

Case report

A family with xeroderma pigmentosum-Cockayne syndrome complex.

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Abstract Xeroderma pigmentosum-Cockayne syndrome complex is the coexistence of two genodermatoses, xeroderma pigmentosum (XP) and Cockayne syndrome (CS) in one patient. The patients of this syndrome present with photosensitivity, freckling on sun-exposed skin, loss of subcutaneous fat from face, prominent ears, dwarfism, microcephaly, mental retardation or other neurological and eye abnormalities. Many similar cases with additional features have been reported in foreign literature. We describe 3 cases of this syndrome along with review of literature.

Introduction

Xeroderma pigmentosum-Cockayne syndrome complex is one of the genodermatoses including photosensitivity, freckling, ocular defects, disproportionately large hands, feet and ears, microcephaly, mental retardation and other neurological abnormalities.^{1,2} Photosensitivity with neurological abnormalities of variable severity can occur in various genodermatoses like xeroderma pigmentosum (XP) and its variants, Cockayne syndrome (CS), trichothiodystrophy and Hartnup disease.¹⁻³ Other differential diagnoses include Bloom's syndrome and progeria.^{1,2,3} In many of these the underlying molecular defects have been demonstrated. These include nucleotide excision repair defects, reduced unscheduled DNA synthesis and increased chromatid exchange.^{2,4} The diagnosis of this group of diseases in our part of the work is based on clinical

features due to lack of facilities for genetic studies. We describe, for the first time, 3 cases who have both the features of xeroderma pigmentosum and Cockayne syndrome.

Case report

Three brothers of ages 12, 7 and 2 years presented at the out-patient department of Paediatric Medicine, Mayo Hospital, Lahore in September 2001 with a history of photosensitivity and black-brown pigmented spots on face and other exposed parts with redness and soreness of eyes. The children were born to a consanguineous couple after an uneventful pregnancy and labour. They were normal at birth and the symptoms began at ages 9, 12 and 17 months, respectively. They developed black-brown pigmented spots and scaly lesions over their faces and back of hands after sun exposure. Their complexion gradually became dark and skin became dry. Two of them also had excessive lacrimation and redness of eyes. The symptoms used to exacerbate particularly during hot weather and febrile illnesses. They also developed anorexia, weight loss and thinning out of nose

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Figure 1 Dry scaly, freckling, atrophy involving face in a butterfly distribution, prominent ears and premature senile appearance.



Figure 2 Long lower extremities with genu valgum.

However, there was no complaint of seizures or hearing deficit in our patients. They remained underweight as compared to their peers. They attained normal motor

milestones but cognitive functions were impaired and the eldest child was the student of class one. They had progressively increasing difficulty in walking with tremulous movements of hands especially when performing any task. Another sibling with similar skin lesion had died at the age of 11 months due to unknown reasons while other family members did not suffer from similar illness.

Physical examination revealed three thin built, anxious looking boys with short stature. They had dry, scaly skin and freckling involving face in a butterfly distribution (**Figure 1**). They had pinched nose, atrophy of the facial skin, loss of subcutaneous fat and prematurely senile appearance. There were no vesiculobullous, eczematous or telangiectatic lesions seen in our patients. Similarly, there were no cutaneous lesions suggestive of malignant transformation. Heights of all three children were less than 5th percentile. Hands and feet were relatively large. Lower limbs were disproportionately long as compared to the trunk in the eldest child (**Figure 2**) while younger children were normal. Ears were relatively large while hair, nails and mucous membranes were normal. They also had carious teeth and skeletal abnormalities which included restriction of knee joint movements with lumbar lordosis and genu valgum (**Figure 2**).

Neurological examination revealed broad-based gait and spasticity, pointing a defect in cerebellum. Other cerebellar signs included intention tremors, past pointing and incoordination. Deep tendon reflexes in the lower limbs were exaggerated with up going plantars. However, there was no nystagmus, choreoathetosis or ataxia in our patients. Photophobia was found in all

the three patients while keratitis was noted in one patient. Hearing was found to be normal. Psychiatric analysis showed lower IQ in all the three patients. Their mental age was assessed to be 6, 4 and 1 year, respectively on portage guide.

Laboratory investigations showed no abnormality. EEG was also normal while CT scan of brain in eldest child showed foci of calcification at basal ganglia. Nucleotide excision repair, unscheduled DNA synthesis and complementation assay studies could not be performed due to unavailability.

Discussion

Cockayne syndrome, first described by a British pediatrician in 1936, is a rare autosomal recessive degenerative disease with cutaneous, ocular and neurological abnormalities.³ The syndrome has classical and non-classical types.⁴ One of the non-classical variety has features of both XP and CS and a number of cases have been reported.^{4,5} The disease usually starts during the second year of life with slowly progressive neurological degeneration, intellectual impairment, deafness, peripheral neuropathy, normal pressure hydrocephalus and microcephaly.¹

The cutaneous findings seen in our patients included photosensitivity with pigmentary abnormalities as seen in XP.¹ A thin nose, large hands and feet with larger lower limbs as compared to trunk are conspicuous of CS.^{1,4} Ocular abnormalities included photophobia in all cases and keratitis in one child, the findings being present in both syndromes while the characteristic 'salt and pepper' appearance of retina, cataract and optic atrophy present in CS were not seen in our cases.^{4,6} We did not find any lesion suggestive of malignant change in our

cases similar to CS in which there is no increase in the incidence of neoplasia.^{1,3} Hypereflexia in lower limbs of our cases is a useful diagnostic feature of CS rather than XP.^{2,5} Although our patients were mentally retarded and had photosensitivity, there were no hair and nail changes, ichthyosis or pellagra-like skin manifestations. Hence the diagnosis of trichothiodystrophy and Hartnup disease were not considered. Dwarfism and premature senile appearance are also features of progeria but photosensitivity, disproportionately large extremities, normal hair and demyelination are not present in cases of progeria. In Bloom's syndrome, the erythema of face and hands is associated with growth retardation, but mental development is normal.

Poor cognition, spasticity, incoordination and upper motor neuron signs in the lower limbs indicate central and peripheral demyelination, the signs of CS.^{5,6} Confirmation of the diagnosis by assay of DNA repair in skin fibroblasts, protein complementation studies and molecular genetic testing of the two genes (ERCC6, ERCC8) could not be done due to lack of facility. The final diagnosis of XP-CS complex could only be made on clinical background. They were prescribed topical sun screen lotions with advice to avoid sunlight. Currently, the patients are under observation with continued treatment.

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