Alkaptonuria is a rare metabolic disorder in the phenylalanine and tyrosine catabolic pathway that is characterized by the excessive excretion of homogentisic acid in the urine, ochronosis, and debilitating arthritis of the spine and large joints. Although it is a very rare disease in most ethnic groups, it is more common in some countries, such as Slovakia and the Dominican Republic. In this report, we report a 58-year-old Jordanian female case with advanced clinical features of alkaptonuria.

Key words: Alkaptonuria; arthritis; dark urine; homogentisic acid; pigmentazione.
Jordan in which we describe the clinical, biochemical, and radiological findings.

**CASE REPORT**

We present the case of a 58-year-old female with a 10-year history of severe chronic lower back and morning stiffness. The patient’s pain became more exacerbated upon the initiation of spinal movements and flexion of the spinal column. She had no symptoms of nerve root compression but had a history of large joint pain in her hips, knees, and shoulders. A physical examination revealed bluish pigmentation over the forehead, cheeks, nose, fingertips, nails, hands, and ear cartilage (Figure 1). In addition, the sclera of both eyes showed dark brown pigment deposits, and there was dark brown pigmentation of the skin, teeth, and gums. When the patient’s urine was left standing for a few hours at room temperature, it turned dark. Furthermore, a dark color was also obtained when ferric chloride was added to the urine sample (Figure 2). According to the clinical examination, the patient had bilateral fixed flexion deformity in both hips with decreased flexion-extension motion with no abduction or adduction. She also had 30-degree fixed flexion bilateral varus knee deformity with decreased flexion-extension range of motion. Additionally, the patient had a fixed kyphotic thoracic spine with decreased lateral flexion in both directions. Regarding her upper limbs, she had normal shoulder range of motion with minimal tenderness in abduction, and both elbows had normal flexion-extension range of motion along with a 50% decrease in pronation-supination. Exaggerated thoracic kyphosis and loss of height were also noted.

Radiographs of the lumbar spine showed extensive degenerative changes with severe narrowing of the joint spaces together with intervertebral disc calcification along the lumbar spine, fusion of vertebral bodies in the upper lumbar spine, osteophyte and bone bridge formation, and loss of lumbar lordosis (Figure 3). Additionally, an X-ray of the knee joints determined that there were degenerative changes with joint space narrowing, and X-rays of both shoulders showed decreased joint spaces with degenerative changes in the articular portion of the humeral head. The patient also complained of difficulty walking and of an inability to move. Eventually, she became disabled. The patient used to have high-protein content meals but had changed her diet to one of low protein since being diagnosed with AKU. She was also prescribed 1 g of vitamin C daily. She has 13 children (two sons and eleven daughters), and there is a family history of AKU, with two sons and six daughters having also been diagnosed with the same disease.

**DISCUSSION**

Although AKU is a rare genetic disorder that is found all over the world (1 in 250,000), high incidence rates have been reported in countries such as Slovakia (1 in 19,000) and the Dominican Republic,[10,11] and so far, 626 patients with AKU have been identified in 40 different countries.[12] In Jordan, the preliminary results of targeted family screening have identified 64 cases. This large number of AKU patients in a small
country with a population of only five million is due
to the large number of consanguineous marriages.[9]

In this study, we reported on our experience
with a patient who had an advanced case of AKU
that had previously gone undiagnosed. Because the
diagnosis occurred at the relatively late age of 58, the
main characteristic features of the disease, such as
involvement of the spine, hips, and knees along with
the typical radiological signs were already present.
Ochronotic spondyloarthropathy is the most common
complication of AKU. This occurs due to the deposition
of ochronotic pigment in the intervertebral discs and
articular cartilage of the large joints.[13] Ochronotic
spondyloarthropathy resembles ankylosing spondylitis
(AS) in its damage to the spine and large joints; however, it differs in that it spares the sacroiliac
joints and does not have the annular ossification,
syndesmosis, or bamboo spine that are associated
with AKU.[14] In addition, AS is also indicated by the
appearance of thin, vertical syndesmophytes, severe
involvement of the apophyseal facet joints, and erosion
and fusion of the sacroiliac joints.[13]

Spinal changes that occur with AKU include
severe disc calcification, disc space narrowing, and
corrosion, primarily in the dorsolumbar spine rather
than the lumbosacral spine.[16] The calcification
of intervertebral discs is pronounced at the periphery
and tends to spare the central nucleus pulposus,
with its wafer-like pattern.[17] Large peripheral joint
involvement usually takes place years after ochronotic
spinal involvement, and the small joints of the hands
and feet, wrists, elbows and ankles are rarely affected.
The knees are the most frequent target, and knee joint
effusion may also occasionally occur. After the knees,
the hips are affected the most, and rapid deterioration
is often seen in these joints with AKU.[18]

No effective treatment exists for AKU. What is
currently offered is primarily supportive in nature
and includes genetic counseling, pain management
with nonsteroidal anti-inflammatory drugs
(NSAIDS), and physiotherapy. It has been reported
that avoiding a diet high in phenylalanine and
tyrosine may be helpful.[19,20] A few studies have
also suggested that vitamin C might be beneficial
because it prevents the oxidation of HGA, thus
preventing the deposition of ochronotic pigments.[21]
However, no clinical studies have shown the long-
term efficacy of these modalities. A drug called
nitisinone has also been mentioned as a potential
treatment for AKU; however, the long-term clinical
efficacy and safety of this drug have also not been
demonstrated.[22] In severe cases of AKU, surgical
intervention is required to replace the severely
affected joints.

Physicians involved in the care of patients with
musculoskeletal problems should be aware of this
rare genetic disease, particularly if a degenerative
arthropathy is far more progressed than would be
expected for the patient’s age.

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