Section: Paediatrics

Case Series

WEST SYNDROME: INTERGRATING RESEARCH FINDINGS INTO CLINICAL PRACTICE

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Abstract

Background: West syndrome (WS), also known as infantile spasms, typically appears in infancy, often reaching its peak around 6 months of age. It is characterized by spasms, developmental regression, and the presence of hypsarrhythmia on electroencephalogram (EEG). The spasms are categorized into symptomatic, idiopathic, and cryptogenic types. While the exact cause of West syndrome is complex, genetic factors, particularly mutations in genes like ARX and CDKL5, have been implicated in its development.

Early diagnosis and prompt initiation of treatment are crucial for improving the prognosis of WS patients. Brain magnetic resonance imaging (MRI) can aid in diagnosis. Our review of medical literature on WS highlights the primary treatment protocols used. Adrenocorticotropic hormone (ACTH), vigabatrin (VGB), and corticosteroids are commonly used as first-line treatments. Further research is needed to assess the efficacy of various therapeutic approaches, particularly in evaluating long-term outcomes after treatment cessation, to enhance treatment effectiveness and patient outcomes.

INTRODUCTION

West syndrome, an epilepsy variant affecting infants, was initially described by English physician William James West in 1841.[1]It affects approximately 2-3.5 in 10,000 live births, showing a higher incidence in males.[8]Symptoms typically appear before the child turns 12 months old and are characterized by a triad of infantile spasms, hypsarrhythmia, and developmental delay.[7] Spasms can present as symptomatic, cryptogenic, or idiopathic.

Genetic mutations in ARX and CDKL-5 are crucial in the syndrome's development. ARX mutations affect brain development, leading to seizures and intellectual disabilities. CDKL-5, a kinase found in cortical neurons, regulates essential brain signaling pathways and its malfunction is directly linked to epileptic spasms.[1]

Treatment usually involves administering ACTH, Vigabatrin, steroids, and other antiepileptic drugs.[4] Brain dysfunction can have prenatal, perinatal, or postnatal origins. Despite treatment efforts, the prognosis for West syndrome remains poor. In the following sections, we'll delve into a detailed discussion of the clinical features and management of patients affected by the symptomatic variant of West syndrome.

CASE PRESENTATION

Case 1

A 3-year-old boy was admitted with a 10-day fever, recent cough, cold, and vomiting. He had Developmental delay. During pregnancy, the mother had anemia treated with Iron Sucrose. The child was born via LSCS due to PROM and fetal distress, resulting in delayed crying. Seizures occurred on day 5, day 8, and during the 7th month, initially presenting as spasms. Milestones were achieved with delay: smiling, eye contact, and neck holding at 5 months, rolling over at 7 months, and bisyllabic speech at 15 months.

Clinical examination revealed increased muscle tone, bilateral clonic limb movements, and bilateral extensor responses in the plantar reflex. Systems appeared normal without organomegaly.

MRI showed periventricular leukomalacia and mild corpus callosum thinning. Visual evoked potential testing indicated delayed responses on both sides, suggesting a bilateral anterior visual pathway defect. Retinoscopy showed temporal pallor. EEG demonstrated modified hypsarrhythmia with mid-parietal localization, exhibiting beta and theta activities. Treatment included steroids, Topiramate, Clonazepam, and sodium valproate.

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Case 2

A 9-month-old boy was admitted to the hospital due to experiencing 2-3 jerks per day, coupled with delayed developmental milestones. He was delivered at full term via a lower segment caesarean section (LSCS), following a previous LSCS, and initially had exaggerated physiological jaundice. The perinatal period was otherwise uneventful. In the family history, the first child had a history of seizures and developmental delays due to hypoxic brain injury, passing away at 11 years old. The current infant's developmental history included rolling over, social smiles, and cooing, but a lack of interest in reaching for objects and no stranger anxiety.

Clinical examination revealed microcephaly (head circumference: 42 cm) and a hypo-pigmented patch on the chest. Tone and anti-gravity movements were normal, with deep tendon reflexes within the normal range. The musculoskeletal and genitourinary systems appeared unremarkable.

Diagnostic investigations, including EEG, showed abnormal findings consistent with modified hypsarrhythmia. The EEG revealed spindle-like activity before and after bursts of epileptiform activity, as well as frequent pseudo-periodic bursts of generalized posterior-dominant spike, polyspike, and slow wave patterns superimposed on high-amplitude slow wave activity. A PET CT scan of the brain demonstrated hypometabolism predominantly in the medial temporal region of the left temporal lobe.

Treatment included Vigabatrin, sodium valproate, Clobazam, and Levetiracetam to manage the symptoms and underlying condition.

Case 3

A 2-year-old male child was brought to our outpatient department by his parents, reporting sudden involuntary jerky movements that began approximately 9-10 months ago. The child exhibits symmetrical myoclonic tonic spasms in both upper arms and neck, each lasting less than 2 seconds, occurring around 10 times per day. The antenatal history was uneventful, followed by a normal vaginal delivery at the general hospital, with a birth weight of 3.25 kg. The child cried immediately after birth, and the neonatal period progressed without any complications. The child achieved developmental milestones appropriately, with no evidence of regression until now. There is no family history of seizure disorders.

Upon examination, the child appeared alert and active, with no signs of fever. Vital signs were within normal limits, with a heart rate of 96 per minute and a respiratory rate of 26 per minute. Weight and height measurements were between the 3rd and 50th centiles, while head circumference was less than the 3rd centile. No focal neurological deficits were observed, and cardiovascular and respiratory examinations were unremarkable. There were no neurocutaneous markers present.

Investigations revealed a hemoglobin level of 10.8g/dl, with all other blood indices within normal ranges. Serum sodium and potassium levels were normal, as were calcium and phosphorus levels. EEG showed a hypsarrhythmic pattern, while MRI of the brain was normal.

The patient's treatment regimen included levitiracetam at a dose of 100mg twice daily, pyridoxine at a dose of 50-100 mg per day, and the parents were advised to implement a ketogenic diet.

Case 4

A 6-year-old female child presented to the outpatient department with complaints of developmental delay, inability to grasp objects, speech delay, and hypotonia. History of spasms was also noted. The antenatal history was uneventful, and the child was born at 36 weeks of gestation with a birth weight of 2.67 kg. She had a history of hyaline membrane disease and feeding difficulties. In the family history, there was a paternal aunt who died in the first week of life with an unknown cause and another paternal aunt who died after epilepsy without any developmental delay. At 5 months of age, the child exhibited spasms, hypotonia, and poor eye contact, with EEG showing hypsarrhythmia. No dysmorphic features were observed.

Treatment included Vigabatrin, Prednisolone, and anti-epileptics, but despite this, there was persistence of spasms with a poor neurological outcome. MRI revealed diffuse cortical atrophy, and the blood karyotype showed no chromosomal imbalance.

Case 5

A 5-month-old female child presented with a history of seizures for the past 2 months, characterized by sudden onset with brief contractions of the neck and extremities. These episodes occurred 3-4 times per day during wakefulness and lasted approximately 3-5 minutes each. The child was initially treated with anti-epileptics (phenobarbitone and sodium valproate) for 4 weeks without any improvement in seizure control. Antenatal history was uneventful, and the baby was delivered via cesarean section due to oligohydramnios at term. The parents were in a non-consanguineous marriage.

Developmentally, the child exhibited no neck control but demonstrated cooing, palmar grasp, and social smile. Physical examination revealed no abnormalities from head to toe, and there were no signs of meningeal irritation. All systems were functioning normally. EEG findings showed hypsarrhythmia. Subsequently, the child was started on Vigabatrin and prednisolone, leading to an improvement in seizure frequency and duration.

Case 6

At 8 months of age, a female child presented with a history of flexor spasms concurrent with fever. She is the firstborn child of parents in a non-consanguineous marriage. The mother conceived at the age of 46 without proper antenatal care, and the baby was delivered at 38 weeks via normal vaginal delivery. By 8 months, the child had not achieved

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head control and displayed hypotonia. Fever was attributed to a viral infection. Physical examination revealed microcephaly, a short neck, brachydactyly, and a single palmar crease.

CT brain results were normal, but karyotyping revealed trisomy 21. EEG findings showed hypsarrhythmia. Treatment began with phenobarbitone, resulting in 18 months of seizure freedom. At 2 years of age, the child experienced status epilepticus alongside a pulmonary infection. Repeat EEG indicated persistent hypsarrhythmia, leading to the initiation of sodium valproate and prednisolone. It is noteworthy that West syndrome is a common cause of seizures associated with Down syndrome.

Case 7

A 10-month-old male child presented to the outpatient department with a history of upper and lower limb spasms occurring 2-3 times daily, accompanied by drooling of saliva. He is the first child of parents in a non-consanguineous marriage, delivered via cesarean section at 39 weeks due to meconium-stained liquor. The baby exhibited delayed crying and fetal bradycardia at birth, with a subsequent history of perinatal asphyxia necessitating the initiation of IV antibiotics and a 15-day ventilator support. At 4 months, seizures developed, with EEG findings indicative of encephalopathy and associated developmental delay. Upon examination, the child was afebrile, with a heart rate of 110 per minute and a respiratory rate of 26 per minute. Systemic examination revealed no abnormalities. The child was receiving syrup sodium valproate. Hypopigmented macules were noted on the face, prompting a ruling out of tuberous sclerosis. Repeat EEG revealed hypsarrhythmia, following which the child experienced respiratory distress, requiring oxygen therapy, antibiotics, and nebulizations. Retinoscopy results were normal, and the patient was subsequently started on tablet prednisolone.

DISCUSSION

West syndrome, observed in infants, presents with three primary symptoms: Infantile spasms, Hypsarrhythmia, and developmental delay. Onset can occur between the first week and 3 years of age, typically peaking around 6 months. Approximately 17% of patients have a family history of epilepsy, and the syndrome usually resolves before the child reaches 5 years old.

Seizures may involve intense jerking of the upper and lower limbs, with spasms affecting flexors, extensors, or both, with the mixed type being most common. Infantile spasms are categorized as Symptomatic, Idiopathic, or Cryptogenic.[6] Symptomatic cases are associated with various causes, including prenatal conditions like toxemia of pregnancy, Trisomy 21, and intrauterine infections, with Tuberous sclerosis being a common factor. [3,5] Perinatal causes include issues such as persistent neonatal hypoglycemia and hypoxic-ischemic encephalopathy (HIE). Postnatal triggers encompass trauma, meningitis, and metabolic disorders like maple syrup urine disease and phenylketonuria. Underlying triggers of West syndrome can induce a stress response, leading to increased corticotropin-releasing hormone (CRH) from the immature brain, thereby causing spasms. An abnormal interaction between the cortex and brainstem structures may also be involved.

Treatment typically includes ACTH, which suppresses CRH via negative feedback, and high-dose oral Prednisolone, which acts similarly by binding to mineralocorticoid receptors.[2]Vigabatrin is primarily used in cases of the cryptogenic or idiopathic type, inhibiting the GABA-degrading enzyme, GABA transaminase.[4] Despite treatment efforts, West syndrome generally has a poor prognosis.[7] However, a more favorable outcome is possible in cases that are cryptogenic or idiopathic, especially if onset occurs after 4 months of age, lacks atypical spasms, seizures, or asymmetrical EEG abnormalities, and shows a short time from onset to treatment, with an early sustained response to treatment.[6]Ketogenic diet therapy neurostimulation techniques and surgeries are exploring alternative options in the treatment of West syndrome.[9]

CONCLUSION

In summary, West syndrome presents a complex challenge with onset in infancy, characterized by infantile spasms, hypsarrhythmia, and developmental delay. Despite progress in understanding its causes and treatment development, the prognosis for affected individuals remains often bleak. However, ongoing research and advances in therapeutic strategies offer hope for better outcomes, especially with early intervention, timely diagnosis, and tailored treatment plans. Further in-depth studies and a deeper understanding of the syndrome's underlying mechanisms are crucial not only for refining current treatments but also for potentially introducing new therapeutic approaches, aiming to enhance the quality of life for those grappling with this intricate neurological condition.

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