Neonatal Hyperekplexia: The Stiff-Baby Syndrome

S.D. Sharma
Anurag Sarna
Sagori Mukhopadhyay

Neonatal hyperekplexia is a rare autosomal dominant startle disorder. Presenting soon after birth, it is often mistakenly diagnosed as spastic quadriparesis, epilepsy etc. While the long-term prognosis is relatively benign, sudden death due to severe spasms have been seen in sporadic cases. We report a case of hyperekplexia with some typical and some unusual findings.

Key words: *Hyperekplexia, Startle, Stiff-baby syndrome.*

Neonatal hyperekplexia is a rare autosomal dominant disorder with onset soon after birth, characterized by exaggerated startle response, rigidity and assumption of a flexed fetal position. Non-habituating symmetrical flexor spasm in response to light tapping of the nose is the clinical hallmark of this disorder(1). Commonly associated features include abnormal intrauterine fetal movements, feeding difficulties, nocturnal myoclonus, undue startle to loud noise or somatosensory stimulation, and hernias. Spasms may be severe enough to cause apnea, bradycardia and death(2). We report a case of hyperekplexia with some typical features along with a peculiar movement abnormality not commonly reported in such cases.

From the Jhanwar Pediatric Gastroenterology Center (JPGEC), Department of Pediatrics, SPM-CHI, SMS Medical College, Jaipur, India.

Correspondence to: Dr. S.D. Sharma, E-2 Doctor's Enclave, Medical College Campus, JLN Marg, Jaipur 4, Rajasthan, India.
E-mail: sdsharmajp@yahoo.co.in

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Case Report

A 9-month-old, female, first born to non-consanguineous parents was admitted with the sole complaint of episodic generalized stiffness since birth. She was a full term, 3 kg home delivered baby who cried immediately following birth. On life day 2, her mother noticed stiffness of the body during handling and a startle to the lightest of auditory or tactile stimuli. The stiffness decreased when the child was asleep. There was no history of feeding difficulties, clonic movements or cyanosis. There was history of operation for umbilical hernia at the age of 3 months. Developmentally child was normal except of a mild delay in gross motor fields. There was no suggestive family history on either side.

On CNS examination, rigidity was seen in all muscle groups including trunk and abdominal wall. Deep tendon reflexes were normal. The patient held herself in a flexed posture, with clenched fists and had an anxious look. Exaggerated nonhabituating startle response along with increased period of hypertonicity were demonstrated on tapping of the nose. She also had stereotypic movements in the form of rocking herself to and fro while lying supine, for long periods of time especially when disturbed by excessive hand ling, loud or sudden sound and on separation from parents. Routine counts and muscle enzyme markers, including creatinine phosphokinase-MB (CPK-MB), SGOT and Lactate dehydrogenasen (LDH) were normal. Muscle biopsy and EMG were also normal. Sonography brain revealed no abnormality. EEG showed no epileptiform discharges.

In light of the suggestive history and normal investigations a diagnosis of "stiff-baby syndrome" was suspected and thera-

peutic trial of clonazepam started at a dose of 0.1 mg/kg. Dramatic response was noted within 72 hrs with a decrease in tone, lessened startle response and straitening of the body to a normal posture.

Self-limiting course of the disease and its genetic mode of inheritance, with probability of the other siblings being affected, was explained to parents.

At one-year follow-up the child has shown continued improvement in the form of increased spontaneous movements, decreased startle and achievement of most of the normal milestones. However, she continues to maintain a slightly flexed posture and walking remains unstable with a tendency to sudden falls. Language development too is mildly delayed, but socially she is active and comparable to her siblings.

Discussion

Hyperekplexia or "startle disease" is a nonepileptic disorder characterized by two abnormal forms of response to unexpected auditory, visual and somesthetic stimuli, namely sustained tonic spasm (tonic extension of both upper and lower limbs or flexion of upper with extension of lower limbs) and the exaggerated startle response (which is a basic alerting reaction with stereotyped features consisting of eye blinking, facial grimacing, flexion of head, elevation of shoulders, and flexion of elbows, trunk and knees)(3).

Additional features include generalized hypertonia decreasing with sleep with hypokinesia, nocturnal myoclonus, increased incidence of congenitally dislocated hips, feeding difficulties with increased incidence of difficult labor and abnormal intrauterine movements(4). Hernias, requiring operative intervention, possibly caused by the persistently raised intra-abdominal pressure, are common, as was present in this case(5,6).

Family history is usually present, though sporadic cases have been documented(7). Our case had no such history. She had both the abnormal responses, qualifying as a major form of the disease. The rocking movements seen were unusual and no mention of such association was found in previously published literature.

Risk of death from apnea caused by severe spasms has been documented and these can be aborted by forced flexion of the head and legs over the trunk(2). Rigidity decreases spontaneously by 2-3 yrs of age when increase in spontaneous activity occurs. However, in some cases mild stiffness reappears in adolescence or adult life and spasms may again be provoked by startle(6). Such episodes are a source of injury. Also the unpredictable timing and outward manifestations of attacks in form of sudden falls or undue startle may make outdoor activities both dangerous and embarrasing resulting in considerable social dysfunction(5). Delayed motor milestones are present while cognitive function normally remains unaffected(8), though low intelligence has been noted in some studies(9).

Diagnosis is mostly clinical; EMG may show shortened latencies with continuous electrical activity at rest, when present it maybe used to monitor progress and response to therapy. Initial spike at frontocentral region followed by slow waves and desyncronization are sometimes seen in EEG. Muscle biopsies are normal.

Hyperactivity of the cortical neurons, decreased sub cortical inhibitory responses and serotonergic pathways has been proposed as pathogenic pathways(1). Linkage analysis demonstrated linkage of disorder with 5q33-35 locus. There is usually a mutation on the α – 1 subunit of the inhibitory glycine receptors (GLRA1) in the caudal pontine

reticular formation leading to neuronal hyperexcitability, by changing the chloride conductance. Low CSF GABA levels have been shown, suggesting a mechanism for the efficacy of clonazepam, a GABA agonist(10). Proton magnetic resonance spectroscopic imaging (MRSI) has shown decreased N-acetylaspartate, choline derivatives and creatinine in the frontal regions of brain.

The disease must be distinguished from other causes of neonatal hypertonia such as tetany, tetanus, Schwartz-Jample syndrome and severe perinatal asphyxia(6).

Therapeutic response to benzodiazepam group is dramatic enough to be diagnostic.

Diazepam and clonazepam are considered the drugs of choice. Valproic acid, 5-hyroxy-tryptophan and piracetam have also produced some benefits(8).

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