Reviewer’s report

Title: Ochronosis as an unusual cause of a valvular defect: a case report

Version: 3 Date: 4 February 2009

Reviewer: Markus Schneemann

Which of the following following best describes what type of case report this is?: New associations or variations in disease processes

Has the case been reported coherently?: Yes

Is the case report authentic?: Yes

Is the case report ethical?: Yes

Is there any missing information that you think must be added before publication?: Yes

Is this case worth reporting?: Yes

Is the case report persuasive?: No

Does the case report have explanatory value?: Yes

Does the case report have diagnostic value?: Yes

Will the case report make a difference to clinical practice?: No

Is the anonymity of the patient protected?: Yes

Comments to authors:

The authors should explain their rationale for conservative treatment, and the type of treatment chosen.

If possible they should give a follow up on this patient after months - until years of their initiation of treatment and now.

This is in the light of most articles who say that there is no established treatment for ochronosis and heart valve disease, see for example:

Alkaptonuric aortic stenosis.
Roser M, Möller J, Komoda T, Knosalla C, Stawowy P.

One step further in their article -
Alkaptonuric ochronosis with aortic valve and joint replacements and femoral fracture: a case report and literature review.
Fisher AA, Davis MW.
- the authors state that therapy with
"Nitisinone, a potent inhibitor of 4-hydroxyphenylpyruvate dioxygenase, dramatically reduces production and urinary excretion of homogentisic acid; however, the long-term efficacy and side effects of such therapy are unknown. Identifying the gene for alkaptonuria offers the potential for a new therapeutic approach (replacement therapy with a recombinant enzyme) in the treatment of alkaptonuric ochronosis.

This review in the New England Journal of Medicine should also be included and discussed (nitisinone is mentioned there, too):
Natural history of alkaptonuria.

In another article the use of nitisinone in 7 patients over one year is presented:
Use of nitisinone in patients with alkaptonuria.

Please include these articles and mention these treatment options.

**Quality of written English:** Acceptable

**Declaration of competing interests:**
I declare that I have no competing interests