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اصول تنظیم قراردادها

آموزش مهارت های کاربردی در تدوین و چاپ مقاله
Werner's Syndrome

Z. Tehranchi Nia, M.D.*, Mah. Seyed Ahadi

Abstract

Werner's syndrome is a rare autosomal recessive premature aging syndrome, characterized primarily by a short stature, premature graying of the hair, hauking, and trophic ulceration of legs. Other features include scleroderma-like skin changes, beak shaped nose, high-pitched voice, stocky trunk with slender extremities, cataract, diabetes mellitus, atherosclerosis, osteoporosis, hypogonadism, and calcification of ligaments, tendons and subcutaneous tissue. A 38-year-old man patient with Werner's syndrome, presenting with ulcers of legs and plantar skin, premature canities, juvenile cataract, and atrophic skin of limbs is described.

Key words: Werner's syndrome, premature aging syndrome, atherosclerosis, juvenile cataract

Introduction

Werner's syndrome is a rare genetic disease that affects connective tissue throughout the body. The manifestations are widespread, and many organs may prematurely undergo changes usually associated with aging. The disease generally becomes apparent around puberty, with growth arrest and thinning and graying of hair. The graying rapidly becomes uniform and is sometimes associated with progressive alopecia. Most patients are of small stature and hypogonadal. Other features are scleroderma-like skin changes, high-pitched voice, cataract, and diabetes mellitus. The incidence of malignancy is high, especially soft tissue sarcoma (1,2,3).

Case report

A 38-year-old Iranian man presented with ulcerations and keratoses of legs and soles (Fig.1). The patient exhibited short stature, gray hair (Fig.2) and generalized atrophic and dry skin. He appeared older than his actual age (Fig.3). The loss of eyebrows, eyelashes and facial hair were prominent. There were sclerodermoid changes of

*Department of Dermatology, Iranian Hospit. Dubai, U.A.E.
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legs, forearms and hands. His toenails showed subungual hyperkeratosis. Both eyes showed severe degenerative changes of cornea. He had also history of operation for cataract. His voice was high pitched. The manifestations of his disease started with graying of the hair at the age of 12, followed by cataract of both eyes at the age of 15 years. His younger brother had features characteristic of Werner's syndrome. The parents were first cousins.

Laboratory investigations including complete blood count (CBC), fasting blood sugar (FBS), glucose tolerance test (GTT), cholesterol, triglycerides and liver and kidney function tests were within normal limits. X-ray studies showed osteoporosis and degenerative changes of bones of legs. Histologic examination demonstrated epidermal atrophy, sparse skin appendages and thickened dermis with fibrosis and hyalinized collagen.

Fig. 3: Premature aging and short stature

Discussion
Werner's syndrome was first described in 1964 by a German ophthalmologist Otto Werner. Werner's syndrome is a rare autosomal recessive disorder classified as one of the premature aging syndromes.

The incidence of Werner's syndrome is 1 to 2.2 cases per million people. Males and females are affected equally. Shortened stature, first evident in adolescence, is usually the initial manifestation of Werner's syndrome. Mean height is 157 cm in men and 146 cm in women. Weight is correspondingly diminished with 45kg for men and 40 kg for women. The hair becomes gray or white at a young age, and there is early thinning and loss of hair. The skin is dry and atrophic with hyperkeratotic calluses and ulcers over bony prominences. Other features include scleroderma-like skin changes, beak shaped nose, stocky trunk with slender extremities. A high pitched voice due to vocal cord atrophy, and bilateral cataract are other manifestations of the syndrome.

Up to 10% of the patients with Werner's syndrome develop malignancies. Mesenchymal neoplasms are the most common visceral malignancies, followed by adenocarcinomas. Malignant melanoma, basal cell carcinoma, bronchiolo-alveolar carcinoma, and erythro leukemia are reported with Werner's syndrome. In this case, investigations were negative for malignancy. Diabetes mellitus or impaired glucose tolerance is frequently associated with Werner's syndrome. In this patient FBS and GTT were normal. Cataract develops between the ages of 20 and 35 in most cases. In this case cataract developed at the age of 15 years.

The average life span of patients is 47 years. The causes of death are vascular diseases (myocardial or cerebrovascular) and malignancies.

Cultured fibroblasts from patients with Werner's syndrome grow poorly in culture and show diminished proliferative response to platelet-derived growth factor and fibroblast growth factor compared to normal controls. Studies of cultured fibroblasts have shown a shortened life span. Cytogenetic analysis of fibroblasts reveals chromosomal abnormalities, including variated translocation, monosomy, increased chromosomal breakage, and sister chromatin exchange.

Urinary excretion of hyaluronic acid is elevated, compared with normal controls, but total urinary glycosaminoglycan excretion is normal.

Biochemical analysis of the scleroderma-like skin has demonstrated increased levels of hexosamines, hydroxyproline, and dermatan sulfate in the dermis.

Lymphocytes from patients with Werner's syndrome show reduced natural killer cell activity irrespective of age or sex, and this may contribute to the high frequency of malignancies in these patients.

The commonest histological findings are epidermal atrophy and dermal hyalinization in scleroderma-like skin. Subcutaneous fat is replaced by dense fibrous connective tissue.
Diagnosis of Werner’s syndrome is based on the clinical symptoms and signs of the disease. This patient and his younger brother fulfilled all diagnostic criteria required of Werner’s syndrome. In this case cataract was associated with severe degenerative corneal changes. In review of the literature cataract is reported between the ages of 20 and 35 years. The occurrence of cataract of this patient at the age of 15 years is interesting.

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