Cockayne Syndrome: A Rare Case Report

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ABSTRACT

Cockayne syndrome (CS) is an autosomal recessive neurological disease caused by defects in DNA repair characterized by progressive cachectic dwarfism, progressive intellectual disability with cerebral leukodystrophy, microcephaly, progressive pigmentary retinopathy, sensorineural deafness, photosensitivity and possibly orofacial and dental anomalies. It is a very rare clinical entity and so far only about 150 cases have been reported in the literature. We report a 3 year old child who was diagnosed as Cockayne syndrome, based on clinical, ophthalmic and radiological findings.

KEYWORDS: Cockayne syndrome, Neill-Dingwall Syndrome

INTRODUCTION

Cockayne syndrome(also called Weber-Cockayne Syndrome or Neill-Dingwall Syndrome) is a rare autosomal recessive degenerative disease with cutaneous, ocular, neurologic and somatic abnormalities. The entity was first described in 1936 by Cockayne. Till now around 150 cases have been reported in the literature [1]. The incidence in Western Europe has been evaluated as 2.7 per million births [2].

3 clinically different classes of CS have been distinguished: A classical form (CS I) which includes the majority of patients, a severe form (CS II) characterized by early onset and severe progression of manifestations and a mild form, typified by late onset and slow progression of disease. Classical CS patients show (a) growth failure, (b) neurodevelopmental delay and neurological dysfunction, (c) cutaneous photosensitivity, (d) progressive ocular abnormalities (pigmentary retinopathy, cataract), (e) hearing loss, (f) dental caries, (g) characteristic wizened facial appearance: bird-like facies. Intracranial calcifications are seen in some individuals. For diagnosis of CS in an infant, the presence of the first two criteria and a few of the other five criteria are required[3].

Mutations in two genes are known to cause Cockayne syndrome:

a) ERCC6. Mutations in ERCC6 cause Cockayne syndrome complementation group type B (CSB), which accounts for 65% of cases[4,5].

b) ERCC8 (previously known as CKNI). Mutations in ERCC8 cause Cockayne syndrome complementation group type A (CSA), which accounts for 35% of cases[6].

Ocular involvement in CS includes pigmentary retinopathy, enophthalmos, strabismus, amblyopia, cataract, optic atrophy, nystagmus, corneal lesions, band keratopathy, recurrent erosions, and poor pupillary response to dilating agents. The pigmentary changes in the retina are fine, involve the periphery, and have been seen in older patients. Visual acuity is often preserved in spite of significant retinal changes and optic atrophy [7].

CASE REPORT

A 3 year old male child was brought to our hospital with history of developmental delay and photosensitive rash over the face since two years. He is the first born and only child of young and otherwise healthy consanguineous parents. The antenatal, intranatal and postnatal periods were unremarkable and the child weighed three kgs at birth. The child had received antitubercular treatment for Primary complex at 18 months of age.

On examination, the weight of the child was 8 kgs, height 81 cms( both <5th percentile for the age). The child had delayed developmental milestones, microcephaly(head circumference 41 cms, < 5th percentile for the age), thin and sparse hair, sunken eyes, prominent nose and ears and hyperpigmented, photosensitive, butterfly-shaped rash in the malar area. (Fig 1.) Cardiovascular, respiratory and per abdominal examination was normal. Examination of the
motor system revealed spasticity, decreased power and exaggerated deep tendon reflexes of both lower limbs.

Fig 1: Characteristic facies and photosensitive malar rash

On ocular examination, the child was orthophoric and was able to fix and follow light. Anterior segment was normal except for enophthalmos and poor pupillary dilatation to cycloplegics. Posterior segment examination showed bilaterally pale optic discs, narrowed arterioles and generalised pallor of the background retina. (Fig 2.) The child was diagnosed to have partial optic atrophy. His dental and ENT examination were normal.

Fig 2: Showing optic disc pallor in right eye and left eye.

Non contrast CT Scan of the brain showed symmetric calcification of bilateral basal ganglia (Fig 3.) generalised cerebral and cerebellar atrophy, curvilinear calcifications at the sulcal depths involving the frontal, parietal and occipital lobes and bilateral paucity of white matter.

Fig 3. CT Scan of the brain showing Bilateral basal ganglia and parenchymal calcification, diffuse cerebral atrophy and ex vacuo hydrocephalus
The parents of the child have been explained the use of sunscreens for the child, oral vitamin A therapy, physiotherapy to prevent contractures and good dental care.

The parents of the child have been counselled about the possibility of recurrence of the condition in the siblings of the child.

DISCUSSION

In summary, a 3-year old boy, a product of consanguineous marriage was diagnosed clinically as a case of Cockayne syndrome because of delayed milestones, spastic paraplegia, dwarfism, ocular fundus changes, typical facies and a photosensitive rash on the butterfly area of the face. A diagnosis of CS was suspected based on the clinical features, neurological, ocular and dermatological signs. CT Scan assisted in the diagnosis, but the definitive diagnosis of CS is by molecular genetic testing or a specific DNA repair assay on fibroblasts [6,8]. Cockayne syndrome has to be differentiated from other conditions having similar clinical features. [Table.1] highlights the conditions to be considered and their differentiating features.

Table 1. Differential diagnosis of Cockayne Syndrome [9]

<table>
<thead>
<tr>
<th>Features</th>
<th>Cockayne Syndrome</th>
<th>Xeroderma Pigmentosum</th>
<th>Bloom’s Syndrome</th>
</tr>
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<tbody>
<tr>
<td>Short stature</td>
<td>+</td>
<td>+</td>
<td>+</td>
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<tr>
<td>Delayed development</td>
<td>+</td>
<td>+/-</td>
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<tr>
<td>Photosensitivity</td>
<td>+</td>
<td>+</td>
<td>+</td>
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<tr>
<td>Unusual facies</td>
<td>+</td>
<td>-</td>
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<tr>
<td>Microcephaly</td>
<td>+</td>
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<tr>
<td>Optic atrophy</td>
<td>+</td>
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<tr>
<td>Retinal degeneration</td>
<td>+</td>
<td>-</td>
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<tr>
<td>Basal ganglia calcification</td>
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The treatment for CS is essentially supportive care. Despite the lack of effective treatment and progressive course of the disease, a correct diagnosis is very important to assist the family with the caretaking of the child and genetic counselling should be done to prevent recurrence of the condition in the family.

REFERENCES


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