Reviewer's report

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

Version: 3 Date: 8 August 2008

Reviewer: Fisher Alex

I am familiar with the literature and believe that this case meets one of the 9 criteria for evaluation in the journal: None

Has the case been reported coherently?: Yes

Is the case report authentic?: No

Is this case worth reporting?: Yes

Is the case report persuasive?: Yes

Does the case report have explanatory value?: No

Does the case report have diagnostic value?: No

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

Is the anonymity of the patient protected?: Yes

Comments to authors:

Alkaptonuria is a rare but possibly under-diagnosed cause of cardiovascular ochronosis with aortic valve stenosis as the most often manifestation. Because of its rarity, any new case-report is justifiable even when it does not contain new scientific or clinical information. Such case-reports keep clinicians alert regarding a wide range of aetiologies of valvular heart diseases, and suggest the importance of a holistic approach to each patient especially when signs of an inherited defect appear.

There is a need to clarify the following issues in Drs A Wilke and D Steverding case report before it can be accepted for publication.

1. The authors presented a 68 year old man with known family ochronosis causing severe arthropathy, renal stones and pigmentation of the sclera in whom they found mild to moderate aortic insufficiency as
well as mitral and tricuspid regurgitation. Although it is possible that the valvular changes in this patient are secondary to the deposition of the ochronotic pigment, this potential pathogenic mechanism has not been proved. In the absence of tissue diagnosis, causes of valvular disease other than ochronosis should be discussed, including infections (rheumatic fever, endocarditis), congenital malformations and degenerative diseases (e.g. calcific aortic valve). The past medical history of the patient needs to be presented.

2. The authors stated “Conservative therapy using ACE inhibitors and diuretics may slow down the progression of valvular dysfunction”. No evidence is presented as to why a patient without symptoms and signs of heart failure should use these medications.

3. In the “Discussion” section it would be reasonable to present a short overview of the current data on genetics (23 HG0 gene mutations), natural history, pathology and heterogeneity of the manifestations of alkaptonuria. Nitisinone, a promising pharmacotherapeutic agent for both prevention and treatment of ochronosis, should also be mentioned.

4. Has dark urine been observed in this patient?

Quality of written English: Acceptable

Declaration of competing interests:
I DECLARE THAT I HAVE NO COMPETING INTERESTS