SVOA Neurology

ISSN: 2753-9180

ScienceVolks Open Access

Case Report

Neglected Alkaptonuric Patients Presented with Symptomatic Degenerative Disc Disorders: Report of Two Cases and Review of Literature

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DOI: https://doi.org/10.58624/SVOANE.2023.04.0110

***Received:** October 28, 2023* ***Published:** November 17, 2023*

Abstract

Alkaptonuria (AKU) is a rare autosomal disorder characterized by the accumulation of excess homogentisic acid (HGA) in connective tissues. Herein, we report the uncommon presentation of degenerative lumbar disc disease occurring in two patients with AKU warranting spinal surgery. We report two cases of symptomatic disc herniation and vertebral canal stenosis, presented with radiculopathy and progressive neurogenic claudication, respectively. During spinal surgery, blackened ligamentum flavum and intervertebral disc raised the suspicion of a metabolic disorder. Re-examination of patients revealed nose and ear cartilage discoloration in only one of them, however, histopathological findings and urinalysis were confirmatory for AKU in both. Notwithstanding the rarity of AKU, spine surgeons must be vigilant in their examination and diagnosis, and should not exclude any possible diagnosis without thorough consideration.

***Keywords:** Alkaptonuria, intervertebral disc, claudication, radiculopathy, vertebral canal stenosis*

Introduction

Alkaptonuria (AKU) is a scarce autosomal recessive syndrome caused by the accumulation of homogentisic acid (HGA) [1]. The early presentation of AKU consists of black discoloration of urine, followed by skin and sclera melanosis [2]. Subsequently, HGA deposits in cartilaginous tissues, large joints, and intervertebral discs [3]. Spinal involvement commonly occurs in the thoracic and lumbar regions [4]. Even though degenerative disc disease (DDD) is prevalent in AKU, intervertebral disc protrusion and gait disorder are uncommon. There are very few cases of patients who were diagnosed with AKU only after undergoing spine surgery on account of symptomatic DDD. Herein, we report two cases of neglected AKU presented with radiculopathy and neurogenic claudication with a thorough review of literature.

Case Presentation

Case 1

A 53-year-old female presented to our neurosurgery clinic with an eight-month history of left lower limb pain and weakness.

Her past medical and family histories were unremarkable except for percutaneous laser disc decompression (PLDD) 20 months earlier. On neurological examination, proximal and distal forces in her left lower limb were 3/5, and toe dorsiflexion was weaker compared with the right foot. She underwent electromyography and nerve conduction studies revealing radiculopathy in L5-S1 levels. Magnetic resonance imaging (MRI) showed disc extrusion at L5-S1 (Figure 1). She underwent surgery for an L5-S1 discectomy, where no skin, muscle, and ligament discoloration were noted. However, the extracted intervertebral disc was found blackened. Histological examination revealed melanin deposits in intervertebral discs. After the operation, she underwent further clinical examination which demonstrated nasal and ear cartilages discoloration. Eventually, urine analysis confirmed the AKU diagnosis by a high-intensity peak of HGA.

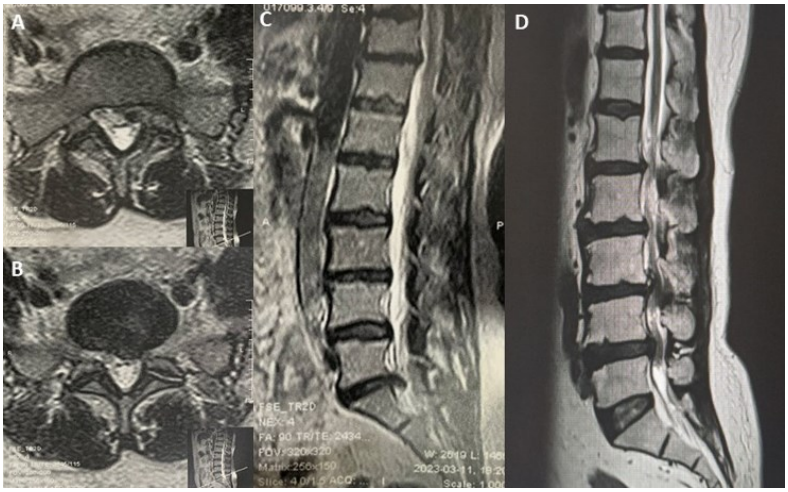

Figure 1: *Axial (A, B) and sagittal (C) images of Case 1 showing extruded intervertebral disc at L5-S1. Sagittal magnetic resonance image (D) of Case 2 revealed lumbar canal stenosis from L1 to L5, disc extrusion at L3-L4, and protrusion at L4-L5.*

Case 2

A 57-year-old man with a history of chronic low back pain, left leg radiculopathy, and progressive neurogenic claudication for almost 18 months was referred to our neurosurgery clinic. His past medical history involved controlled hypertension. No history of trauma or surgery to the spine was mentioned and he had an unremarkable family history. He did not report any bowel and bladder problems. An MRI was requested showing severe vertebral canal stenosis from L1 to L5 as well as lumbar disc extrusion and protrusion at L3-L4 and L4-L5, respectively (Figure 1). Decompressive laminectomy was performed at L2, L3, and L4 levels followed by L3-L4 and L4-L5 discectomy and posterior fusion. The ligamentum flavum appeared to be black in color. Histopathology results were indicative of melanin-like pigmentation and degeneration of the ligamentum flavum. Afterward, the patient was re-examined and no pigmentation of the sclera, nasal, ear cartilages, or skin was found. However, a high level of HGA on the subsequent urine analysis was confirmatory of AKU.

Discussion

AKU is an autosomal recessive metabolic disorder happening as a result of failure to metabolize HGA [5]. Excessive amounts of HGA are excreted in the urine, and sweat and accumulate in different tissues which is attributable to bluish-black pigmentation known as “ochronosis”[5]. Ochronosis mostly occurs in the ear and sclera in early adulthood [6], while DDD usually is seen between the third and fifth decades of age [7].

There are several non-specific radiographic findings in AKU patients including, osteoporosis, decreased lumbar lordosis, extensive disc calcification, and intervertebral space narrowing [8]. Having said that, a majority of patients with mild AKU are asymptomatic during their adulthood and might insidiously develop symptoms [9]. Consistently, both of our patients started to have neurological symptoms in their 6th decade of life. Having reviewed the literature, we found nine cases of neglected AKU patients who were diagnosed after spinal surgery. To the best of our knowledge, we present the third case of ligamentum flavum hypertrophy due to HGA deposition (Case 2).

AKU diagnosis is established based on ochronosis of tissues, ligaments, facet joints, black-colored discs, and black discoloration of urine after alkalization [10]. Retrospective examination of patients usually reveals signs of ochronotic deposits in tissues including ear, nose and sclera [10]. Likewise, after observation of extracted black intervertebral disc and re-examination of our patient (Case 1), we found nasal and ear discoloration as well as positive urine analysis. However, our second case had no clue of ochronotic deposition with the exception of his blackened ligamentum flavum and high level of urinary HGA. It is worth mentioning that our first patient had undergone PLDD in another center for right lower limb radiculopathy and experienced recurrence of symptoms after almost 20 months. Reviewing the patients' documents showed that she had not met the eligibility criteria for PLDD [11], leading to disc herniation recurrence.

There is no definitive treatment for AKU at the moment and supportive management is the cornerstone of treatment. Dietary limitations on phenylalanine and tyrosine kinase, while increased use of oral vitamin C is proposed to curb the production and accumulation of HGA (14-16). Surgery is deemed to be effective for patients with spinal or peripheral large joint involvement to refine the quality of life (19,20). Here we have reviewed the features of neglected AKU patients who were diagnosed after spinal surgery for symptomatic DDD (Table 1).

Table 1. Demographic characteristics of neglected AKU patients who underwent spinal surgery.

Study/year	Age/sex	Symptoms	Physical re-examination
Present study			
Case 1	53/F	Left leg pain and weakness	Discoloration of nasal and ear cartilages
Case 2	57/M	LBP, left leg pain, and neurogenic claudication	No pigmentation
Vakilzadeh et al.[12] /2021	28/M	LBP and left foot drop	Discoloration of nasal and ear cartilages
Yucetas, Ucler.[10] /2019	71/M	LBP and neurogenic claudication	Discoloration of sclera, cornea and skin
Mirzashahi et al[13]. / 2015	51/M	LBP and right leg pain	No pigmentation
Kahveci et al.[14] /2013	45/M	LBP and left leg pain	No pigmentation
Gurkanlar et al. [15]/2006	45/M	LBP and left leg pain	Discoloration of nasal and ear cartilages
Farzannia et al.[16] /2003			
Case 1	30/F	LBP and left leg pain	Discoloration of nasal and ear cartilages
Case 2	28/M	Lumbago and right leg pain	Discoloration of sclera and nose
Case 3	36/M	LBP and left leg pain	Discoloration of nasal and ear cartilages and fingernails
Choudhury et al[6]./2000	35/M	LBP and right leg pain	No pigmentation

M: male, F: female, LBP: low back pain, MRI: magnetic resonance imaging, CT: computed tomography, NA: not available

Conclusions

Our paper highlights the paramount significance of early diagnosis and proper treatment of complications so as to curtail morbidities, especially in patients with no other sign of AKU. Thus, we urge spine surgeons to meticulously consider metabolic disorders such as AKU as the differential diagnosis of degenerative disc diseases.

Ethics Approval and Consent to Participate

Ethics committee approval was not considered necessary because it was a case report.

Informed Consent

Written informed consent was obtained from the patient for the publication of this case report and accompanying images.

Funding

None.

Conflict of Interests

None declared.

Authors' contributions

S.R.E.B., M.J.B., S.D. contributed to writing the paper, data collection, interpretation, and leadership responsibility for the research activity planning and execution, including mentorship external to the core team. B.S.S., D.M.V., D.K. and S.A.S.R. contributed to data collection and interpretation. M.T. and N.F. contributed to the study concept or design, and interpretation.

Acknowledgments

None.

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Citation: Bakhtiari SRE, Begijonovich MJ, Sharafiddinovich BS, Valievich DM, Kheradmand D, Delasaeimarvi S, Razavi SAS, Taghdisi M, Faraji N. Neglected Alkaptonuric Patients Presented with Symptomatic Degenerative Disc Disorders: Report of Two Cases and Review of Literature. *SVOA Neurology* 2023, 4:6, 184-188.