Answers for the reviewers

Reviewer #1:

Specific comments: There is a good effort by the authors for writing this case report about a complication of alkaptonuria i.e., ochronosis arthropathy. Overall, the manuscript is well-written according to guidelines. The only thing I need to highlight is the grammatical mistakes in the manuscript which should be rectified by the authors.

Answer: Thank you for your suggestion. We have sent our revised manuscript to a professional English language editing company to polish the manuscript. A new language certificate along with the manuscript will be provided.

Reviewer #2:

Specific comments: 1. Although Ochronosis is a rare genetic disorder, case reports of Ochronosis with hip lesions are not rare. The patient report had hip arthroplasty after the onset of the disease in 2019. The patient reoccurred with the same hip arthroplasty, which was not innovative in the diagnosis and treatment process. 2.The article mentions genetic screening and does not specify the specific patient's genetic alterations. The patient was not genetically screened at either admission and no gene therapy was administered to the patient. 3.Lack of innovation in the treatment of hip joint necrosis by ochronosis. 4.The image of the consent for treatment form or document is not clear, please re-upload the full English consent for treatment form or document and high definition image. 5. The classification of Ochronosis into endogenous and exogenous is not stated in the case report, as the clinical manifestations of endogenous and exogenous are different and need to be clarified. 6. Skin changes in Ochronosis are not described.

Answer: Thank you for your suggestions.

1. This study mainly introduces the surgical treatment of bilateral hip arthritis caused by a patient with alkaptonuria. The final treatment is based on joint

replacement surgery to restore the patient's mobility. In this case, we finally came to the right diagnosis through initial misdiagnosis, intraoperative findings and additional postoperative physical and blood tests.The position of the bilateral hip prosthesis was good and the patient's functional recovery was satisfactory. At present, there is no effective method regarding gene therapy. We strongly advised the patient to follow a low-protein diet, which can slow down the progression of the disease.

2. Alkaptonuria is defined as an autosomal recessive genetic disease. The pathogenesis of this disease has been clearly defined; the symptoms and signs of this disease can be diagnosed based on intraoperative findings and specific blood/urine screenings. The incidence rate and gene screening are relatively small. This case report is about the surgical treatment of ochronotic arthropathy from the perspective of misdiagnosis which has certain clinical significance.

3. We use joint replacement as a surgical method to treat the bilateral hip joint and restore the function of patients. Total hip replacement has been used for decades and with its latest innovation, we deemed that it was the best overall option to improve the patient’s quality of life.

4. It has been re-uploaded.

5. Exogenous skin browning

This disease is caused by long-term local use of hydroquinone, phenol and other phenol intermediates. Urinary melanic acid oxidase contains a hydrophobic group (-SH), therefore, its activity can be inhibited by certain chemicals and drugs such as phenol, phenol intermediates, resorcinol, hydroquinone, picric acid, acetaminophen, mipaline, etc., as well as by certain antimalarials drugs, resulting in the accumulation of uronic acid in the collagen fibers of the local skin.

The patient, in this case, has not taken any special drugs orally. Therefore, the disease was of endogenous origin.

6. We did not find any specific observations related to alkaptonuria on the skin and during physical examination. These notes will be added on the revised manuscript.