Blue-Black Discolouration

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A 70-year-old male of Asian descent presents to the walk-in clinic for an incidental skin problem. Striking blue-black discolouration of his face and ears is noticed. When you enquire about the nature of the problem he reassures you that it is a harmless condition. The patient was born in China and was told by his mother that he had sustained "gun powder burns" to his face in infancy during World War II. He has lived with this disfigurement all his life. He states many physicians have seen him in the past and he was not interested in undergoing investigations. He also denies the use of bleaching creams to his face. Functional enquiry reveals chronic low back pain. He has never had a history of discoloured urine in the past and there is no history of heavy metal exposure through well water ingestion.

Examination

On examination, he appears well and is in no distress. He has Fitzpatrick type IV skin complexion. There is prominent blue-black discolouration of both cheeks with involvement of the ears. There is no sclera involvement, no evidence of surface scarring nor induration on palpation of the ears and no cervical lymphadenopathy. Remainder of integumentary exam is unremarkable except for his tinea pedis for which topical antifungal medication was prescribed.

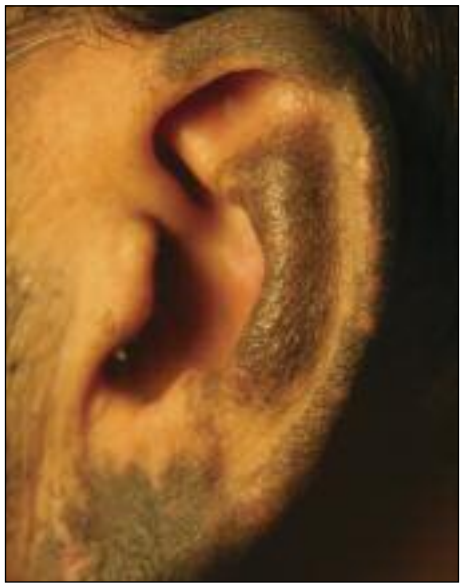

Figure 1. Blue-black discolouration of the face and ears.

What is your course of action?

a. Respect his decision and treat him only for his present complaint
b. Refer him to a cosmetic camouflage make-up clinic
c. Suggest a urine test for homogentisic acid

Answer: Suggest a urine test for homogentisic acid

What's your diagnosis?

a. Nevus of Ota
b. Argyria
c. Sturge-Weber syndrome
d. Alkaptonuria (primary ochronosis)
e. Exogenous ochronosis

Answer: Alkaptonuria (primary ochronosis)

About Alkaptonuria

Alkaptonuria is an autosomal recessive genetic disorder of tyrosine metabolism. Affected patients have a deficiency of the hepatic enzyme, homogentisate 1, 2-dioxygenase. This deficiency leads to a build up of the tyrosine intermediate, homogentisic acid, which can be excreted by the kidneys. Homogentisic acid is a pigment-like polymeric compound which rapidly turns black upon exposure to air. Hence, one of the earliest presenting signs of alkaptonuria is black staining urine on the diapers during infancy.

The incidence of alkaptonuria worldwide is estimated to be much lower than the 1 in 25,000 live births reported in some prevalent areas. Patients are asymptomatic in childhood and early adult life since the kidneys are able to excrete most of the homogentisic acid.

However, there is some collagenous transformation of the circulating homogentisic acid into a blue-black polymer-like substance in the cartilages of the body. The gradual accumulation of this polymer-like compound may initiate onset of arthritis in affected joints. Thus, patients often present with lumbosacral back as well as hip and knee pain by the third decade of life. Blue-gray discolouration may be noted in the sclera and ears (ochronosis). Some patients can develop calcification of their heart valves. Patients seldom give a personal history of black urine.

Diagnosis and management

The presence of homogentisic acid in the urine can be determined by gas chromatography/mass spectrography. It is absent in healthy subjects.

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Spinal x-rays may reveal disc degeneration combined with calcification, similar to osteoarthritis. A chest x-ray is recommended to rule out cardiac valve involvement. CT scans may help further delineate the extent of the disease. Surgery may be required for severely affected joints.

Medical therapy is aimed at retarding the conversion of homogentisic acid into the polymeric substance. High doses of vitamin C (1 gram per day) is recommended for older children and adults. Dietary restriction of tyrosine may be of some benefit in childhood but not adult life. Life expectancy is normal, however, patients should be monitored for development of cardiac disease. Experimental use of nitisinone, a tyrosine degradation inhibitor, has been reported. Genetic counselling and family screening is advised.

Back to the case

Urine test was positive for homogentisic acid. Skeletal x-ray revealed mild degenerative changes. He was started on vitamin C supplementation and referred for genetic assessment.

Addendum

Exogenous (secondary) onchronosis is a paradoxical hyperpigmentation of the skin caused by prolonged uses of hydroquinone containing bleaching medications.

Argyria is a condition whereby the skin develops a blue-grey colour due to oral ingestion of elemental silver and related compounds, often for purported homeopathic benefits. Dx

Resource
1. Phornphutkul C, Introne WJ, Perry MB, et al: Natural History Of Alkaptonuria. N Engl J Med 2002; 347(26):2111-21.