Arthritis, clubbing and periosteal reaction in liver failure

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A 20-year-old male with end-stage liver disease presented with progressively worsening pain and swelling in ankles, feet, knees, wrists, hands and elbows for one year. He denied any fever, chills, painful red eyes, oral or genital ulcers, urinary tract infections, sexual activity, travel, contact with a tuberculosis patient, diarrhea, rashes, cough, shortness of breath and back pain. He underwent an orthotopic liver transplant for biliary atresia while six months old and was being worked up for another transplant. On exam, significant clubbing was present. Joint examination revealed swollen wrists, metacarpophalangeal and proximal interphalangeal joints, knees, ankles and metatarsophalangeal joints. Pertinent laboratory findings included hemoglobin of nine (13.5-17.5 g/dL), platelets of 80 (150-400 K/uL), international normalization ratio of 2.0, total bilirubin of 16.6 (0.2-1.2 mg/dL) with the direct component of 11, mildly elevated transaminases, erythrocyte sedimentation rate of 52 (0-15 mm/hr), C-reactive-protein of 35.8 (0.0-10.0 mg/dL).

At this point in time, based on his immune suppression, a wide differential diagnosis was entertained. This included reactive arthritis, bowel disease associated arthritis, seronegative inflammatory arthritis, psoriatic arthritis, Still's disease, viral arthritis, chronic fungal or tuberculosis infection, cyclosporine toxicity, thyroid acropachy and hypertrophic osteoarthropathy. Workup including synovial analysis, echocardiogram and chest x-ray was negative. Imaging showed periosteal reaction (Figures 1 and 2).

Clubbing can be primary or related to a variety of medical conditions: mostly malignancies, gastrointestinal inflammatory disorders, and chronic infections, particularly pulmonary. Periosteal reaction of the bones can be seen as a primary condition, in metabolic disorders, malignancies, venous stasis, trauma, and due to drugs.

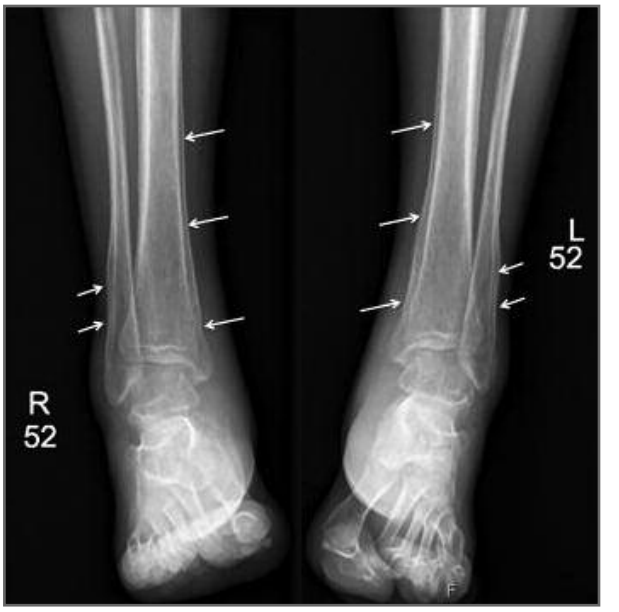

FIGURE 1. Periosteal reactions

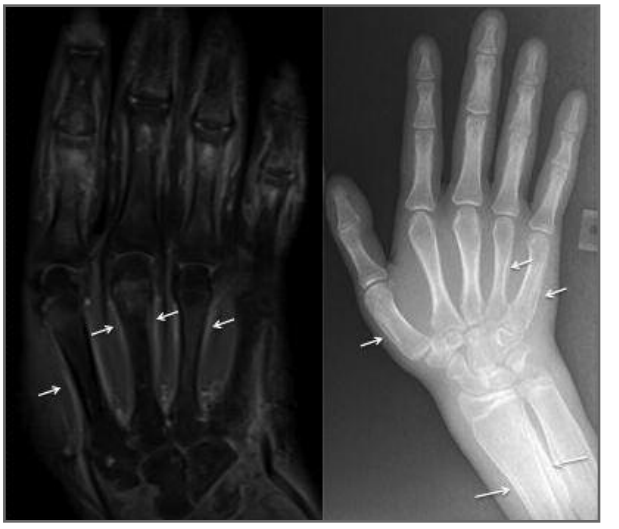

FIGURE 2. Periosteal reactions

In this case, hepatic hypertrophic osteoarthropathy was diagnosed based on the classic triad of clubbing,

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arthritis and periosteal reaction[1]. Only six such cases due to biliary disease were reported till 2008.2 Non-clearance of a putative growth factor by the liver or a hepato-pulmonary syndrome exposing the circulation to growth factors is postulated to cause the periosteal reaction[2]. One such candidate is the vascular endothelial growth factor[3]. The tibia and fibula near the ankle joint are the most frequently involved joints and should be used for screening. The periosteal reaction may precede clubbing and bone pain may precede clubbing[4]. Patients with end stage liver disease may present with bone pain and one differential for consideration should be hepatic hypertrophic osteoarthropathy. In this context, it may be important to pursue a bone scan in these patients presenting with bone pain. Transplant is curative. Successful treatment with bisphosphonates has been reported[5]. Our patient died before treatment could be initiated.

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