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Case report/Kazuistyka

West syndrome associated with Down syndrome: Case report and literature review

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ABSTRACT

West syndrome is the most frequent cause of epilepsy in Down syndrome. West syndrome is often associated with poor long-term prognosis in most of children. We report a girl with West syndrome associated with Down syndrome which occurred at 8 months of age for repetitive flexor spasms and electroencephalography (EEG) showed hypsarrhythmia. She had Down syndrome facies, microcephaly, psychomotor development delay and axial hypotonia. Computed tomography of the brain was normal. Her karyotype was 47, XX, +21. Phenobarbital therapy was immediately effective with good clinical control of seizures, while the EEG monitored after one month was unchanged. At 2 years of age, the patient had hypertonic status epilepticus following a lung infection. The EEG showed a persistence of hypsarrhythmia. Sodium valproate and hydrocortisone therapy was effective with good seizure control but her psychomotor development was severely impaired. After a follow-up of 7 years, the patient presents growth retardation, microcephaly, severe psychomotor development delay, generalized hypotonia and tetraparesis. Knowledge of West syndrome in Down syndrome allows the early detection and prompt management of this neurological complication in order to optimize psychomotor development and improve the quality of life of these children.

Introduction

West syndrome or infantile spasms are a rare form of severe epilepsy, described for the first time by West in 1841. Epileptic spasms must be associated with a psychomotor regression and electroencephalography (EEG) hypsarythmia to make the diagnosis of West syndrome [1, 2]. It is well known that the incidence of major forms of epilepsy is higher in children with Down syndrome than in the general population, and West syndrome is the most frequent and most severe form of epilepsy in these children [3, 4].

In the general population of children, the incidence of West syndrome ranges from 2.2 to 4.5 per 10 000 live births

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[5, 6]. However, this incidence is much higher in children with Down syndrome. It has been reported that 6.4 to 8.1% of patients with Down syndrome had epilepsy, and 12.8–32% of these epileptic patients with Down syndrome had West syndrome [2, 7]. The West syndrome begins during the first year of life in 90% of those affected children. The peak age of onset is usually between 3 and 7 months. However, onset after 18 months is rare, though onset up to 4 years of age has been reported [8].

The association of infantile spasms with Down syndrome is considered a symptomatic form because of preexisting psychomotor development delay. However, the prognosis seems to be better in this association than in cryptogenic forms. This prognosis is linked to early diagnosis and rapid initiation of adequate treatment, but the long-term prognosis is often very poor in most of these children [1, 4]. We report a case of West syndrome in a girl with Down syndrome and we discuss the clinical characteristics, management and prognosis of this association.

Case report

An 8-month-old girl developed repetitive flexor spasms associated with fever, and was referred to the department of pediatrics. She was the first child of healthy non-consanguineous parents. Her mother was 46-year-old, and pregnancy was not followed. She was born at term with vaginal delivery without incident and neonatal period was unremarkable. Her psychomotor development was abnormal with hypotonia and disability of head control. At 8 months, she had flexor spasms several times a day, occurring in series. At admission, she was fever to 38.4 °C, Down syndrome facies, microcephaly, short neck with skin folds, brachydactyly and single crease in the palm, psychomotor development delay and axial hypotonia. The following laboratory tests were normal: complete blood counts, serum chemistry results, and serum electrolytes. The fever was linked to a viral infection, but no viral studies were performed. The thyroid function was normal. The transfontanellar ultrasound was normal. Computed tomography of the brain did not demonstrate any abnormalities. The karyotype showed 47, XX, +21. The initial EEG showed hypsarrhythmia and she was diagnosed as having Down syndrome associated with West syndrome. She was treated with phenobarbital before the result of EEG at a dose of 3 mg/kg/day and her seizures disappeared immediately with good control of these seizures for 16 months, while the EEG monitored after one month of admission was unchanged.

At 2 years of age, the patient was readmitted for hypertonic status epilepticus following a lung infection. The EEG showed a persistence of hypsarrhythmia. Thus, she was treated with Sodium valproate at a dose of 30 mg/kg/day and hydrocortisone at a dose of 2 mg/kg/day and her seizures disappeared immediately. Thereafter, hydrocortisone was stopped after 3 months and sodium valproate was continued at the same dose. At long-term, valproate therapy was effective with good seizure control but her psychomotor development was severely impaired. After a follow-up of 7 years, the patient presents growth retardation, microcephaly, severe psychomotor development delay, generalized hypotonia, tetraparesis and epilepsy well controlled by sodium valproate.

Discussion

Down syndrome is the most common genetic cause of mental retardation with a reported prevalence of epilepsy of 6.4–8.1%. Infantile spasms or West syndrome is the most frequent epilepsy syndrome in children with Down syndrome. West syndrome occurs in 0.6–13% of children with Down syndrome, representing 12.8–32% of seizures in these children [2, 7].

The mechanisms that raise susceptibility to infantile spasms in patients with Down syndrome have yet to be thoroughly uncovered. However, several authors suggest a potential epileptogenic role for the interaction of various Down syndrome-specific structural abnormalities of the brain, such as lower rates of inhibitory interneurons, decreased neuronal density, abnormal neuronal lamination, persistence of dendrites with fetal morphology, primitive synaptic profiles or altered membrane potassium permeability [1, 2].

The diagnosis of West syndrome is often easy when the infantile spasms are associated with arrest or regression of psychomotor development, and a specific EEG pattern of hypsarrhythmia [1, 5]. The clinical symptoms of infantile spasms are very different than any other type of seizure because of the absence of paroxysmal motor phenomena, such as convulsions or loss of consciousness. This lack of more typical of seizure phenomena may lead to initial misdiagnosis of infantile spasms by pediatricians at the first medical consultation. Recently, it was reported that approximately one third of infants with infantile spasms were not suspected of having epilepsy during the first medical consultation [9, 10]. Infantile spasms in infants are usually symmetrical and manifested by a repetitive flexor, extensor or flexor–extensor spasms with sudden and brief axial contraction, predominating in the upper limbs, with upper deviation of the eyes [11].

It is estimated that approximately 60–90% of children with West syndrome have an associated with a brain abnormality such as brain injury or cortical and subcortical malformations of the brain due to abnormal development, present in isolation or associated with other diseases such as Down syndrome [8, 12]. The magnetic resonance imaging is required to study the brain with great precision and detect brain malformations in some children [12]. In our case, the computed tomography of the brain did not demonstrate any abnormalities but magnetic resonance imaging of brain has not been made because this magnetic resonance imaging is not available in our hospital and parents do not have the means.

Medical treatment of infantile spasms should be effective and initiated as early as possible. Evaluation of treatment effectiveness includes cessation of spasms, a resolution of hypsarrhythmia on the EEG and reduction the cognitive decline associated with epilepsy. Currently, vigabatrin and adrenocorticotropic hormone (ACTH) are the only drugs whose effectiveness was approved to suppress clinical spasms and abolish the hypsarrhythmia on the EEG. In the literature, different treatment protocols were used, but the

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