Author’s response to reviews

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

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Version: 4 Date: 18 February 2009

Author’s response to reviews:

Dear Sir or Madam,

Please find enclosed a revised version of our manuscript entitled "Ochronosis as an unusual cause of a valvular defect: a case report". All changes are highlighted in red. For our response to the comments of the reviewers please see below. All issues raised by the reviewers have been addressed point-by-point or have been rebutted (point 3, information on pathology).

I look forward to hearing form you

Yours sincerely,

Dietmar Steverding

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Reply to the comments of the reviewer

Reviewer 1:

1. We have included other causes of valvular heart disease in the discussion (page 7, lines 5-8). We have presented the past medical history of the patient (page 3, lines 16-24).

2. We have provided evidence for the treatment (page 7, line 28 to page 8, line 3; page 8, line 14; and Ref. 20).

3. We have included data on the genetics (page 5, line 29; and Ref. 6). However, the total number of HGO mutations is 67 according to ref. 6. Information on the
natural history is now included (page 6, lines 8-11, lines 14-17 and lines 19-20; page 7, line 13). In our opinion, we have already mentioned the pathology of alkaptonuria in the discussion. Information on the heterogeneity of the manifestations of alkaptonuria is now provided (page 6, lines 8-11, line 17 and lines 19-20). The drug nitisinone is mentioned in the discussion (page 7, lines 18-21, and Refs. 6, 18 and 19).

4. That the patient had dark urine in now mentioned (page 4, lines 15-16).

Reviewer 2:

1. The rational for the conservative treatment is now mentioned in the discussion (page 7, line 28 to page 8, line 3; page 8, line 14; and Ref. 20). The type of treatment is now stated (page 5, line 14).

2. Information on the follow-up on this patient is provided at the end of the case presentation (page 5, lines 15-17).

3. The article by Roser et al. is cited in the text (Ref. 16; page 7, line 16).

4. The treatment options are now mentioned (page 7, lines 18-24). The articles by Fisher & Davis, Phornphutkul et al. and Rubin et al. are mentioned (Refs. 6, 18 and 19).