Imbalance in production between vascular endothelial growth factor and endostatin in patients with rheumatoid arthritis. *J Rheumatol* 2000; 27: 2339-42.
5. O'REILLY MS, BOEHM T, SHING Y *et al.*: Endostatin:An endogenous inhibitor of angiogenesis and tumor growth. *Cell* 1997, 88: 277-85.
6. SASAKI T, FUKAI KM, MAUN K, GÖHRING W, OLSEN BR, TIMPL R: Structure, function and tissue forms of the C-terminal globular domain of collagen XVIII containing the angiogenesis inhibitor endostatin. *EMBO J* 1998; 17: 4249-56.
7. BUSSOLINO F, MANTOVANI A, PERSICO G: Molecular mechanisms of blood vessel formation. *TIBS* 1997; 22: 251-6.

Inflammatory polyenthesopathy in a patient with X-linked osteomalacia

Sirs,

X-linked hypophosphatemia (XLH) due to a renal tubular defect in phosphate transport and a mutation of the phosphate regulating gene, is the most common inherited form of rickets in developed countries (1-3). While the main radiographic feature in childhood is rickets, in adult life one predominatly sees generalised calcific enthesopathy (1, 4-6).

Polisson *et al*. (1) suggested that the enthesopathy of XLH cannot be attributed to the other two common causes of generalised enthesopathy, i.e. diffuse idiopathic skeletal hyperostosis (DISH) or spondyloarthritis and, on the basis of histologic evaluation performed in selected patients, excluded the possibility of an inflammatory form. However, we would like to report the case of a patient with XLH who presented many aspects suggesting an inflammatory enthesopathy.

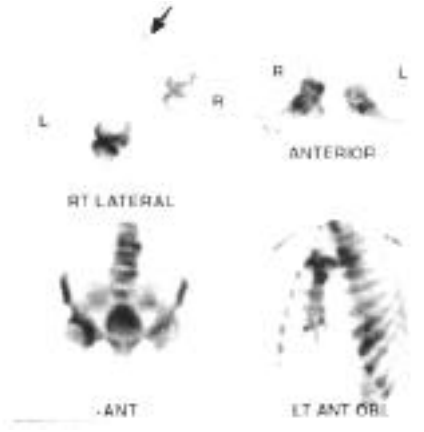

Fig. 1. ^{99m}Tc-MDP bone scan demonstrates intense uptake in the left knee and right coxo-femoral region. Note the deformity in the right femur and the small hyperactive area in the distal portion of the diaphysis. Milder hyperactivity can also be seen in the chondral part of numerous ribs and in the right tarsal region.

A 42-year-old male patient presented with a 5-month history of diffuse joint pain and stiffness, mainly involving the shoulders and knees, which started abruptly after a long bicycle ride. The patient had been affected since the age of 18 months by an XLH for which, from the age of 5, he underwent several osteotomies in the legs. Treatment with phosphate and low dose vitamin D was introduced at the age of 15 and continued for 5 years. He was then well until the present episode. The family history was negative.

Physical examination revealed short stature (163.2 cm), bow legs, and loss of range of motion in the hips, knee and shoulders without significant swelling, but with tenderness and warmth over the shoulders and knees. Laboratory investigations revealed only a slight elevation of the ESR (35 mm/ h) and a CRP of 1.7 mg/dl (normal < 0.6 mg/dl). X-rays detected extensive calcified enthesopathies on the supero-lateral patella, femoral metaphysis and pelvis, and multiple areas of hyperostosis in the tibia and fibula. In the left femur the diaphyseal bowing was associated with a mid-diaphyseal lateral active Looser-Milkman zone. Bone scintigraphy (Fig. 1) revealed intense up-take mainly in the left knee, right coxo-femoral area, and a small area in the diaphysis corresponding to the Looser-Milkman zone.

X-rays clearly demonstrated features of an enthesopathy that,due to the abrupt onset of symptoms, the elevated ESR and CRP, and the intense activity of the clinically affected areas shown on bone scintigraphy, seemed to be of the inflammatory type. However, no sacroiliac involvement or HLA-B27 were found. The patient was treated with 150 mg/day of sodium diclofenac for 3 months, and experienced a satisfactory recovery from his symptoms. Two years later he experienced some severe flares, mainly in the shoulder and knees, which occurred every 2-3 months and lasted approximately one week.

In 1985 Polisson *et al.* (1) reported that 69% of 26 patients with XLH were affected by generalised enthesopathy. These aspects should be considered as an integral part of XLH and are very frequent, being found in 33% of patients under the age of 30 with XLH, and in all those over this age (7).

The pathogenesis of the enthesopathy associated with XLH is unclear and seems to be unrelated to therapy. Unlike DISH, it is relatively symmetric and does not show significant spinal ligament hyperostosis. The differential diagnosis from spondyloarthritis was made based on the absence of sacroiliac involvement, subchondral bone erosions or syndesmophytes. Thus,the inflammatory features found in our patient are unusual and difficult to explain. A possible cause could be the disruption in tissues surrounding the microcrystals contained in calcified deposits of the enthesopathies, probably induced by traumatic or metabolic changes, in our patient provoked by an unusually long bicycle ride.

L. PUNZI[1], *MD, PhD, Associate Professor*
P. ZUCCHETTA[2], *MD, Assistant Professor*
R. STRAMARE[3], *MD, Assistant Professor*
M. PODSWIADEK[1], *MD, Fellow*
R. RAMONDA[1], *MD, PhD, Rheumatologist*
S. TODESCO[1], *MD, Prof., Division Chief*

[1]Division of Rheumatology, Department of Medical and Surgical Sciences; [2]Division of Nuclear Medicine; [3]Department of Radiology, University of Padova, Italy

Address correspondence to: Dr. Leonardo Punzi, Division of Rheumatology, University of Padova, via Giustiniani no. 2, 35128 Padova, Italy. E-mail: punzireu@unipd.it

References

1. POLISSON RP, MARTINEZ S, KHOURY M *et al.*: Calcification of entheses associated with X-linked hypophosphatemic osteomalacia. *N Engl J Med* 1985; 313: 1-6.
2. DIXON PH, CHRISTIE PT, WOODING C, TRUMP D, GRIEFF M, HOLM I *et al.*: Mutational analysis of PHEX gene in X-linked hypophosphatemia. *J Clin Endocrinol Metab* 1998; 83:3615-23.
3. ARNSTEIN AR, FRAME B: Primary hypophosphatemic rickets and osteomalacia: A review. *Clin Orthop* 1966; 49:109-18.
4. HARDY DC, WILLIAM AM, SIEGEL BA, REID IR, WHYTE MP: X-linked hypophosphatemia in adults:Prevalence of skeletal radiographic and scintigraphic features. *Radiology* 1989; 171:403-14.
5. BURNSTEIN MI, LAWSON JP, KOTTAMASU SR, ELLIS BI, MICHO J: The enthesopathic changes of hypophosphatemic osteomalacia in adults:Radiological findings. *Am J Roentgenol* 1989: 153:785-90.
6. STEINBACH HL, NOETZLI M: Roentgen appearance of the skeleton in osteomalacia and rickets. *Am J Roentgenol* 1964; 91: 955-72.
7. REID IR, HARDY DC, MURPHY WA, TEITELBAUM SL, BERGFELD MA, WHYTE MP: X-linked hypophosphatemia:A clinical,biochemical, and histopathologic assessment of morbidity in adults. *Medicine* 1989; 68: 336-52.
8. CHALMERS J: Enthesopathy as the presenting feature of X-linked hypophosphatemia. A case report. *Acta Orthop Scand* 1993; 64: 221-3.
9. VERA CL, CURE JK, NASO WB, GELVEN PL, WORSHAM F, ROOF BF *et al.*: Paraplegia due to ossification of ligamenta flava in X-linked hypophosphatemia. *Spine* 1997; 22: 710-5.
10. VERGE CF, LAM A, SIMPSON JM, COWELL CT, HOWARD NJ, SILINK M: Effects of therapy in X-linked hypophosphatemic rickets. *N Engl J Med* 1991; 325: 1843-8.