Alkaptonuria, a rare inherited disorder: a case report and review of literature

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Case report

A 70 year old male patient from Erbil city, Iraq, complaining of gradually increasing pain and stiffness in the lower back over the last 50 years. He consulted many doctors and was misdiagnosed as having (prolapsed disc, Ankylosing spondylitis, Osteoarthritis). He was put on analgesics, anti-inflammatory drugs, hard bed .It gave him some relief but the pain and stiffness recurred again over a large area of the spine on stopping the treatment. For the past 20 years, the patient had pain in his hip joints too. There was no history of fever, trauma, oral ulcers, acute abdominal pain, dysuria or recurrent diarrhea. The urine had normal color when voided but the patient has also had brownish black staining of underwear since childhood.

Examination revealed undernourished patient with bluish discoloration of face (Fig 1) & both index fingers, pigmentation of both eyes sclera &ear (Fig 2), no anemia, cyanosis, jaundice or edema of the feet

Tenderness was positive over the lumbar spine with marked limitation of movements. schober test were positive and movements at both the hip joints were limited and painful. There is decreased in chest expansion at respiration. Marked restriction in rang of movement at both shoulders &knee joints with cripitus.

Investigations: His hemoglobin was 13.0 gm%, WBC count was 6600/cmm., with Neutrophil 66%, Lymphocyte 31%, Monocyte 1% and Eosinophil 2%. Serum uric acid was 3.5 mg%; E.S.R., 17mm in the 1st hour; fasting blood sugar 86 mg%; serum cholesterol 180 mg%; and Urine was of normal color when voided (Fig 3) but turned black over variable periods spontaneously (Fig 4) or addition of FeCl3 ; latex test and ANA are negative. E.C.G. was normal. Mother's, father's, brother's and his three sons' urine was negative for any history of changes in color. X-rays of the spine revealed narrowing of disc spaces and calcification of intervertebral discs (Fig 5); sacroiliac joints were normal. X-rays of pelvis show narrowing of the joint space of the hips with sclerosis, no prostatic or renal calculi were seen, and an X-ray of shoulders showed the same narrowing.

Abdominal ultrasound showed small spots of calcification on the mild enlarged prostate. Echo study of the heart showed mild Aortic regurgitation otherwise normal Echo study.

Discussion

ALKAPTONURIA (AKU) is a rare inherited genetic disorder of tyrosine metabolism characterized by the triad of homogentisic aciduria, ochronosis and arthritis clinically manifested by blue-black pigmentation of connective tissues and cartilages and arthritis of weight bearing joints. and the urine turns dark on standing and on alkalization due to elimination of excessive amounts of homogentisic acid (HGA).The condition is rare, Males and females are equally affected, though symptoms tend to be more severe in males and most severe in those individuals with impaired kidney function.3 Here we report case of alkaptonuria in a 70 year old man presented with typical feature in whom the case was missed.

Alkaptonuria is affecting one in 250,000 to one million people worldwide. Cases have been reported from UK, Germany, Lebanon, Sudan, Saudi Arabia, Turkey and other parts of the world.1, 2. It is of interest to note that the disease was identified in 1500 BC in an ancient Egyptian

mummy[3]. Alkaptonuric patients are usually asymptomatic as children or young adults. When they get older, pigmentation of the sclera or the cartilage of the ear start to appear, or the skin, giving these areas a dusty coloration. The widespread deposition of pigment in alkaptonuric patients is called ochronosis [4] a term used to describe the darkening of tissues, which is due to a slow accumulation of the black polymer of homogentisic acid in the cartilage and other mesenchymal tissues.

Arthritis is the only disabling effect of this condition, and occurs in almost all patients with advancing age[5]. The earliest symptoms are usually in the hips, spine and knees, the large weight-bearing joints. The radiological picture is of severe osteoarthritis. In contrast to osteoarthritis, the large joints at the hip and shoulder are most commonly involved, whereas the sacroiliac joints are spared contrary to that of Ankylosing Spondylitis. The degenerative changes in the lumbar spine are quite characteristic, with narrowing of joint spaces and fusion of vertebral bodies, resulting in marked limitations of motion with ultimate ankylosis. Ochronotic arthropathy in the hips and the knees may be so severe as to require total joint arthroplasty.[6] the disease is more severe in men, although the incidence in the two sexes is equal.

There is a high incidence of heart disease, [7] commonly due to mitral and aortic valvulitis. Secondary calcification of the aortic valve may be so severe as to necessitate aortic valve replacement.[8]

The diagnosis is made by measurement of homogentisic acid in the urine and characteristic radiographic changes to the spine. Homegentisic acid turns black upon exposure to oxygen or alkali treatment.

Individuals with alkaptonuria are counseled to avoid occupations in which the large joints and spine are subjected to stress. There have been attempts to prevent symptoms by consuming a low protein diet especially low in phenylalanine and tyrosine in combination with ascorbic acid.9. However, these regimens have no effect on the disorder. Other treatment is symptomatic and supportive. Anti-inflammatory medication may be used to treat pain. Joint and aortic valve replacement may provide symptomatic relief. A new medicine (Nitisinone) that inhibits the enzyme, which produces HGA is on trial for the evaluation of long-term therapy.10

As a conclusion, This case report from Erbil, Iraq highlight the importance of early detection of this rare inherited disease to avoid misdiagnosis. The detection of this disorder is not without benefit for the affected individual as the administration of un-necessary drugs can be avoided.

References

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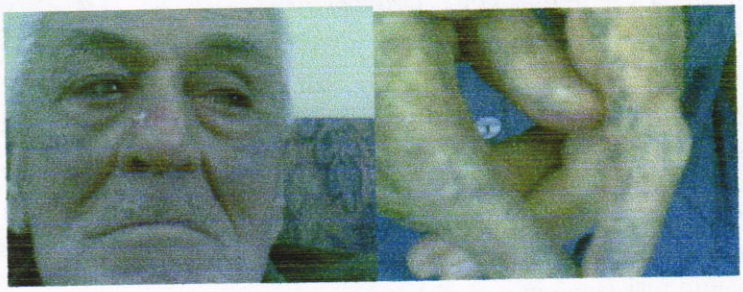
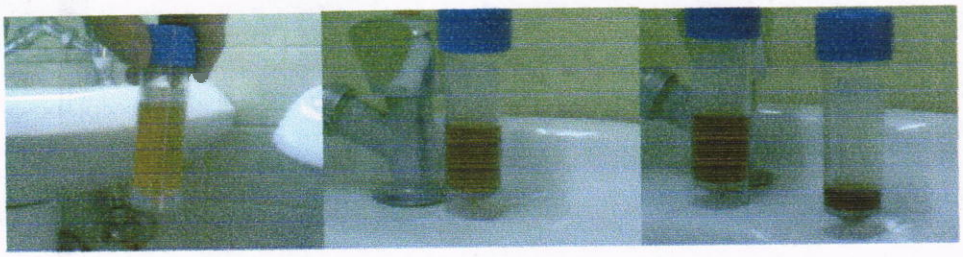


(Fig 1)

(Fig 2)



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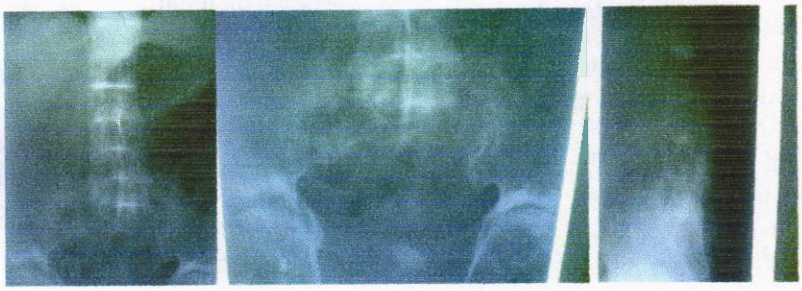

(Fig 5)