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Cockayne Syndrome

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Abstract
Cockayne syndrome is one of the rare genetic disorders. The pattern of inheritance is autosomal recessive. The characteristic features of cockayne syndrome include short stature, pigmentary retinopathy, birdlikefacies, poor weight gain, microcephaly and photosensitivity. Associated features may include deafness, dental decay and neurological abnormalities. Cockayne syndrome have 3 subtypes, Type I or classical form is characterized by early onset symptoms (usually within 1-2 years) and type II is severe form of disease and signs and symptoms are usually present at birth it's also called pena-Shokeir syndrome. The mildest variety of cockayne syndrome is type III in which the symptoms are mild and usually present later in childhood. We present here a case of 7 year old female child who was admitted to us with complaints of non attainment of motor milestones like standing or walking and decrease vision and hearing since 2-3 years. The characteristic facies, microcephaly, bat like ears, dwarfism, photosensitivity and bilateral optic atrophy lead us to the diagnosis of cockayne syndrome.
Keywords: *Cockayne syndrome, neuroregression, photosensitivity, bat like ears*

Introduction

Cockayne syndrome is an autosomal recessive disorder usually characterized by facial erythema in a butterfly distribution after sun exposure, followed by loss of adipose tissue and development of thin, atrophic, hyperpigmented skin, particularly over the face. Associated features include dwarfism, mental retardation, large protuberant ears, long limbs, disproportion-ately large hands and feet, which are sometimes cold and cyanotic, pinched nose, carious teeth, unsteady gait with tremor, limitation of joint mobility, progressive deafness, cataracts, blepharoconjunctivitis, retinal degeneration, optic atrophy, decreased sweating and premature graying of the hair[1]. Diffuse extensive demyelination of the peripheral and central nervous systems ensues, and patients generally die of athermanous vascular disease before the third decade[2]

We describe here a case of Type I Cockayne syndrome in which the manifestations started in between 1 to 2 years of age. The patient presented with characteristic facies, developmental delay (inability to stand or walk) and regression of milestones (loss of vision and hearing) on examination there was microcephaly, dwarfism, bat like ears, bilateral equinous deformity of legs and diffuse loss of adipose tissues. The characteristic features and the fact that it presented

in between 1-2 years of age led us to the diagnosis of classical or type i Cockayne syndrome.

Case report

A 7 year old female child, first by order of birth was brought with complaints of inability to stand and walk since 1-2 years of age. Also there was history of reduced vision and hearing since 2-3 years. For these complaints patient was taken to many general practitioners and was investigated and treated for rickets on multiple occasions in the past. Meanwhile because the patient didn't respond to any type of treatment he was also given homeopathic treatment intermittently. Despite all these efforts she has not shown any improvement. Later she was referred to this hospital for further evaluation and management.

On admission the patient was haemodynamically stable. Clinical examination revealed dwarfism, cachexia, microcephaly and mental retardation (IQ 50%) Characteristic facial features like large protrubent ears, beaked nose, hyperpigmented skin, relatively small mandible, dental caries, equinous deformity of legs and contractures of joints with decreased joint mobility were strikingly present.

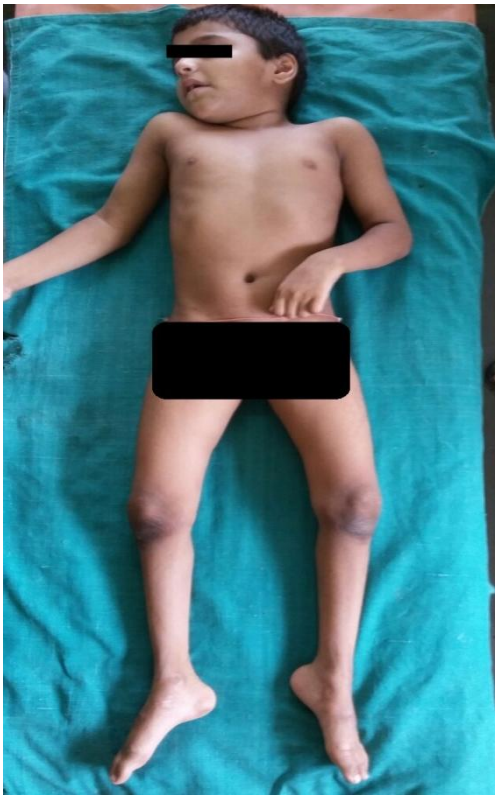

Fig 1: Characteristic features of Cockayne syndrome: large protrubent ears, beaked nose, small mandible long limbs, absence of subcutaneous fat, contractures of joints of upper limbs and equinous deformity of legs.

An ophthalmological and ENT consultation was done in view of complaints of decreased vision and deafness. EEG was done which was normal. MRI findings were significant and showed bilateral optic atrophy.

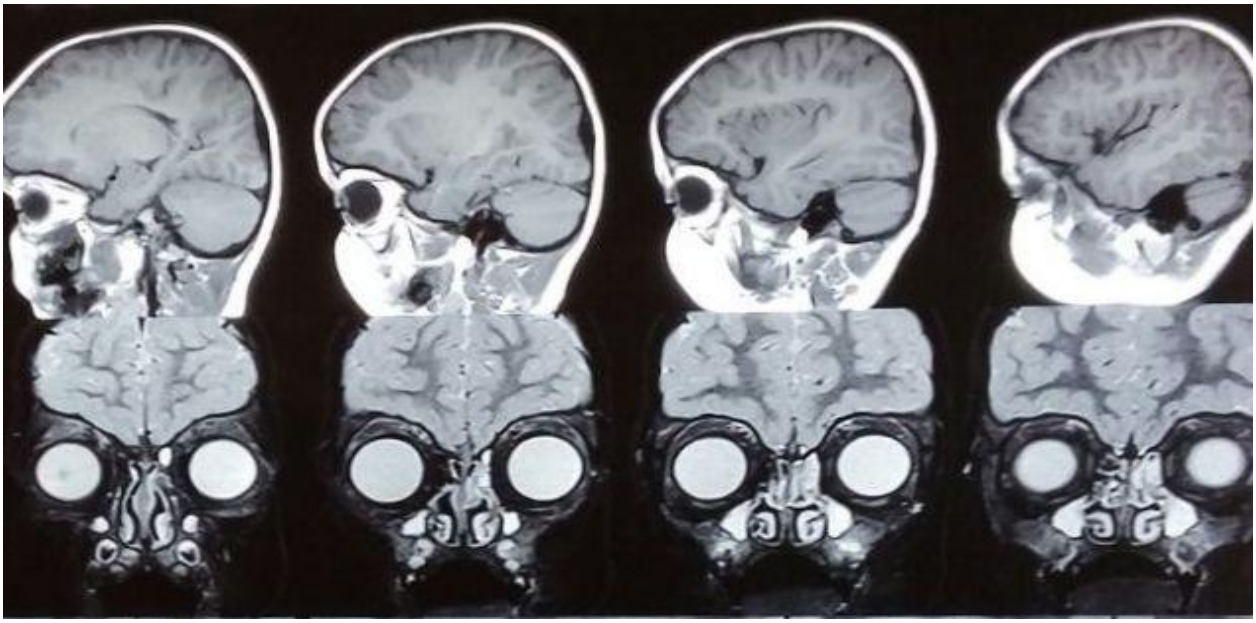

Fig 2 : MRI Brain revealed bilateral optic atrophy.

Electromyography was normal. In view of dysmorphic facies karyotyping was done which was normal. Characterstic facial features, cachexia, dwarfism, developmental delay and regression of milestones along with mental retardation led us to the diagnosis of cockayne syndrome. The age of presentation completed the diagnosis to be Cockayne syndrome type I.

Discussion

Cockayne syndrome is a rare autosomal recessive disorder. 2 types of genes, CSA and CSB, are responsible for CS[3]. Photosensitivity seen in CS is due to impaired repair of UV-induced DNA damage[4].

There are 3 known types of Cockayne Syndrome

Type I or classical Cockayne syndrome is characterized by normal prenatal growth. Developmental abnormalities start manifesting within first 2 years of life. The patients universally have dwarfism, failure to thrive and microcephaly. Neurological abnormalities may present as ataxia, deafness and blindness. The quality of life is seriously affected by neuroregression and death usually occurs in first or second decade[5].

Type II is most severe form of Cockayne syndrome and also called cerebrooculo-facioskeletal syndrome (COFS) or Pena-Shokeir syndrome type II. This form of CS presents with severe affection since birth. Affected children have severe form of skeletal deformities like kyphoscoliosis. Structural abnormalities of eyes and cataracts may be present. This type of CS is characterized by no or very little neurological development since birth. Life span is severely affected and death usually occurs within 1st decade[5].

Type III is the mildest form of CS and usually doesn't have growth or cognitive developmental abnormalities. Though early senility is also a feature of Cockayne syndrome it is usually distinguished from progeria by presence of ocular abnormalities and photosensitivity in Cockayne syndrome[5].

All patients of CS present with dwarfism[6]. There is usually history of inability to walk, ataxia or unsteady gait. Some authors have reported it to be associated with demyelinating peripheral neuropathy and pathological lesions consisting of neuronal and myelin loss with deposits of calcium and iron about the vessels in the cerebellum, basal ganglia and cerebrum[7]. The dermatological finding typical of CS is a photosensitive rash which characteristically heals with atrophic scarring. There is diffuse loss of subcutaneous tissue. Morphological features include dwarfism, large, protuberant ears, long limbs, disproportionately large hands and feet, which are sometimes cold and cyanotic, pinched nose, carious teeth, limitation of joint mobility and premature graying of the hair. In later stages of CS diffuse extensive demyelination of the peripheral and central nervous systems ensues, and patients generally die of atheromatous vascular disease. Sometimes Cockayne syndrome is associated with Nephrotic syndrome[8]. The life span depends upon the type of CS with type II being most lethal to type III being mildest form[9].

As there is no cure as of now for CS management usually is supportive and treatment of associated conditions and prevention of complications. Photoprotection with sunscreen and clothing is recommended to prevent or reduce photosensitivity. Hearing loss needs a prompt referral to ENT for further evaluation and management in the form of cochlear implants[10] or speech therapy depending upon the severity of loss of hearing. Since CS is a disease of early senility many diseases of advanced age like diabetes mellitus, renal impairment and cardiac ischemia needs to be detected and treated early in time[11]. Other referrals which may be needed are dental, occupational therapy and physiotherapy. Ophthalmological consultation for decreased vision may also be needed.

Conclusion

Cockayne Syndrome should be suspected in any child with characteristic facial features along with photosensitivity and developmental delay. Early

senility associated with CS requires the treating pediatrician to be vigilant to detect the diseases like diabetes mellitus and renal failure in these patients. Associated features like dental caries, hearing and visual impairment and mental retardation needs referral to respective specialities. As CS is incurable the essential part of management is supportive and prevention of complications. Another important aspect is prevention of recurrence of CS in other sibling. Identification of gene defects involved makes it possible to offer genetic counseling and antenatal diagnostic testing to the parents who already have one affected child.

Conflict of interest: None

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