The Journal of Laryngology & Otology (2011), ***125***, *1059–1061.*

doi:10.1017/S0022215111001903

CLINICAL RECORD

An unusual dark pigmentation on the tympanic membrane

M SAGIT[1], M ULUDAG[2], I SAN[3]

[1]Department of Otorhinolaryngology-Head and Neck Surgery, Kayseri Training and Research Hospital, and the Departments of [2]Physical Medicine and Rehabilitation and [3]Otorhinolaryngology-Head and Neck Surgery, Faculty of Medicine, Harran University, Sanliurfa, Turkey

Abstract

Objective: To report an extremely rare case of dark pigmentation on the tympanic membrane due to alkaptonuria, and to discuss the probable association between this condition and hearing loss.

Case report: A 58-year-old man with alkaptonuria was admitted with tinnitus and hearing loss in both ears. Physical examination showed bluish-black pigmentation on the helixes of both ears and both sclerae. Otoscopic examination revealed dark discolouration of both tympanic membranes. Audiological evaluation revealed mixed high frequency hearing loss in both ears. Tympanometric examination revealed type A tympanograms bilaterally, and absence of acoustic reflexes both ipsilaterally and contralaterally. Computed tomography of the temporal bones revealed no abnormality.

Conclusion: Clinicians should consider alkaptonuria in the differential diagnosis of patients with abnormal tympanic membrane pigmentation and hearing loss.

Key words: Hearing Loss; Pigmentation; Alkaptonuria; Tympanic Membrane

Introduction

Alkaptonuria is a rare autosomal recessive metabolic disorder caused by deficiency of homogentisic acid oxidase within the tyrosine and phenylalanine degradation pathway.[1] Homogentisic acid is a metabolic product of phenylalanine and tyrosine. In patients with alkaptonuria it accumulates, polymerising to form a dark pigment that is selectively deposited in connective tissues.[2] This pigment has a high affinity for fibrillary collagens surrounded by abundant mucopolysaccharide substances, in various tissues including hyaline cartilages, intervertebral discs, skin, sclera, and the concha and helix of the ear.[3–6] However, tympanic membrane involvement has previously been described in only one case report.[7]

We report otoscopic and audiological findings for a patient with alkaptonuria, and we discuss the probable association between this condition and hearing loss.

Case report

A 58-year-old man was admitted to our department complaining of tinnitus and hearing loss in both ears for one year. The patient had no history of otological surgery, infection, trauma, otorrhoea, tympanic membrane perforation or drug use. Upon questioning, he also complained of a 10-year history of chronic, nonspecific lower back pain and stiffness. In 2005, he had been admitted to the department of physical medicine and rehabilitation for lower back pain, and had been diagnosed with alkaptonuria, with typical dark urine.

Physical examination showed bluish-black pigmentation on both sclerae and on the helixes of both ears. There was no other skin discolouration.

Otoscopic examination revealed dark discolouration of both tympanic membranes (Figures 1 and 2).

Audiological evaluation revealed mixed high frequency hearing loss in both ears.

Tympanometric examination revealed type A tympanograms bilaterally, and the absence of acoustic reflexes both ipsilaterally and contralaterally.

Computed tomography of the temporal bones showed no abnormality.

Discussion

Clinical manifestations of alkaptonuria include ochronosis and arthritis. Patients with alkaptonuria are generally asymptomatic until 30 years of age, after which ochronosis develops. The major clinical features of ochronosis relate to deposition of homogentisic acid within connective tissues: ochronotic pigment deposits are seen in connective tissue in hyaline cartilage, tendons, ligaments and muscles. Consequently, these tissues become weak, brittle, and prone to chipping, cracking and rupture, leading to rapid degeneration of the joints.[2] The condition involves large joints such as the spine, hip and knee; rarely, small joints can also be involved.[8]

The present report reveals peculiar ochronotic pigment deposition on the tympanic membrane, in addition to previously diagnosed lower back involvement. Our patient

Accepted for publication 21 February 2011 First published online 5 August 2011

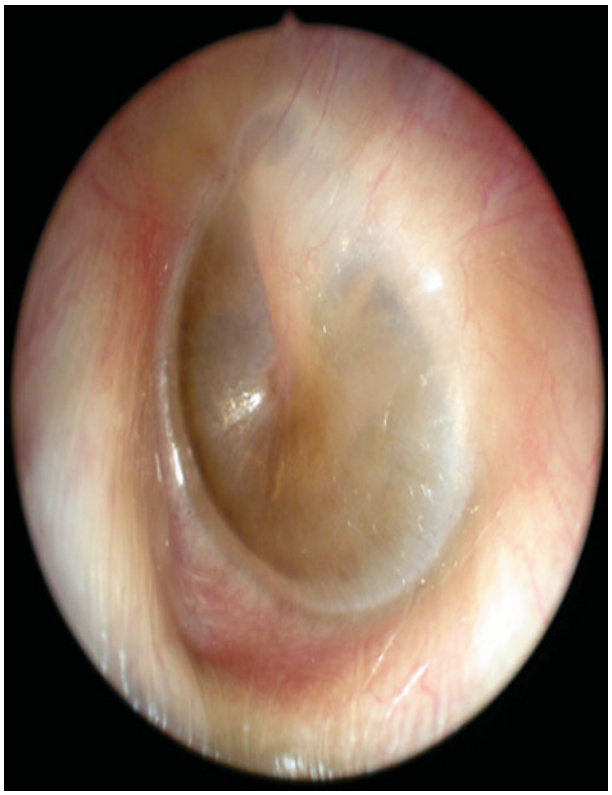

FIG. 1
Dark pigmentation on the anterior-inferior and anterior-superior part of the left tympanic membrane.

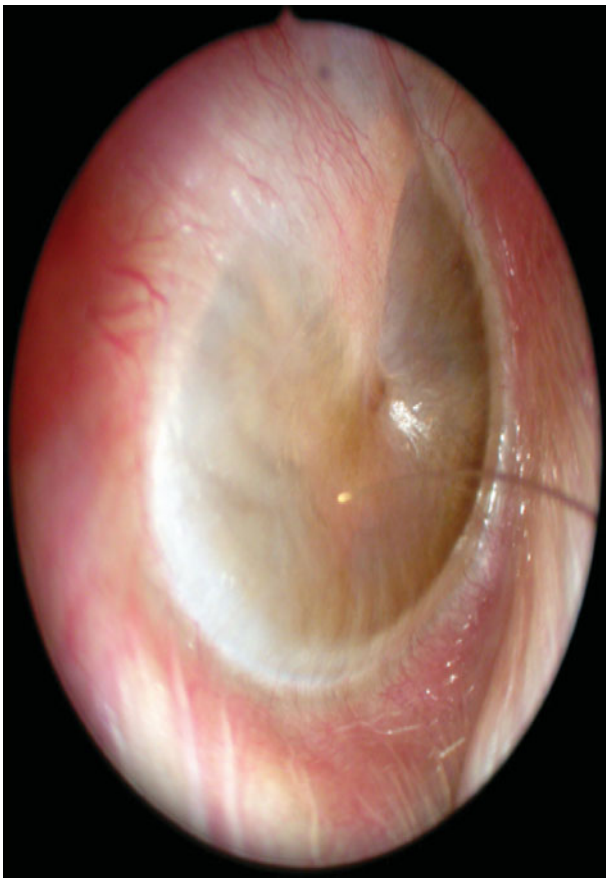

FIG. 2
Dark pigmentation on the anterior-inferior and anterior-superior part of the right tympanic membrane.

also had mixed high frequency hearing loss. The conductive component of this hearing loss would have developed as a consequence of progressive ochronotic pigment deposition and consequent altered tympanic membrane elasticity, or as a consequence of ochronotic impairment of the incudomalleolar and incudostapedial joints.

This pattern of abnormal tympanic membrane discolouration can result from a variety of causes, including haemotympanum, cholesterol granuloma, jugular bulb dehiscence, glomus tumours and prolonged drug use (e.g. minocycline).[9–13]

- **Alkaptonuria is a rare autosomal recessive metabolic disorder; homogentisic acid oxidase deficiency results in dark pigmentation of connective tissues**
- **The presented, alkaptonuric patient had dark tympanic membrane pigmentation and mixed high frequency hearing loss**
- **The conductive hearing loss component can be explained by ochronotic alteration of tympanic membrane elasticity or ossicular joint mobility**
- **Alkaptonuria should be considered in the differential diagnosis of abnormal tympanic membrane pigmentation with hearing loss**

The diagnosis of alkaptonuria is verified by detection of homogentisic acid in the urine.[14] Pigmentation of the ear auricle and sclera, and/or altered urine colour, are typical clinical manifestations and can aid diagnosis. Our patient had pigmentation of the sclerae and ear auricles, together with altered urine colour.

There is no effective treatment for alkaptonuria, although various therapeutic modalities have been employed, such as ascorbic acid, nitisonine and a low protein diet.[5] However, there is no evidence that these drugs can prevent the development of ochronosis, treat existing pigmentation, or affect bone metabolism. Currently, symptomatic treatment of alkaptonuria appears to be the sole therapeutic option.[2]

This case emphasises the fact that clinicians should consider alkaptonuria within the differential diagnosis of dark tympanic membrane pigmentation coexisting with hearing loss.

References

1 Fernandez-Canon JM, Granadino B, Beltran-Valero de Bernabe D, Renedo M, Fernandez-Ruiz E, Penalva MA *et al*. The molecular basis of alkaptonuria. *Nat Genet* 1996;**14**:19–24
2 Keller JM, Macaulay W, Nercessian OA, Jaffe IA. New developments in ochronosis: review of the literature. *Rheumatol Int* 2005;**25**:81–5
3 Hamdi N, Cooke TD, Hassan B. Ochronotic arthropathy: case report and review of literature. *Int Orthop* 1999;**23**:122–5
4 Ferreira M, Sanches M, Lobo I, Selores M. Alkaptonuric ochronosis. *Eur J Dermatol* 2007;**17**:336–7
5 Ibrahim FA, El-din Selim MM, Al-Ansari H. Ochronosis-A Review. *The Gulf J Dermatol Venereol* 2002;**9**:1–8
6 Maathuis PG, Driessen AP. Painted black. *Ann Rheum Dis* 2002; **61**:100–1
7 Pau HW. Involvement of the tympanic membrane and ear ossicle system in ochronotic alkaptonuria. *Laryngol Rhinol Otol* 1984;**63**:541–4

https://doi.org/10.1017/S0022215111001903 Published online by Cambridge University Press

8 Zhao BH, Chen BC, Shao de C, Zhang Q. Osteoarthritis? Ochronotic arthritis! A case study and review of the literature. *Knee Surg Sports Traumatol Arthrosc* 2009;**17**:778–81
9 Balatsouras DG, Dimitropoulos P, Fassolis A, Kloutsos G, Economou NC, Korres S *et al*. Bilateral spontaneous hemotympanum: case report. *Head Face Med* 2006;**2**:31 doi:10.1186/1746-160X-2-31, http://www.head-face-med.com/content/2/1/31
10 Gadre AK. Cholesterol granuloma. *Ear Nose Throat J* 2005; **84**(5):264
11 Williams J, Sharma A, Prinsley P. Bilateral jugular bulb dehiscence in achondroplasia. *Int J Pediatr Otorhinolaryngol* 2006; **1**:164–6
12 Neto ME, Vuono IM, Souza LR, Testa JR, Pizarro GU, Barros F. Tympanic paragangliomas: case reports. *Braz J Otorhinolaryngol* 2005;**71**:97–100
13 Suwannarat P, Phornphutkul C, Bernardini I, Turner M, Gahl WA. Minocycline-induced hyperpigmentation masquerading as alkaptonuria in individuals with joint pain. *Arthritis Rheum* 2004;**50**:3698–701
14 Peker E, Yonden Z, Sogut S. From darkening urine to early diagnosis of alkaptonuria. *Indian J Dermatol Venereol Leprol* 2008; **74**:700 DOI: 10.4103/0378-6323.45142

Address for correspondence:
Dr Mustafa Sagit,
Kayseri Eğitim ve Araştırma Hastanesi KBB Kliniği,
Sanayi Mah. Atatürk Bulvarı Hastane Cad. No: 78
38010 KAYSERİ/TURKEY

Fax: +90 352 320 73 13
E-mail: musagit@yahoo.com

Dr M Sagit takes responsibility for the integrity of the content of the paper
Competing interests: None declared