CASE REPORT

COCKAYNE SYNDROME

• *a case report* •

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INTRODUCTION

Cockayne Syndrome (CS) is a multisystem sun-sensitive genetic disorder associated with a specific defect in the ability to perform transcription-coupled repair of active genes after UV irradiation. Two complementation groups have been identified (CS-A and CS-B), and 80% of patients have been assigned to the CS-B complementation group. The Cockayne syndrome A is caused by homozygous or compound heterozygous mutation in the gene encoding the group 8 excision-repair cross-complementing protein (ERCC8; 609412) on chromosome 5q11, and the Cockayne syndrome B (133540) is caused by mutation in the ERCC6 gene (609413) on chromosome 10q11. This syndrome has an estimated incidence of 1 for 200.000 newborns and is characterized by 'cachectic dwarfism', abnormal and slow growth and development, cutaneous photosensitivity, retinopathy – 'pepper-and-salt' chorioretinitis, a progeroid appearance, thin, dry hair, progressive pigmentary sensorineural hearing loss, dental caries, microcephaly, delayed neural development and severe progressive neurologic degeneration resulting in severe mental retardation, and intracranial calcification. The phenotype includes disproportionately long limbs with large hands and feet, and flexion contractures of joints are usual skeletal features. Knee contractures can result in a 'horse-riding stance.' There are cases described in literature of normal pressure hydrocephalus in children having the recessively inherited Cockayne's syndrome. The mean age at death in reported cases is 12.5 years, by inanition and infection in most cases. There are also relates of decreased or undetectable thyroid hormone. Hypertension and renal disease are frequent complications of Cockayne syndrome. There is a theory that Cockayne syndrome is a leukodystrophy. This theory is supported by studies that found segmental demyelination and/or remyelination with onion-bulb formation in sural

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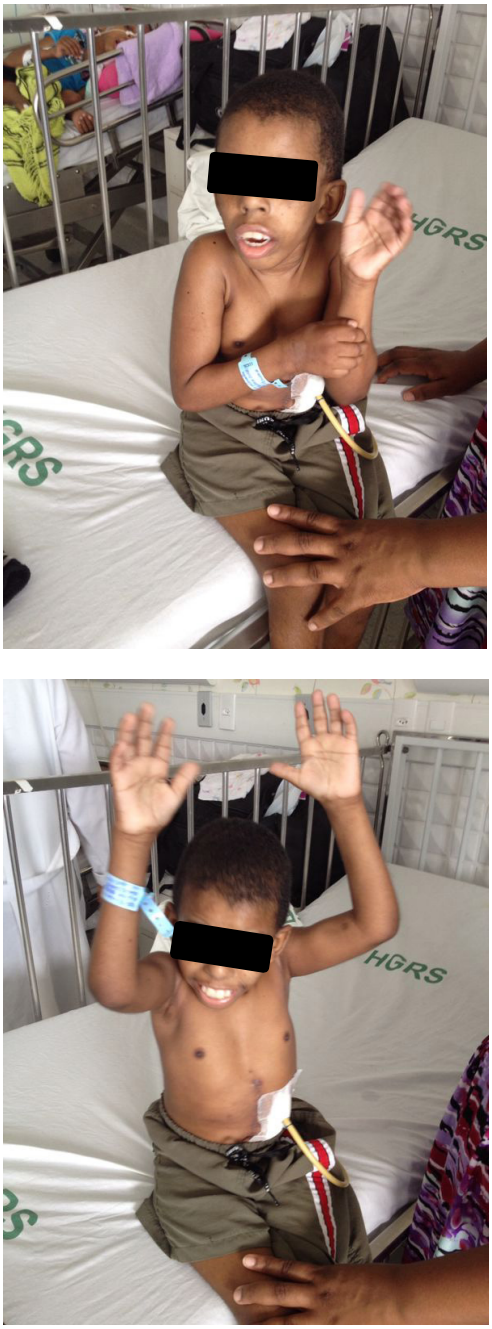
nerve biopsies. Visual disturbances and brainstem auditory evoked responses could be indicative of central nervous system demyelination, also.

CASE REPORT

L.A.C., 12 years old, black, male, born and raised in Salvador-Bahia-Brazil, sought medical attention due to hipoactivity, cough and refusal to eat. Associated with this clinical picture, had developed mental delay, besides he did not walk or talk and he interacted only with social smiles, held his neck up and sat down after his first year of life. Furthermore, he had severe malnutrition due insufficient intake of to proteins and calories. After the patient had been checked by neurologist and phonoaudiologist, he underwent a gastrostomy.

In his obstetric history, mother experienced an earlier miscarriage. Neonatal history: vaginal birth at full term without complications, weighing 2.920g. He didn't undergo any Newborn screening test. This patient has 1 healthy sibling and no report of congenital diseases in family history. Parents are first-degree consanguineous.

In the first evaluation of the patient, call attention his premature aging. Physical exam demonstrated a moderate state of health and emaciated (W = 9.5 kg), appearance of a cachectic dwarfism. Microcephaly, symmetrical skull, sunken eyes, with opaque areas in the iris, gengival hypertrophy, dentition in poor condition were also observed. Neurological examination showed: severe cognitive impairment, social contact only with smile, did not respond to commands, emited weeping and incomprehensible sounds, pupils equal round and reactive to light, symmetrical muscular stiffness and also symmetrical hyperreflexia. Cutaneous photosensitivity brands were disseminated in the skin. Genetic laboratory evaluation showed a normal karyotype – 46X,Y. Computerized tomography scan demonstrated diffuse cortical atrophy, extensive cerebral calcifications and enlarged cerebrospinal fluid space in the posterior fossa with probable communication with the fourth ventricle – a possible variant of Dandy Walker malformation. A geneticist evaluated the patient and a clinical diagnosis of Cockayne syndrome was made. The picture shown below was taken with the consent form signed by the patient's mother.



Patient with clinical features of the Cockayne Syndrome

DISCUSSION

The clinical features of Cockayne syndrome are discussed in the cases reported in the literature. [1-4] Importants neurological disorders, especially neuropsychiatric developmental delay, weakness,

muscle atrophy, abnormal movements such as tremor and myoclonus, changes in tonus, seizures and headache have been described. Are characteristic of the syndrome: ocular changes as decreased lacrimation, cataracts, optic atrophy or hypoplasia.[2-4] Other manifestations as hearing loss, nasal mucosa atrophy, hypertrophic tonsils and palate and dental abnormalities such as cavities, delayed tooth eruption, malocclusion, hypoplastic or absent[2-4] teeth, are normally seen in this syndrome. The clinical evaluation and detailed physical examination are important aspects to suggest the diagnosis. It is also important to perform imaging tests such computed tomography or magnetic resonance image that can show or not changes in the white matter.[2] Assessment should also be performed with an ophthalmologist to rule out ocular pathology associated with the syndrome as well as molecular genetic testing to confirm the Cockayne syndrome diagnosis.[2,3]

Specific tests for the syndrome were not performed in this case report, but the suggestive clinical picture and two imaging exams compatibles with the syndrome were key figures that suggested the diagnosis. The importance of addressing the issue described is to consider the main clinical characteristics of the disease in order to think in this diagnosis in potential. In this situation, it is desirable a limited sun exposure, physical therapy to reduce muscular symptoms, besides evaluation and genetic counseling of the patient's family.

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