Case Report

Progeria-First Case Report from Pakistan

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ABSTRACT

Progeria is characterized by premature aging and the clinical manifestations part of the well known Hutchinson-Gilford syndrome. We present the first known case of Progeria in Pakistan. (Rawal Med J 2008;33;266-267).

INTRODUCTION

The term Progeria means "prematurely old.” It has an incidence of 1 in 8 million newborns, with a slight male predominance\(^1\) (M: F ratio of 1.5:1) and a significant susceptibility for Caucasians (97% of patients).\(^2\) There have been about 100 reported cases since the
first diagnosis in 1886 by Jonathan Hutchinson. The Progeria syndrome is usually diagnosed in the first or second year of life and alters the internal systems of children to age rapidly resulting in cardiovascular, pulmonary and metabolic complications. The resulting accelerated atherosclerosis lead to premature death during the initial decades of life.

**CASE PRESENTATION**

A 6 year old girl presented to the clinic with delayed developmental milestones and failure to thrive with the classical symptoms of premature and rapid aging with short stature and low weight. There were typical senile skin changes with prominent superficial blood vessels. The head was macrocephalic and the eyes were protruding accompanied by other characteristic facial features such as a thin and beaked nose, facial hypoplasia and micrognathia with thin lips (Fig 1). She displayed light downy scalp hair with predominant alopecia, loss of eyebrows and eyelashes. A faint peri-oral cyanosis was noted with a malformed oral cavity showing crowded and discolored irregular teeth with
cavities. The skin showed diffuse scleroderma-like lesions, with irregular pigmentation; the nails were hypoplastic and brittle with yellowish discoloration. Her past history was significant for intra-uterine growth retardation, cleft palate with feeding difficulties, delayed ossification of fontanels, recurrent respiratory tract infections and oral ulcers. She developed joint stiffness along with other associated musculo-skeletal abnormalities such as osteoporosis and skeletal dysplasia of multiple bones.

**Fig.1. Typical facial features of patient.**

She had elevated serum lipid levels, anemia with anisocytosis and increased platelet count. Hyaluronic acid level was elevated in the urine and radiological examination displayed extensive
calcification in soft tissues around multiple joints. X-rays of the skull showed diastasis of the sagittal suture with numerous wormian bones and absence of certain air-filled cavities of the skull; and a hypoplastic mandible with infantile angle. Radiograph of the chest showed osteoporotic changes in the ribs and clavicles, while the spinal images showed deformed vertebrae. Images of the terminal digits revealed resorption of the bones, however, the bone age corresponded to the chronological age. The Ultrasonographic and ECG findings were normal.

DISCUSSION
This is the first reported case of Progeria in Pakistan. There are few proposed theories as to the underlying etiology of this disease, the most widely accepted of which is based on a mutation of the Lamin A gene.\textsuperscript{4} This gene regulates fibroblast function, a mutation of which results in altered splice sites resulting in fibroblasts with a truncated Lamin A. Though the majority of reported cases have shown an autosomal dominant inheritance pattern, factors such as
paternal and maternal ages have also shown to influence the inheritance of this disease. There are a few cases, however, which do not support the theory of a mutated Lamin A, including pituitary growth hormone deficiency, faults in vitamin E metabolism, and lastly, a mutation altering the regulation of decorin gene transcription.

Patients of Progeria initially present with premature and rapid aging, macrocephaly characteristic facial features and develop insulin resistance. However, the complication with the highest mortality remains the processes of arteriosclerosis and atherosclerosis. The main tools to utilize are a detailed clinical evaluation and specialized tests including routine X-rays, blood studies, DEXA scans and Cardiac studies. Persistently positive findings in all patients include elevation of blood cholesterol and phospholipids levels as well as hyaluronic acid; abnormal fibroblasts on skin histopathology; extensive lipofuscin deposition in cells; and reduced level of activity of certain primary antioxidant enzymes, such as glutathione peroxidase [GPx] and catalase. The
age at death ranges from 7 to 27.5 years, with a median age of 13.4 years.\textsuperscript{7} A few have survived until age 26.\textsuperscript{8} There is no effective treatment till to date. The only available treatment option targets a multidisciplinary approach towards symptomatic treatment and timely identification and prompt management of complications.

REFERENCES


