

## Commentary

Alkaptonuria is a rare autosomal recessive disorder of tyrosine degradation that is associated with a deficient homogentisate 1,2-dioxygenase activity in the liver. In patients with alkaptonuria, the gene for homogentisate 1,2-dioxygenase is mutated. Homogentisate 1,2-dioxygenase deficiency leads to excretion of large quantities of homogentisic acid in the urine. In urine and in collagen-rich connective tissues, homogentisic acid oxidizes to benzoquinones, which in turn form melanin-like polymers that cause its dark color changes. Accumulation of homogentisic acid and its metabolites causes ochronosis in collagen-rich connective tissues with darkening of cartilage and bone. These changes lead to arthritis, joint destruction and deterioration of the spine and large joints. Furthermore, cardiac valvular disease and renal and prostate stones occur, however generally at a later stage of disease.<sup>[1,2]</sup>

Ochronotic arthropathy is common in alkaptonuria. Various cases of ochronotic arthropathy have been

described in different anatomical regions. In most of these cases surgical reconstruction with arthroplasty has been performed.<sup>[3,4]</sup>

A novel therapy for alkaptonuria could be Nitisinone, which is a potent inhibitor of the second enzyme in the tyrosine catabolic pathway.<sup>[5]</sup> In a prospective, randomized clinical trial in 40 patients over a 3-year period the use of Nitisinone could demonstrate a 95% reduction of homogentisic acid in urine and plasma. Clinically, the primary outcome parameter was hip total range of motion and measures of musculoskeletal function serving as secondary parameters. In both, however, no statistically significant benefit of Nitisinone could be shown.<sup>[6]</sup>

In this issue, Rana *et al.* report about a patient with alkaptonuria and ochronotic arthropathy of the shoulders that was treated with bilateral total shoulder

joint arthroplasty.<sup>[7]</sup> Furthermore, they report about psychological distress due to alkaptonuria in their patient. Psychological distress hasn't been recognized often and gained attention in alkaptonuria patients yet. Generally, psychological issues are associated with various musculoskeletal conditions.<sup>[8]</sup> So, this seems to be an interesting and important point that needs further attention and should be addressed in future studies.

**Lukas A Holzer**

*Department of Orthopaedic Surgery, Medical University of Graz,  
Graz, Austria*

**Address for correspondence:**

Dr. Lukas A. Holzer,  
Department of Orthopaedic Surgery, Medical University of Graz,  
Auenbruggerplatz 5, 8036 Graz, Austria.  
E-mail: lukas.holzer@medunigraz.at

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