

Case Report

A case report of cockayne syndrome- five cases in a single family

Pooja Kondadi*, Siddalingappa Karjigi, Kallappa C. Herakal, Sreelekha Challagundla

Department of Dermatology, Venereology and Leprosy, Navodaya Medical College Hospital and Research Centre, Raichur, Karnataka, India

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*Correspondence:

Dr. Pooja Kondadi,

E-mail: pooja.kondadi@gmail.com

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ABSTRACT

Photosensitive genodermatoses are a group of disorders presenting with photosensitivity, short stature, systemic manifestations and susceptibility to malignancy these include cockayne syndrome (CS), rothmund– thomson syndrome, Trichothiodystrophy, Xeroderma pigmentosum etc. CS is a rare disorder characterized by the presence of three cardinal signs growth retardation i.e. short stature, abnormal sensitivity to light (photosensitivity), prematurely aged appearance. A 12-year-old girl had photo sensitive rash over the face with short stature. Four of her cousins (two brothers and two sisters) also had similar features. Clinical and lab investigations were suggestive of CS. Early detection and differentiating the syndrome from other congenital disorder is essential as the prognosis of each disorder differs.

Keywords: Cockayne syndrome, Photosensitivity, Congenital disorder

INTRODUCTION

Cockayne syndrome (CS) is an autosomal recessive disorder caused by defect in the repair of damaged DNA¹. CS affects both sexes equally. CS was first reported in 1946 by the British pediatrician Cockayne as “a case with a marked decrease in growth accompanied by atrophy of the optic nerve and hearing loss.”² There are no indications of ethnic or racial partiality. The incidence of CS is less than 1 in 250,000 live births in the U.S. as of 1992, about 140 cases of CS had been reported in the literature. The gene responsible for CS-type I has been mapped to chromosome 5 and is called ERCC8, and for CS-type II its mapped to chromosomal locus 10q11 and is called ERCC6. A recent study showed that two-thirds of CS cases are caused by mutations in excision-repair cross complementing group 6 (ERCC6) gene while remaining cases are caused by mutations in ERCC8 gene, although the clinical symptoms are indistinguishable.³

CASE REPORT

A 12-year-old girl presented with photosensitive rash over the malar area of the face (Figure 1).



Figure 1 (A and B): Photosensitive rash over the butterfly area of face.

Her height and weight were below the third percentile for her age. She had a history of delayed developmental milestones. On examination, the patient had photosensitive rash on face, sunken eyes, pinched nose, senile look and hearing loss. Ophthalmic examination showed corneal opacity (Figure 2). Fundoscopy revealed a “salt and pepper” type fundus. Dental examination revealed multiple caries. Patient has aphasia.



Figure 2: Corneal opacity with multiple dental caries.

Patients four cousins has same complaints except one among them did not have hearing loss (Figure 4). Skin biopsy of the affected area revealed non-specific histological findings. Haematological investigations are within normal range. X-ray showed thickened skull. CT scan revealed calcification of basal ganglia and other structures. MRI showed atrophy and demyelination of the cerebrum and cerebellum. On the basis of history, clinical examination and laboratory investigations, we diagnosed this case as CS.



Figure 3: Patients four cousins with similar complaints.

DISCUSSION

CS also called Neill-Dingwall syndrome, is a rare form of dwarfism. It is an inherited disorder whose diagnosis

depends on the presence of three signs growth retardation, photosensitivity, progeria. Symptoms of photosensitivity start to occur around six months after birth.⁴ Almost all patients with CS over 2 years of age have microcephaly, cachectic dwarfism, cataracts and loss of subcutaneous fat.^{5,6}

In the classical form of (CS type I) the symptoms are progressive and seen after the age of one year. An early onset or congenital form (CS type II) is apparent at birth. CS type III (CS type III), that presents later in the child's development and is generally a milder form of the disease. A fourth form, now recognized as xeroderma pigmentosa-cockayne syndrome (XP-CS), combines features of both of these disorders.

The symptoms of all forms of CS are similar. The age of onset defines the type.

CS type I is characterized by a normal appearing newborn whose symptoms may become apparent after the first year. Height, weight and other indicators of size and growth are within the 5th percentile. Vision, hearing, and nervous system functioning (central and peripheral) gets worse over time and severe disability may result.

The few reported cases of congenital CS type II are characterized by growth failure at birth along with little or no neurological development after birth. Serious visual impairments are usually present at birth. Early skeletal aberrations occur as well. It is likely that CS type II includes some patients previously diagnosed with cerebro-oculo-facial syndrome (COFS) and pena-shokeir type II syndrome due to the identification of a common gene defect in these patients.

CS type III is rarer and is characterized by essentially normal growth and mental development during the early years but interrupted by the late onset typical symptoms of CS.

XP-CS is the rarest form and includes the features of both diseases. Widespread freckling and early skin cancers and short stature, mental retardation and sexual underdevelopment are seen.

Children with CS have unusual distinctive facies due to prognathism, large malformed ears, enophthalmos, prominently beaked nose, and microcephaly, due to which a wizened appearance is seen. There may be congenital absence of few permanent teeth, an unusual amount of dental decay due to the abnormal placement of the teeth, delayed eruption of the primary teeth, partial macrodontia and caries. Affected individuals have limbs disproportionate to body size. Joints may be abnormally large, flexed with kyphosis.

Other symptoms of CS may include cyanosis of arms and legs, which may feel cold on touch, hypohidrosis, decreased lacrimation, and premature graying of hair.

Neurological symptoms may include tremors and ataxia. CS is characterized by both failure of brain development and loss of brain volume, attributable in part to progressive leukoencephalopathy, and calcified leptomeningeal vessels.^{7,8} Affected children may experience varying degrees of mental retardation, partial loss of hearing, and progressive loss of previously acquired intellectual abilities. Mental deficiency undoubtedly potentiates the effects of hearing loss, and both contribute to the severe disorder of communication in this condition.⁹

The ocular symptoms may include cataracts, optic atrophy, degeneration of the retina, abnormal retinal pigmentation, salt and pepper type of fundus.

Some people with CS may also have hypertension, hepatomegaly and arteriosclerotic disease. Adults may be sexually under developed.

Photosensitivity is due to failure of repair of damaged DNA, caused due to ultraviolet rays.

It is likely, that some of the genes which cause CS are also involved in protein synthesis, and hence clinical signs of CS are due to the production and accumulation of abnormal proteins in the cell.

If both the parents have defective gene 25% may be affected and 50% may be carriers with each pregnancy. The risk is equal for males and females.

The treatment of CS is symptomatic and supportive. Specialized imaging testing (MRI) may demonstrate the loss of the fatty covering (demyelination) on some nerve fibers in the brain.

Establishing an unequivocal diagnosis in CS is important for proper management of the patient, to empower families in caring for affected individuals, and to provide accurate genetic counseling to parents and siblings.¹⁰ Definitive diagnosis of CS can be done by DNA repair assay or molecular testing.

A supportive team approach including special education, physical therapy, medical, social, vocational services and genetic counseling should be done to parents.

CONCLUSION

Based on a detailed history, clinical examination, lab investigations we have arrived at a conclusion that these are cases of CS.

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