ALKAPTONURIA AND KERATOELASTOIDOSIS MARGINALIS - AN UNUSUAL ASSOCIATION

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INTRODUCTION

Alkaptonuria is a multisystem, genetic disorder with an autosomal recessive inheritance. The disease is typically characterized by a triad of dark urine, cutaneous hyperpigmentation, and arthropathy [1]. The diagnosis may easily be made during infancy when an observant mother notes dark staining of diapers; however clinical signs and symptoms usually develop following the deposition of pigment in connective tissues in the fourth decade of life. Cutaneous pigmentation, an important signs of disease, is more pronounced in sun-exposed sites and in areas with high sweat gland density. Bluish discolouration of skin overlying cartilages, especially on the ear and nose, may be one of the earliest signs of the disease [1]. We report a patient who presented with hyperpigmentation and acrokeratoelastoides marginalis like lesions on palms alongwith cutaneous and systemic manifestations of disease.

CASE REPORT

A 48 year fruit seller presented with the thickening of palm and soles for the last 10 years along with history of recurrent joint pains and difficulty in walking. There was no history of any drug intake or significant systemic symptom. On examination he had bluish black pigmentation of hands along with bluish yellow hyperkeratotic papules and plaques along the margins of palms, sides of fingers and thumbs suggestive of keratoelastoidosis marginalis (fig. 1). Similar pigmentation was also prominent on his cheeks, forehead, ear lobes and axillae. Oral mucosa and hairs were normal but nails were markedly discolored. His eyes showed dark brown to black pigment deposition in the sclerae between the cornea and the outer and inner canthi and a gray blue band on the sclera just peripheral to the iris (fig. 2). Skeletal survey revealed swollen and tender left knee joint with restricted movements. Systemic review was otherwise normal. The color of lesions was suggestive of ochronosis (Alkaptonuria) and on further questioning he told that his urine became dark on standing for sometime and it was also confirmed clinically (fig. 3). Investigations including haemogram, liver function tests and renal function tests were normal. Skin biopsy from a pigmented lesion on hand revealed hyperkeratosis and hypergranulosis and dermal elastorrhexis with yellow-brown (ochre) coloured pigment within the collagen bundles and also freely in the deeper dermis consistent with oochronosis and acrokeratoelastoidosis. X ray of knees showed osteoarthritic changes and X-ray lumber spine revealed intervertebral disc calcification. Diagnosis was confirmed by screening tests for alkaptonuria. He was advised symptomatic treatment and regular follow-up to monitor any cardiac or renal complications. Orthopedic consultation was sought for further management of his arthritis.

DISCUSSION

Alkaptonuria is a rare disorder of protein metabolism. It was initially described by Virchow in 1866 and was recognized as an autosomal recessive inborn error of metabolism by Garrod in 1902 [2]. It is caused by deficiency of homogentisic acid 1, 2-dioxygenase, typically due to a mutation of its gene on chromosome 3q. Since it is the sole catabolic enzyme for homogentisic acid (HGA), an intermediate metabolite of

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phenylalanine and tyrosine catabolism, its deficiency leads to elevated plasma levels of HGA [3]. This results in deposition of HGA in different tissues, especially fibrous and cartilaginous tissues, as well as its increased urinary excretion, upto 4-8 g/day. HGA excreted in urine gets oxidized by either exposure to air or alkalinization and leads to black discoloration of urine3. Black colour is due to HGA polymer which is formed once HGA is oxidized. HGA deposited in tissues is similarly oxidized by tissue homogentisic acid polyphenoloxidase, an enzyme present in mammalian tissues, to form a melanin-like pigment. It results inblue-black pigmentation (ochronosis) most evident in the ears, nose, and cheeks. The more serious consequences of ochronosis, however, stem from deposits of the pigment in the articular cartilages of the joints and organs like kidneys, heart and blood vessels. Pigment deposition in articular cartilage makes it brittle and susceptible to fragmentation resulting in osteoarthrosis in weight bearing joints. Furthermore ensuing inflammatory changes lead to dystrophic calcification which is most prominent in the lumbar intervertebral discs [4]. Pigment deposition and calcification in genital and urinary tracts may lead to renal and prostatic stones at an early age [5]. Heart is affected by valvular dysfunction, due to calcification of valves. Pigment deposition in the blood vessels wall makes it prone to atherosclerosis leading to ischemic heart disease [6].

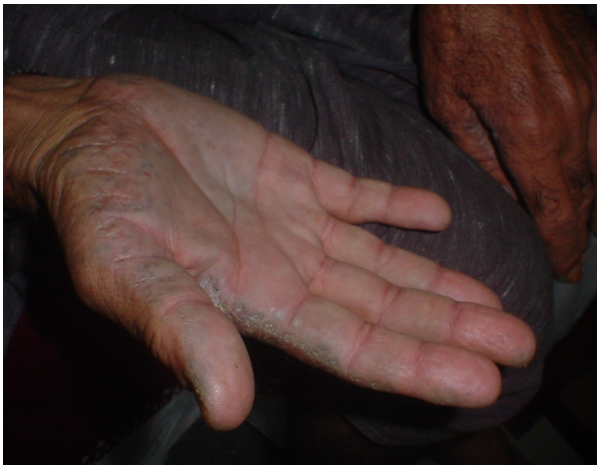

Fig. 1: Pigmented Lesions of Keratoelastoidosis on the Margins of Hand

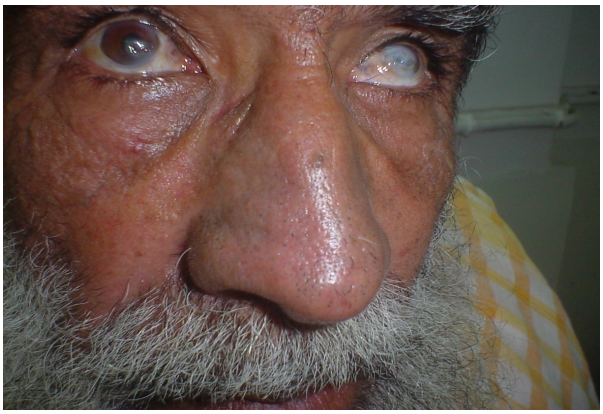

Fig. 2: Gray Blue Band Peripheral to Iris and Pigmentation of Sclera

Fig. 3: Comparison of Colour of Freshly Voided Urine and Urine after 24 Hours

Skin gets discoloured due to deposition of ochronotic pigment granules in the dermis. In early childhood the only evident sign may be black coloured cerumen. By the time of puberty a patient may notice brown discoloration of the axillae and groin probably due to chronic exposure to pigmented sweat. Characterstic pigmentation usually becomes evident in the sclera and external ear after the age of 30 years. In the eyes it is prominent between the cornea and the outer and inner canthi. Ear involvement usually starts in the concha and antihelix and later involves the tragus also. Occasionally dark-stained tendons

can be seen when the hand is made into a fist. Blue finger nails may also be noticed in some patients [1, 3, 4, 8].

Keratoelastoidosis marginalis is a rare variant of solar elastosis [7]. Long-term ultraviolet radiation exposure and chronic trauma secondary to manual labor are considered to be inciting factors. It usually presents as asymptomatic cornified hyperkeratotic yellowish papules distributed along the margins of hand and feet, an isolated finding with no other lesions else where on the body and no defect in protein metabolism.

Hyperkeratotic linearly arranged blue papules along the lateral fingers and hands have been reported in several patients with alkaptonuria [8] but to the best of our knowledge co-existence with keratoelastoidosis marginalis has not been reported earlier and needs further exploration to establish this association.

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