again increased and the laboratory markers including erythrocyte sedimentation rate: 92 mm/h, C-reactive protein: 1.31 mg/dl (0-0.8) were elevated, an abdominal computed tomography was performed. It was suggestive of Hepatocellular carcinoma (HCC). Magnetic resonance imaging of the liver was also relevant with HCC. After the liver biopsy confirmed the diagnosis, chemoembolization was carried out. In the last control visit, the patient was free of arthritic findings with prednisolone 2 mg/day and hydroxychloroquine once daily.

Wilson arthropathy generally presents with pain, stiffness, gelling, joint hypermobility and attacks of acute polyarthritis resembling rheumatic fever or acute rheumatoid arthritis.^{1,2} The pathogenesis is yet unclear but there seems to be no correlation between arthritis and the systemic findings. In the synovial biopsy, there is inflammation together with hyperplasia of cells surrounding the synovium.³ In some synovial membranes accumulation of copper was shown and also cartilage matrix glycoprotein resembling ceruloplasmin has been defined.² Eventual articular findings may comprise premature osteoarthritis, subchondral bone fragmentation, cyst formation, cortical irregularity, periostitis, chondromalacia patella, osteochondritis dissecans and chondrocalcinosis.²⁻⁴ In our patient, acute polyarthritic involvement of the knee, wrist and metacarpophalangeal joints were compatible with Wilson arthropathy.

On the other hand, patients treated with penicillamine can suffer penicillamine-related arthritis which can not be distinguished from rheumatoid arthritis.^{5,6} In a study of 32 patients with Wilson

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arthropathy, five patients had acute polyarthritis which appeared to be due to penicillamine. The arthritic findings had resolved with decreased penicillamine dose in four of the cases; however one of the patients had recurrent attacks leading to discontinuation of the drug.² According to the hepatologist's suggestions, penicillamine treatment could not be stopped in our patient; therefore the contribution of the drug to the arthritic process could not have been ascertained. The overall treatment for her arthritis was also tailored together with the hepatologist.

In our patient, the scenario was even more challenging with the presence of an underlying psoriasis. The clinical spectrum of psoriatic arthritis encompasses five different forms; prominent distal joint involvement, arthritis mutilans, oligoarthritis, polyarthritis and spondyloarthritis. In general, the most prominent features of psoriatic arthritis is distal interphalangeal joint involvement, enthesitis, periosteal bone formation, asymmetric oligoarthritis and spondylitis.⁷ Our patient had polyarthritis, arthralgia, stiffness in the hands and the wrists which were compatible with psoriatic arthritis.

Last but not least, our patient was eventually diagnosed to have also HCC during the follow up. Cancer induced polyarthritis is a well-known entity where the spectrum of arthritic findings may be quite wide.⁸ On the other hand, although metabolic paraneoplastic syndromes are recognized in HCC, polyarthritis is very rare.⁹ However, considering the time period of both the onset of arthritis and the diagnosis of HCC, one can not definitely exclude paraneoplastic polyarthritis in the differential diagnosis of our patient.

In closing, presenting our interesting patient in whom the extent of each disease's influence remains unclear, we call attention of physicians to relevant scenarios of arthritis where the diagnosis might be 'blurred'. Further, the treatment of such cases might also be as challenging as the diagnosis. In this regard, multidisciplinary approach seems to be of paramount importance.

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