Title
Ochronotic Arthropathy

Journal
Arthritis & Rheumatology, 69(11)

ISSN
2326-5191

Authors
Jafri, Kashif
Gensler, Lianne S
Link, Thomas M

Publication Date
2017-11-01

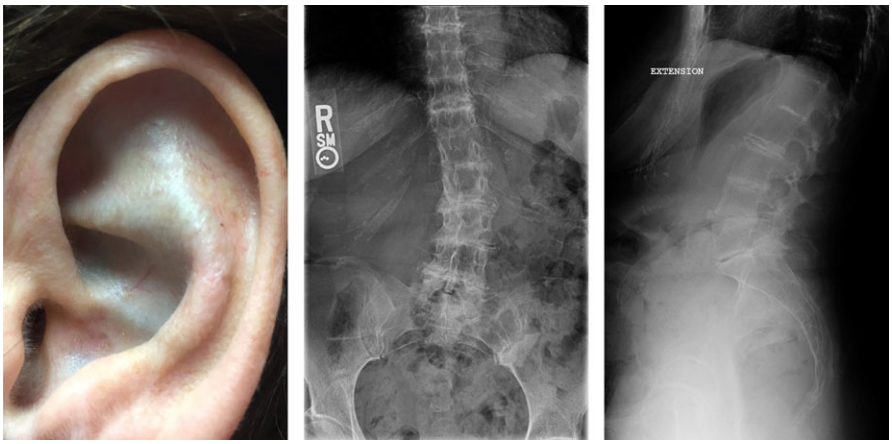
DOI
10.1002/art.40184

Peer reviewed

in Sjögren's syndrome–associated lymphoproliferation. Arthritis Rheum 2013;65:1085–96.
9. Vitali C, Bombardieri S, Jonsson R, Moutsopoulos HM, Alexander EL, Carsons SE, et al, and the European Study Group on Classification Criteria for Sjögren's Syndrome. Classification criteria for Sjögren's syndrome: a revised version of the European criteria proposed by the American-European Consensus Group. Ann Rheum Dis 2002;61:554–8.
10. Meffre E. The establishment of early B cell tolerance in humans: lessons from primary immunodeficiency diseases. Ann N Y Acad Sci 2011;1246:1–10.
11. Yurasov S, Wardemann H, Hammersen J, Tsuiji M, Meffre E, Pascual V, et al. Defective B cell tolerance checkpoints in systemic lupus erythematosus. J Exp Med 2005;201:703–11.
12. Kinnunen T, Chamberlain N, Morbach H, Cantaert T, Lynch M, Preston-Hurlburt P, et al. Specific peripheral B cell tolerance defects in patients with multiple sclerosis. J Clin Invest 2013;123:2737–41.
13. Shlomchik MJ, Craft JE, Mamula MJ. From T to B and back again: positive feedback in systemic autoimmune disease. Nat Rev Immunol 2001;1:147–53.
14. Kinnunen T, Chamberlain N, Morbach H, Choi J, Kim S, Craft J, et al. Accumulation of peripheral autoreactive B cells in the absence of functional human regulatory T cells. Blood 2013;121:1595–603.
15. Ittah M, Gottenberg JE, Proust A, Hachulla E, Puechal X, Loiseau P, et al. No evidence for association between 1858 C/T single-nucleotide polymorphism of PTPN22 gene and primary Sjögren's syndrome. Genes Immun 2005;6:457–8.

DOI: 10.1002/art.40184

Clinical Images: Ochronotic arthropathy



The patient, a 56-year-old woman with progressively worsening back pain, was referred to our rheumatology clinic for ankylosing spondylitis (AS) evaluation after being informed that she had spinal ankylosis on radiographs. Her medical history was significant for a childhood diagnosis of alkaptonuria. On physical examination, she had bluish-black discoloration of her external ears (**left**) and sclerae. Spine radiographs showed severe disc space narrowing with calcification of the degenerated lower lumbar spine discs (**middle**), fusion of the upper lumbar spine disc spaces (**right**), and severe osteopenia; the sacroiliac joints were patent. Alkaptonuria is a rare autosomal-recessive metabolic disorder in which a homogentisate 1,2-dioxygenase enzyme deficiency leads to an accumulation of homogentisic acid (HGA) (1,2). The classic clinical triad of alkaptonuria is homogentisic aciduria, ochronosis, and ochronotic arthropathy. The tissue deposition of the pigmented oxidation products of HGA results in ochronosis, which is the dark pigmentation of connective tissues (e.g., external ear, sclera, and intervertebral disc) in alkaptonuria. Ochronotic arthropathy commonly affects the thoracolumbar spine and the weight-bearing joints, and contributing mechanistic factors include deposition of pigmented HGA polymers, loss of cartilage elasticity, altered mechanical loading transmission, and aberrant bone remodeling (3). This case highlights an important mimic of AS.

1. Ventura-Ríos L, Hernández-Díaz C, Gutiérrez-Pérez L, Bernal-González A, Pichardo-Bahena R, Cedeño-Garcidueñas AL, et al. Ochronotic arthropathy as a paradigm of metabolically induced degenerative joint disease: a case-based review. Clin Rheumatol 2016;35:1389–95.
2. Gil JA, Wawrzynski J, Waryasz GR. Orthopedic manifestations of ochronosis: pathophysiology, presentation, diagnosis, and management. Am J Med 2016;129:e1–6.
3. Gallagher JA, Dillon JP, Sireau N, Timmis O, Ranganath LR. Alkaptonuria: an example of a "fundamental disease"—a rare disease with important lessons for more common disorders. Semin Cell Dev Biol 2016;52:53–7.

Kashif Jafri, MD
Lianne S. Gensler, MD
Thomas M. Link, MD, PhD
University of California, San Francisco