Case report

Cockayne syndrome: picture story

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Introduction

Cockayne syndrome is a rare autosomal recessive neurodegenerative disorder with multisystem involvement, described by Edward Alfred Cockayne in 1936[1]. It is caused by a defect in DNA repair system. There are two gene mutations reported; *ERCC6* in 65% of individuals and *ERCC8* in 35%. It is characterized by progeria, cachectic dwarfism, progressive intellectual disability with leukodystrophy, photosensivity, sensorineural deafness and progressive pigmentary retinopathy[2].

We report a 12-year-old boy diagnosed with this rare syndrome, based on clinical, ophthalmological and radiological features.

Case report

A 12-year-old male child was evaluated for progressive difficulty in walking due to unsteadiness. He is the third child of second degree consanguineous parents with unremarkable family history of any neurological disorder. Antenatal, birth and neonatal history were uneventful. However, his birth weight was only 1.8 kg. Since birth his growth was significantly affected in spite of normal nutrition and absence of any systemic illness. His development was globally affected since birth; only mildly initially. The signs of unsteadiness of gait with tremor around 6 years of life were the first clinical signs noticed by the parents. This progressively worsened over the years with significant impairment of manual functions such as feeding and writing due to the tremor. Later he was noted to have a dysarthria. Appearance of lentigines over the sun exposed areas of his face was noted around 6 years which also gradually increased in number. Though he commenced school in main stream he had to be moved to special education.

He presented to us at 12 years, at which point appeared as a progeric and examination revealed a cachectic dwarf. All his growth parameters were well below third centile. The examination of face revealed a small skull with large sunken eyes, a beaked nose, large prominent ears, relatively small mandible, dental crowding, evidence of cutaneous photosensitivity and dry scaly skin with facial lentigenes (Figure 1). His neurological examination revealed cerebellar signs. He was hypotonic with muscle power of grade 4 and normal reflexes. His cognitive function at current age of 12 years was compatible to that of 6 years according to the TONI 3 (Test of nonverbal intelligence). Eye examination revealed a pigmentary retinopathy, bilateral pale discs, poorly defined fovea ([Figure 2) and a refractive error. Other system examination was normal.

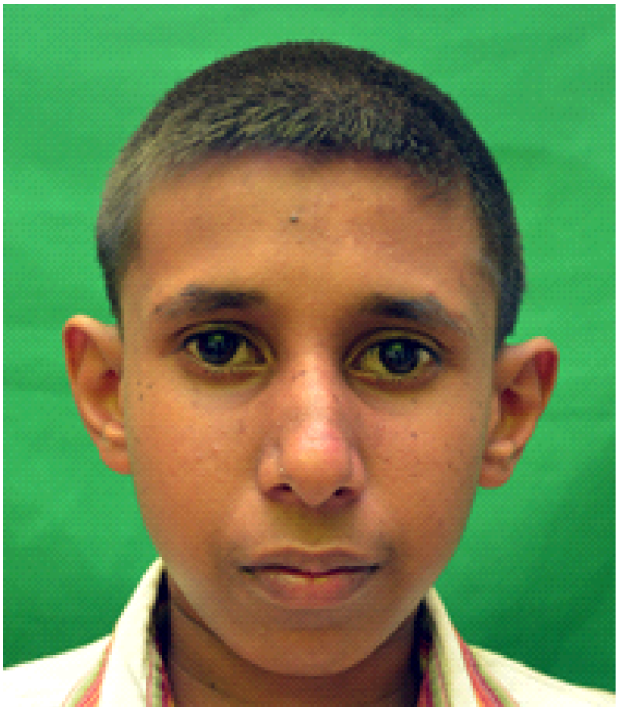

Figure 1. Characteristic facial appearence

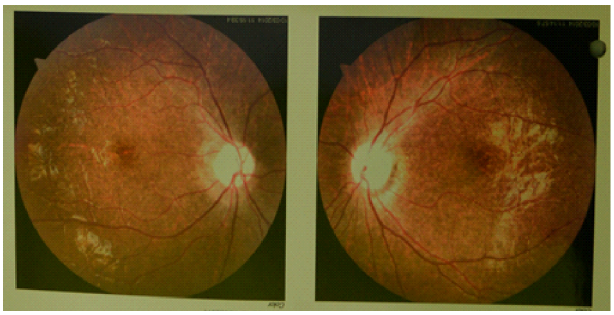

Figure 2. Fundal photograph showing pigmentary retinopathy

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Basic investigation revealed elevated liver enzymes with normal fasting blood sugar and renal functions. Computerized tomography (CT) showed evidence of bilateral basal ganglia calcification ([Figure 3) and his magnetic resonance imaging (MRI) brain showed evidence of early leukodystrophy characterized by T2 and flair hyperintensities in the white matter and cerebral and cerebellar atrophy (Figure 4). Audiogram and renal ultra-sonogram were normal.

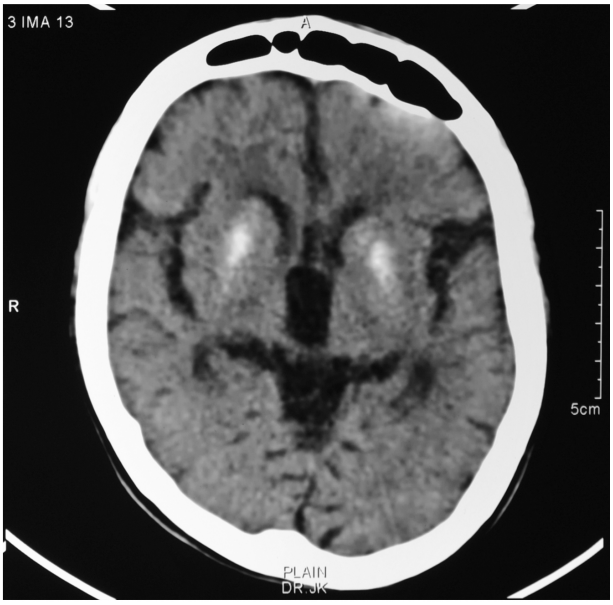

Figure 3. CT showing bilateral basal ganglia calcification

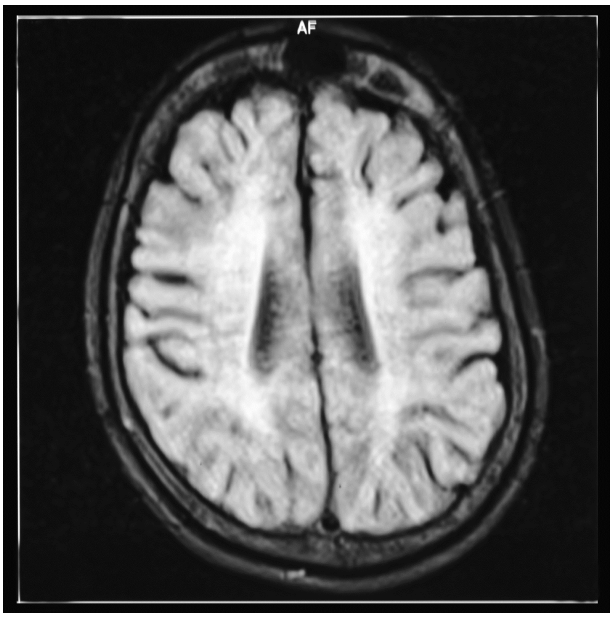

Figure 4. MRI T2 flair showing leucodystrophy

Discussion

Cockayne syndrome is a rare condition with a variable age of onset and rate of progression[2]. The degeneration begins in the second or third year of life. The mean age of death in reported cases is 12 years and three months[5]. The phenotypic spectrum of Cockayne syndrome can be divided into four general clinical presentations: Type 1 (intermediate/ classic form), Type 2 (severe early onset form), Type 3 (mild/ atypical form) and Type 4 (adult form)[6]. CS type I which is characterized by postnatal growth failure with early developmental delay, followed by progressive behavioral and intellectual deterioration is the most likely spectrum in this child. Premature aging is the cardinal feature and is due to defect in DNA repair system. Characteristic cutaneous findings include photosensitivity, thin skin, dry scaly skin and thin dry hair. Ophthalmologic changes are pigmentary degeneration of the retina (pepper and salt appearance); the hallmark of the disease and cataracts, optic atrophy or optic disk pallor[2,6]. Most patients have mild to moderate sensory neural hearing loss.

Neurocognitive decline with variable onset is due to pericapillary calcifications in the cortex and basal ganglia at an early age, severe neuronal loss in the cerebral cortex and cerebellum, leukodystrophy and demyelinating neuropathy[4,6]. These changes correlate with the physiologic changes of aging. Characteristic neurological findings are increased or decreased muscle tone and reflexes, unusual gait resulting from leg spasticity, ataxia, and contractures of the hips, knees, and ankles.

Less frequently found symptoms in Cockayne syndrome include major structural anomalies of the renal system, cryptorchidism or testicular hypoplasia, delayed puberty, irregular menstrual cycles, arteriosclerotic disease, hepatomegaly and hypertension. Our patient did not have any of these.

There is no definite treatment for Cockayne syndrome[6,2]. However, physical therapies, sunscreen, avoiding excessive sun exposure, hearing aid, visual aid, gastrostomy tube feeding, psychological therapy and genetic counseling are some important aspects in the management.

Conclusion

The characteristic facial features, cachectic progeric dwarfism, microcephaly, intellectual disability, cerebellar signs, photosensitivity, pigmentary retinopathy, characteristic CT and MRI findings lead us to the diagnosis of Cockayne syndrome in this child.

References

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