Letter to the Editor / Editöre Mektup

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Turk J Osteoporos

A Rare Cause of Inflammatory Back Pain: A Case of Alkaptonuria Mimicking Axial Spondyloarthritis

Nadir Bir Enflamatuvar Sırt Ağrısı Nedeni: Aksiyel Spondiloartriti Taklit Eden Bir Alkaptonüri Olgusu

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Dear Editor,

A 59-year-old male was referred to our outpatient clinic with a 15-year history of progressive inflammatory low back and hip pain, accompanied by morning stiffness lasting longer than 30 minutes. The patient had previously been evaluated for a suspected rheumatological condition based on his chronic symptoms. At an external centre, he had been misdiagnosed with ankylosing spondylitis and subsequently treated accordingly. Upon clinical examination, melanotic discolouration was observed in both sclerae and auricles, suggestive of ochronosis (Figure 1A, B). There was marked thoracic kyphosis, and range of motion was limited in the spine, hips, and particularly in the lumbar region. There were no signs of nerve root compression.

Routine blood investigations, including complete blood count, C-reactive protein, liver function, and renal function tests, were all within normal reference ranges. Interestingly, the patient reported that his urine darkened noticeably upon standing at room temperature for a few hours. This observation was supported biochemically by elevated homogentisic acid levels in the urine.

Molecular genetic analysis revealed a homozygous pathogenic variant in exon 3 of the *homogentisate 1,2-dioxygenase (HGD)* gene: c.175del (*p.Ser59Alafs*52*), classified as a frameshift mutation (*rs397515517*).

Radiographic evaluation demonstrated wafer-like calcification of the intervertebral discs, predominantly in the thoracolumbar region, with thoracic kyphosis (Figure 1C). The sacroiliac joints appeared abnormal, with unilateral narrowing and sclerosis on one side and complete ankylosis on the opposite side (Figure 1D). Magnetic resonance imaging (MRI) of the sacroiliac joints demonstrated chronic structural changes without evidence of active inflammation. No bone marrow edema, synovitis, or joint effusion was detected on short tau inversion recovery and T1-weighted sequences.

Based on the clinical, biochemical, radiological, and molecular findings, a diagnosis of alkaptonuria was established. The patient was managed conservatively with a combination of dietary modification, a home-based physiotherapy programme, ascorbic acid supplementation, and non-steroidal anti-inflammatory drugs and was subsequently referred for ongoing multidisciplinary follow-up involving cardiology and metabolic medicine.

Alkaptonuria is a rare inherited metabolic disorder transmitted in an autosomal recessive manner. It results from a defect in the catabolic pathway of phenylalanine and tyrosine (HGD enzyme), leading to the systemic accumulation of homogentisic acid. This accumulation is particularly pronounced in connective tissues, including cartilage, tendons, and ligaments, ultimately giving rise to a condition known as homogentisic aciduria (1,2). Deposition of brown-black pigment occurs predominantly in connective tissues, with a particular affinity for cartilage, while cutaneous and scleral involvement is observed less frequently (3). Involvement of the

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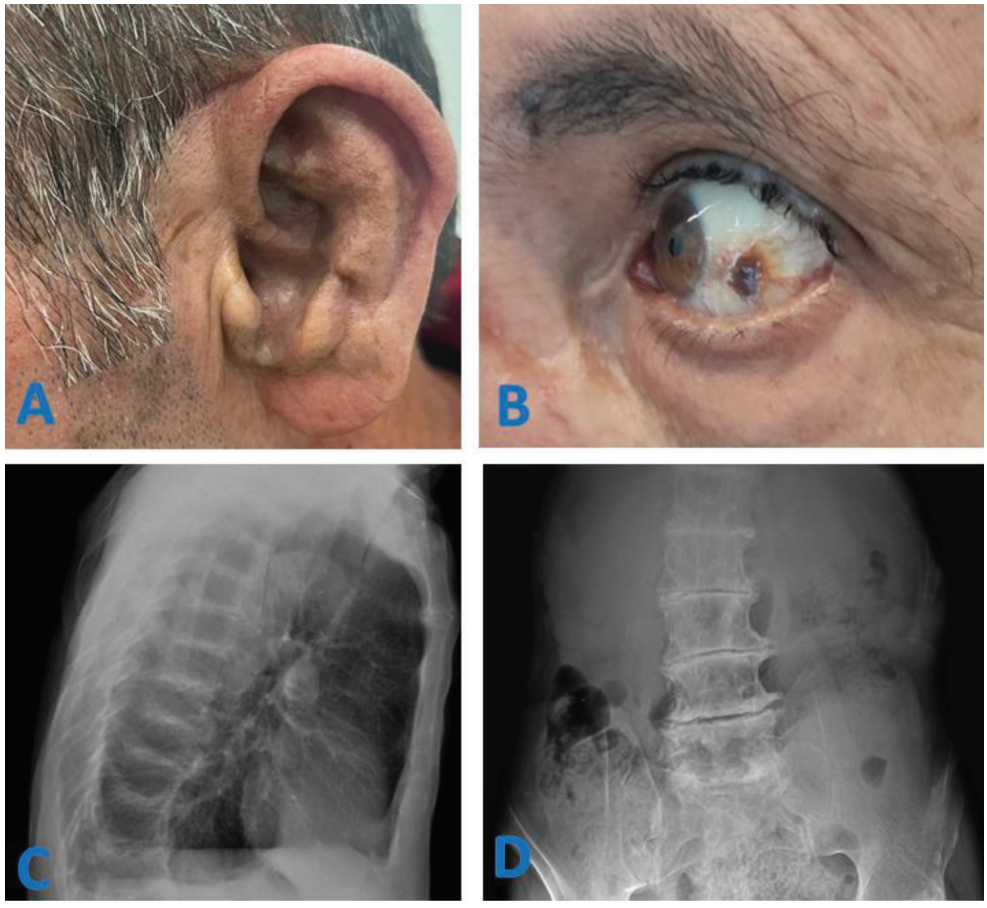

Figure 1. (A) Ochronotic pigmentation of the auricle, characterised by bluish-brown discolouration of the helix and antihelix. (B) Brown-black pigment deposition visible in the sclera (ocular ochronosis), a classic sign of systemic homogentisic acid accumulation. (C) Lateral thoracic spine radiograph showing thoracic kyphosis and intervertebral disc calcification. (D) Anteroposterior radiograph of the lumbar spine demonstrating wafer-like intervertebral disc calcification and reduced disc space height, along with unilateral sacroiliac joint space narrowing and subchondral sclerosis on one side, and ankylosis on the contralateral side

Note: Written informed consent was obtained for publication of the case report and accompanying images.

musculoskeletal system, notably the lumbar intervertebral discs and various peripheral joints, is a major source of functional impairment and morbidity in patients with alkaptonuria. As the disease progresses, the accumulation of pigment within connective tissues leads to stiffening, early degenerative changes in spinal joints, and the development of marginal osteophytes along the vertebral bodies. Characteristic imaging findings include widespread narrowing of intervertebral disc spaces, often accompanied by a "wafer-like" disc calcification pattern (4). Except for darkening of urine after 1-2 hours in the first years of life, most clinical symptoms typically manifest in the fourth decade of life. In addition to the musculoskeletal system, alkaptonuria may involve a wide range of other tissues, including the cardiovascular, genitourinary, integumentary, and ocular systems (5).

Ochronotic pigment accumulates primarily in collagen-rich connective tissues, which can lead to complications such as valvular heart disease, renal and prostatic calculi, and skin and scleral pigmentation. The progressive involvement of the axial and peripheral joints, along with features such as low back pain, stiffness, and intervertebral disc calcifications, may closely resemble other rheumatologic disorders, particularly ankylosing spondylitis, osteoarthritis, calcium pyrophosphate deposition disease or diffuse idiopathic skeletal hyperostosis (6). In our case, the patient had previously been misdiagnosed with ankylosing spondylitis and treated accordingly. We believe this misdiagnosis was likely driven by the presence of sacroiliac joint involvement and prolonged morning stiffness, which are commonly associated with spondyloarthropathies, and by the absence of an early MRI evaluation that could have excluded active inflammatory changes (7).

This clinical overlap, particularly when active inflammatory changes are not excluded by MRI, carries a substantial risk of misdiagnosis as axial spondyloarthritis. Clinicians should remain alert to the possibility of alkaptonuria in patients presenting with early-onset degenerative changes, atypical sacroiliac joint imaging features, and combined axial and large peripheral joint involvement. Early and accurate diagnosis, supported

by biochemical and genetic testing, is crucial to guiding appropriate management, avoiding unnecessary exposure to immunosuppressive agents, and ensuring timely multidisciplinary follow-up.

Yours sincerely,

Footnotes

Authorship Contributions

Surgical and Medical Practices: A.N.D., A.U., Concept: A.N.D., A.U., Design: A.N.D., M.E.U., A.U., Data Collection or Processing: A.N.D., M.E.U., A.U., Analysis or Interpretation: A.N.D., U.G.D., M.E.U., A.U., Literature Search: A.N.D., U.G.D., M.E.U., A.U., Writing: A.N.D., U.G.D., M.E.U., A.U.

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