COCKAYNE SYNDROME: REPORT OF TWO CASES WITHIN A FAMILY

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Abstract - The clinical and phenotypic features of two siblings (a 12 years old girl and her 7 year old brother) with Cockayne syndrome are described. The main problems were mild to moderate mental retardation, dwarfism, clumsy gait, photosensitive skin lesions and progeroid (senile like) appearance. Brain CT - scans revealed symmetrical, well defined areas of calcification mainly located at lenticular nuclei, in both patients. The brainstem auditory responses also showed increased hearing thresholds and absolute wave latencies. that were more prominent in the older sister. The older patient had a healthy twin sister with normal mental function and phenotypic appearance. Acta Medica Iranica 37 (2): 115 - 118; 1999

Key words: Cockayne syndrome, mental retardation, photosensitive skin lesions, progeroid appearance, basal ganglia calcifications, brainstem auditory evoked potentials

INTRODUCTION

Cockayne reported this disorder in siblings in 1946 for the first time. Thereafter more than 150 cases have been reported. This rare syndrome is transmitted as an autosomal recessive trait. A defect in DNA metabolism has been documented in fibroblasts that involves increased sensitivity of cells to ultraviolet light, decreased RNA synthesis following UV exposure and normal excision repair. Main clinical features are senile (progeroid) changes beginning in infancy, retinal degeneration, impaired hearing and photosensi - tivity of thin skin (1). There may be additional features such as growth deficiency with early loss of adipose tissue, mental retardation, clumsy gait, tremor and other abnormal movements, corneal opacity, cataract, small cranium and large calvarium, loss of facial adipose tissue with slender beak - like nose, moderately sunken eyes, cool hands and feet, sometimes cyanotic extremities (1), intracranial calcifications especially in the basal ganglia in brain CT-scan (1,2,3,4), hypersignal intensity areas distributed through cerebral white matter revealed by brain MRI (1,2,3,4), abnormal waves in brainstem auditory evoked potentials (5). Peripheral neuropathy has also been reported as a rare presenting feature of Cockayne syndrome (6). Although prenatal growth deficiency has occasionally been documented, only one case has been reported in the neonatal period (7). Growth and development usually proceed at a normal rate in early infancy and it is not until two to four years of age that the pattern of defect is clearly evident (1). Prognosis is not favorable in the affected patients. The progressive course of disease finally leads to functional disability and the patient becomes bed ridden at the end of the second decade of life. Death usually occurs due to respiratory and other infections (1).

Case

Two siblings (a 12 years old girl and her 7 years old brother) were referred because of low academic achievements and unsteady gait (Fig. 1). Their parents were first cousins and the other three offsprings were quite well. The older affected sibling had a normal phenotypic twin sister with good psychomotor development (Fig. 2). She weighed 36kg and had a head circumference of 53cm. She had finished only the first grade and could not continue primary school. On neurologic examination both patients had ataxic gait with some extrapyramidal signs like coarse tremor, titubation and mild choreic movements. The neurologic findings were more prominent in the older sister. Mental state was normal according to their mental ages. Language and speech were compatible with mental ages of

Fig. 1. The affected siblings.

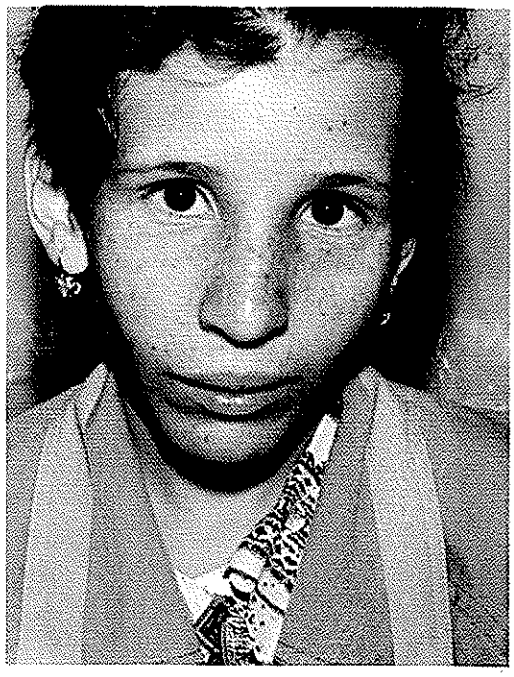

Fig 3. The older affected sister

Fig. 2. The normal twin sister in comparison with affected twin.

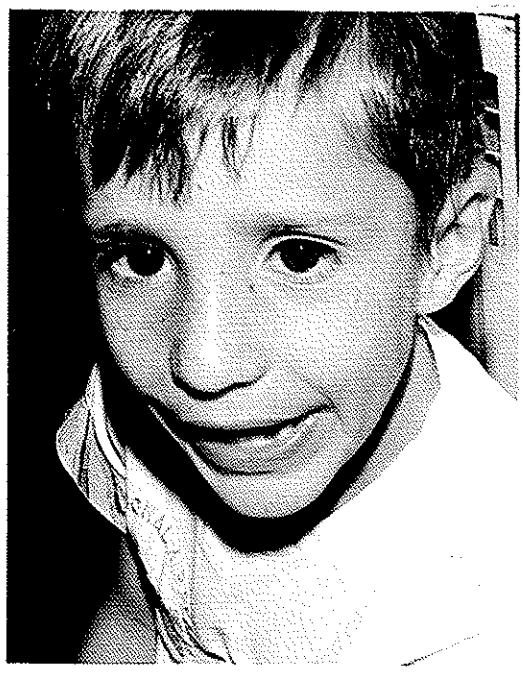

Fig. 4. The younger affected brother.

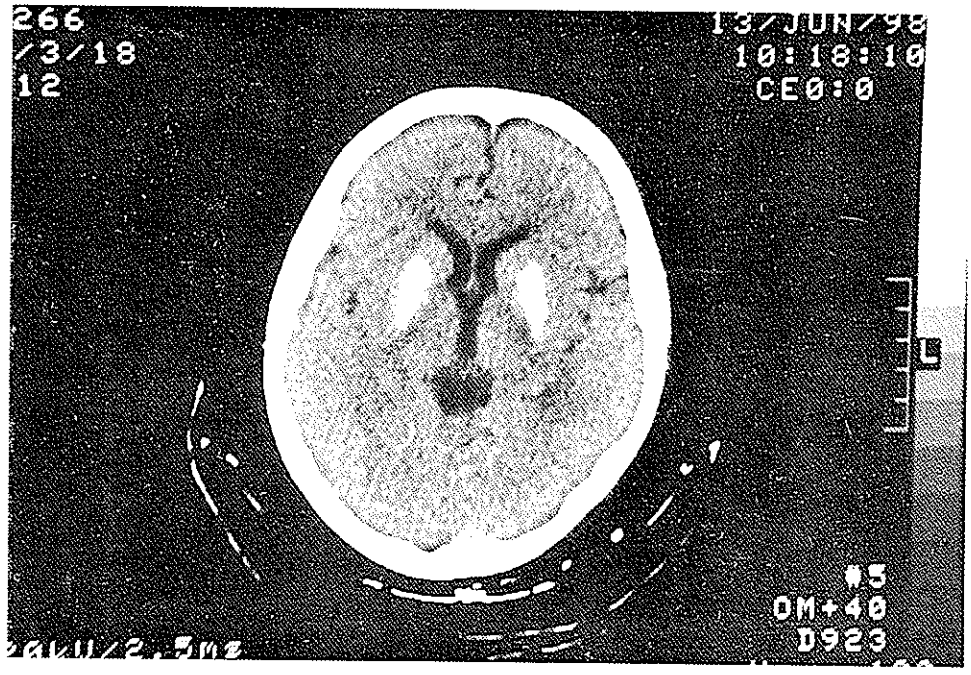

Fig. 5. Calcifications of both lenticular nuclei

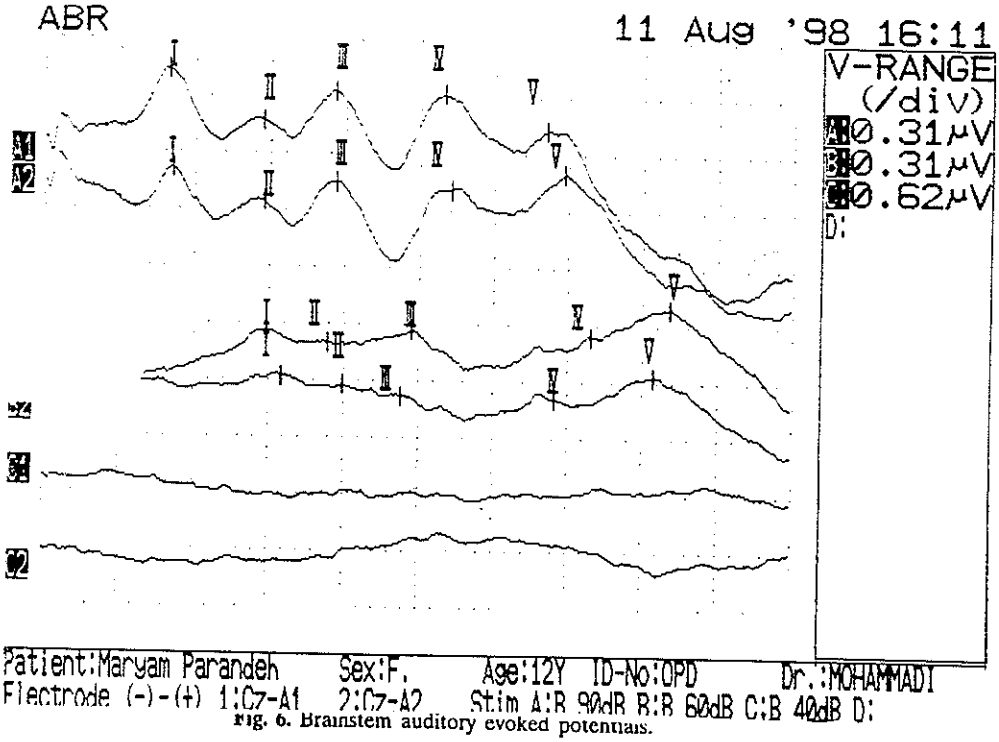

Fig. 6. Brainstem auditory evoked potentials.

two affected siblings and completely normal in the normal twin sister but there was a very mild scanning speech in both affected siblings. Deep tendon reflexes were slightly decreased in ataxic children. They had peculiar facies and physical appearance: dwarfism, slender facies with beakshaped nose and mild sunken eyes. There were also butterfly skin rashes accentuated by direct sunlight exposure (Fig. 3-4).The older affected sister had a body weight of 27 Kg and occipitofrontal circumference of 51 cm. The younger affected brother had a body weight of 15 Kg and a head circumference of 48.5 cm. There were no symptom or signs of kidney involvement. The affected siblings had normal deep tendon reflexes. The complete ophthalmologic and especially fundoscopic examinations were normal. There was also no tearing abnormality, retinitis pigmentosa, cataract, blindness and pendular nystagmus. Their brain CT-scan revealed symmetrical calcifications of basal ganglia (lenticular nuclei) (Fig. 5). Brainstem auditory evoked potentials also showed increased hearing threshold and prolonged absolute latencies with no increment of interpeak intervals (Fig. 6). Because of normal hearing thresholds on BAEPs, pure tone audiometry was not carried out. There was no sign of hearing loss. EMG, NCV studies and also somatosensory evoked potentials were normal. Lumbar puncture was not done. Complete blood biochemistry (including serum calcium, phosphorus, alkaline phosphatase, PTH and kidney function tests) and also metabolic studies were within normal limits. Other tests including serum alpha fetoprotein levels and immunoglobulin electrophoresis were within normal limits.

DISCUSSION

Cockayne syndrome is a very rare disorder with certain phenotypic, functional and paraclinical features (1). This article is the first case report of the Cockayne syndrome in Iran. Two siblings are reported within a family. The parents are related. One of the affected sibs is the product of a heterozygote twin pregnancy. Both the twins were female, one of them being affected and the other quiet normal. Familiarity with the characteristic features of the syndrome will guide us to an early clinical diagnosis. This gestalt approach to syndromic diagnosis will help us to avoid some sophisticated, unnecessary and luxurious paraclinical diagnostic tests and also to have clear and practical therapeutic and educational plans. We can thereby predict the natural history and also have a fruitful genetic consult.

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