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Diagnosing Alkaptonuria after a Discectomy Case - A Case Report

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Abstract

Alkaptonuria is a rare genetic disorder characterized by the excessive production of homogentisic acid, leading to the formation and deposition of pigment polymers throughout the body. It is extremely rare, affecting only around 1 in 100,000 individuals.Despite the normal life expectancy, it can cause severe morbidities.

Alkaptonuria is typically managed supportively with pain medication, dietary modifications, and surgical interventions, which considered to be the gold standard of therapy.In this report, we present a case of a 33-year-old male with no previous medical or surgical history who presented with severe acute back pain radiating to the left leg. Genetic testing confirmed a homozygous pathogenic variant for alkaptonuria.

This case highlights the challenges in diagnosing alkaptonuria, emphasising the significance of early detection and clinical evaluation for improved outcomes. Furthermore, it underscores the need to consider alkaptonuria as a multidimensional disease, necessitating further researches to enhance our understanding and develop effective management. Therefore, this case report serves as an opportunity for future trials and studies aimed at dig deeper into the intricacies of alkaptonuria to increase our understanding and establish comprehensive management plans for affected individuals.

Categories: Orthopedics
Keywords: discectomy, ochronosis, alkaptonuria, black urine, alkaptonuria

Introduction

Black urine disease, AKA, Alkaptonuria or alkaptonuria is a rare autosomal recessive inborn error of metabolism as defined in 1902 [1]. The defect lies in the catabolism of tyrosine and the deficiency of the HGO enzyme, which is responsible for the formation of homogentisic acid that is, upon contact with air, converted to a pigment polymer that is causing the blackish discoloration of the standing urine [2]. This pigment can deposit throughout the body and mainly throughout cartilaginous tissues. This process of deposition/pigmentation takes years and is often presented in adulthood usually beginning from the third decade, in contrast, although usually asymptomatic, some of the earliest signs of presentation are blackish diaper staining and black urine through childhood [3]. Because it is autosomal recessive, chances of development are equally distributed throughout genders. Yet, males tend to have sooner and worse clinical outcomes [4]. Alkaptonuria Causes significant morbidity in patients in which patients usually suffer severe arthritic Sx and back pain requiring medical attention [3].The pigment can also be deposited in valves causing valvular calcification and cardiac manifestations [5]. Using gas chromatography, homogentisic acid can be identified in the urine suggesting alkaptonuria. Disk degeneration plus calcification of imaging can be helpful for diagnosis. Valvular involvement can be assessed by chest x-ray or CT. Histological evaluation will show pigment deposition outside the cells in a sample taken from cartilage. Treatment of Alkaptonuria often relies on dietary modification and surgical management. Surgical options include removal of involved disks with fusion and the replacement of the involved joint if necessary [6].

Case Presentation

We present a case of a 33-year-old male with no prior medical or surgical history who presented with severe acute back pain and radiating to left leg pain. The patient symptoms began two days after lifting a heavy object and and getting worse day by day. In addition to weakness and numbness in the left leg., initial assessment indicated signs of cauda equina syndrome, leading to an urgent lumbar MRI. The MRI revealed a paracentral left disc herniation at the L5-S1 level, along with Modic type 1 changes on the inferior endplate

of the L5 body (Figure *1*). Further evaluation with a CT scan was performed to assess the presence of any bony abnormalities causing compression and confirmed the absence of bony osteophytes (Figure *2*). The patient was initiated on intravenous analgesia and oral pain medications. Upon reassessment, weakness affecting the L5-S1 level was noted, with a strength grade of 3/5, along with decreased sensation and radiating pain throughout the entire leg. Consequently, a decision was made to proceed with a microscopic discectomy of the left L5-S1 disc the following day. The surgical approach employed a minimally invasive posterior technique, and no abnormalities were observed in the skin, connective tissues, or bone. During the surgery, upon incision of the annulus fibrosus, the disc material appeared black and dark in color. After removing all loose disc material, inspection of the extracted disc revealed fragile and black tissues (Figure *3*). Following the surgery, the patient experienced a favorable outcome, with a return of strength and significant improvement in pain and numbness. A retrospective evaluation of the patient's history and physical examination revealed a positive report of dark urine to varying degrees, although no pigmentation was observed in the cartilage or sclera. This prompted an investigation for alkaptonuria. Urine homogentisic acid was collected and sent for gas chromatography, with fresh urine appearing normal in color. An echocardiogram (ECHO) was performed, ruling out any valve abnormalities. The patient also mentioned having a sibling in their thirties who presented with similar complaints of back pain and disc disease. The patient's recovery progressed well, without any complications. After the patient's one-year follow-up, it was observed that the patient exhibited no symptoms or signs of the previously diagnosed disease. This outcome indicated a complete resolution or remission of the condition. The follow-up period not only provided reassurance about the patient's well-being but also allowed for a comprehensive assessment of their long-term health status. In order to gain further insights into the genetic aspects of the disease, genetic testing was performed on the patient's siblings. This testing aimed to identify any potential genetic predisposition or inherited factors that could contribute to the development of the disease. The genetic analysis involved examining specific genes or genetic markers associated with the condition and it was positive for a homozygous pathogenic variant was identified in HGD gene which confirmed the genetic diagnosis of autosomal recessive alkaptonuria. In addition to genetic testing, histopathological testing was conducted. This type of testing involves studying the microscopic structure of tissues obtained from the patient. The purpose of histopathological examination was to confirm the presence of disease-related cellular or tissue changes. In this case, the histopathological testing yielded positive results, suggesting the presence of disease-specific abnormalities in the affected tissues. Overall, the patient's positive clinical outcome in the follow-up, combined with the genetic and histopathological findings, provided valuable information for understanding the nature and potential hereditary aspects of the disease. These insights can contribute to improved diagnosis, treatment, and genetic counseling for the patient and their family members.

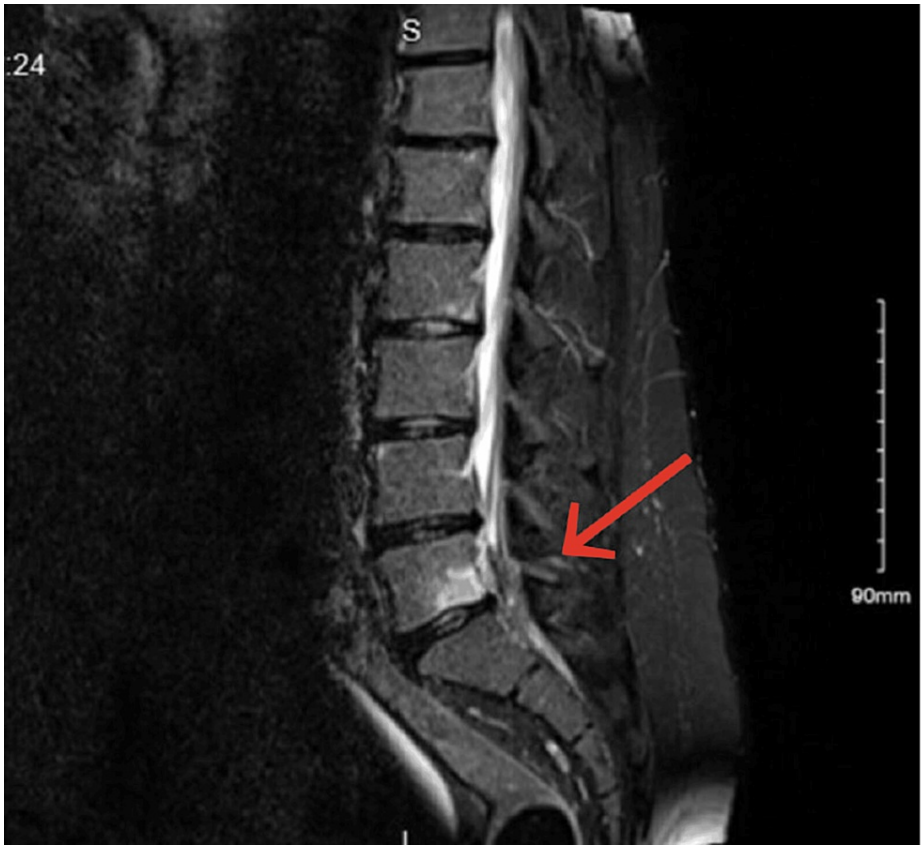

FIGURE 1: The MRI revealed a paracentral left disc herniation at the L5-S1 level, along with Modic type 1 changes on the inferior endplate of the L5 body

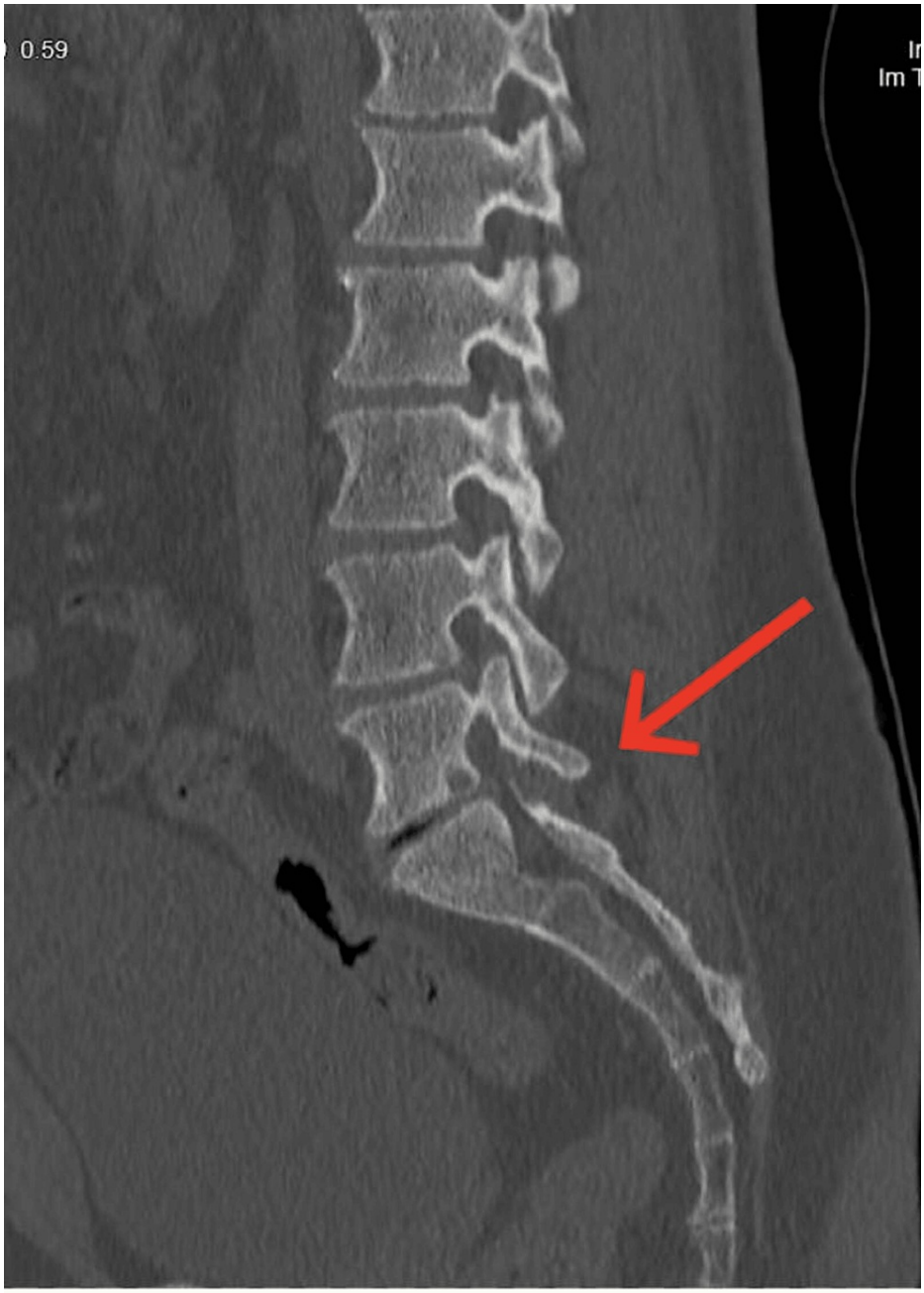

FIGURE 2: CT scan confirmed the absence of bony osteophytes

FIGURE 3: inspection of the extracted disc revealed fragile and black tissues

Discussion

Alkaptonuria is an autosomal recessive genetic disease ,which was first reported by Garrod as an inborn error of protein metabolism in 1902 [1]. The defected gene has been mapped to chromosome 3 by Pollak et al [1]. AKU results in accumulation of homogentisic acid in connective tissues due to the deficiency of HGD enzyme [1,7]. The accumulated HGA oxidizes to form melanin-like polymer which is responsible for the dark yellow pigmentation of cartilage and other tissues [1] . The majority of the patients are usually asymptomatic until the third and fourth decades [8]. One of the earliest signs is darkening of the urine upon standing [8]. In the age of forty, external signs of bluish-black discoloration, ochronosis, begin to appear [9]. The pigmentation tend to be more prominent in the sun exposed, cartilage, high sweat gland density sites of body [8]. Approximately fifty percent of patients present with ochronotic arthropathy, musculoskeletal manifestation of alkaptonuria, involving weight-bearing joints leading to arthritis and significant back pain [10,11]. Patients often present with back stiffness, with eventual loss of lordosis and exaggerated thoracic kyphosis occurring earlier than the peripheral joints and the spine [12].

Intervertebral calcification at numerous levels and vacuum phenomena with radiolucent gas collections are typical radiologic findings that indicate areas of severe degeneration [12].

AKU affects males and females equally. However, Males typically experience more severe and earlier-onset arthritic symptoms than females [13]. The diagnosis of AKU is frequently not made until it is identified intraoperatively during orthopedic surgery, when the affected joint shows the distinctive bluish-black coloring, due to the disease's rarity and symptoms that mimic other types of arthritis.

Currently, there's no effective treatment for alkaptonuria. However, low tyrosine and phenylalanine diet, physical therapy, NSAIDs ,and antioxidants have been recommended [1,10].

Conclusions

In conclusion, Alkaptonuria is a frequently underdiagnosed disease that requires greater understanding and earlier clinical evaluation. Detecting this condition early is crucial for preventing and treating various systems in the body, as it not only presents with skin changes but also affects the renal, cardiovascular, and liver systems. Therefore, it is essential to raise awareness among healthcare practitioners about the importance of assessing albuminuria in cases of unexplained musculoskeletal manifestations, as Alkaptonuria is commonly involved in such presentations. Since there is currently no effective treatment for Alkaptonuria, it is advised to approach it as a multidimensional disease, and further research is necessary. This case report provides an opportunity for trials and series to delve deeper and gain more knowledge about this disease.

Additional Information

Disclosures

Human subjects: All authors have confirmed that this study did not involve human participants or tissue. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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