

## Alkaptonuria

Umer Feroze Malik, MD

Sheela Kapre, MD



**A** 56-year-old man presented to our orthopaedic clinic due to increasingly severe back pain. Physical examination revealed black discoloration of the sclera (**Image A**) as well as of the tendons of the digits (**Image B**) and the ear. History revealed that the patient took no medications or supplements. A clinical diagnosis of alkaptonuria was made based on the physical examination findings of spine pain and ochronosis. A urine sample was not obtained, and thus the diagnosis could not be confirmed by demonstrating homogentisic aciduria. The patient did not return for follow-up.

Alkaptonuria is an inborn error of metabolism inherited as an autosomal recessive disorder that is caused by deficiency of the enzyme homogentisic acid dioxygenase, resulting in the deposition of polymerized homogentisic acid in collagenous tissues (ochronotic pigment) and destruction of connective tissue.<sup>1-3</sup> Other important but rare consequences of alkaptonuria are cardiovascular (mainly valvular abnormalities) and urinary tract involvement (usually calculi in the kidneys, ureters, and prostate).<sup>4</sup>

Hallmarks of the disease include bluish-black pigmentation of collagenous tissues (ochronosis), early onset of severe arthritis, and the presence of homogentisic acid in the urine. The classic presentation includes urine that stains diapers or clothing black or turns black on standing or exposure to alkaline agents.

Alkaptonuria must be considered when early onset of arthritis is coupled with the classic bluish-black discoloration of skin, sclera, and connective tissue and cartilage. In the case patient, the ear ochronosis was not in the typical area of the helix but rather was located between the tragus and antitragus. Scleral and tendinous ochronosis varies and may be subtle or essentially absent in younger patients or in milder cases.<sup>4</sup> Spine pain is commonly the initial complaint of patients, and flattening and calcification of vertebral discs on spine radiographs are highly suggestive of the disease. The diagnosis can be confirmed by detecting an elevated level of homogentisic acid in the urine or blood. **HP**

### REFERENCES

1. Fisher AA, Davis MW. Alkaptonuric ochronosis with aortic valve and joint replacements and femoral fracture: a case report and literature review. *Clin Med Res* 2004;2:209-15.
2. Ffolkes LV, Brull D, Krywawych S, et al. Aortic stenosis in cardiovascular ochronosis. *J Clin Pathol* 2007;60:92-3.
3. Sieckert RG, Gibilisco JA. Discoloration of the teeth in alkaptonuria (ochronosis) and parkinsonism. *Oral Surg Oral Med Oral Pathol* 1970;29:197-9.
4. Phornphutkul C, Introne WJ, Perry MB, et al. Natural history of alkaptonuria. *N Engl J Med* 2002;347:2111-21.

---

*Dr. Malik is a resident, and Dr. Kapre is chairperson and program director, Internal Medicine Residency Program, San Joaquin General Hospital, French Camp, CA.*

Copyright 2008 by Turner White Communications Inc., Wayne, PA. All rights reserved.