

Neonatal Hyperekplexia: A Case Report

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Abstract

Hyperekplexia is a rare non-epileptic disorder characterized by an exaggerated and persistent startle reaction to the unexpected tactile and acoustic stimuli. The disorder is occasionally associated with generalized muscular rigidity and has the clinical hallmark of positive nose tapping test.

The disease is inherited in an autosomal dominant fashion. Recessively inherited and sporadic forms of the disorder are also seen.

Neonatal hyperekplexia is extremely rare but important because, if undiagnosed and untreated, the disease can be fatal. Hyperekplexia is easily mistaken for commoner disorders such as spastic cerebral palsy and epilepsy. Clonazepam is of benefit, but it does not always stop the prolonged spasms. Forced flexion of baby's head toward the trunk is the most effective treatment.

We report a young female infant who presented with excessive jerky movements of the limbs in response to tactile stimuli, associated with episodic generalized stiffness and irritability since her birth. Marked improvement was seen following the use of clonazepam.

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Keywords • Hyperekplexia • seizures • infant • newborn

Introduction

Hyperekplexia, also known as familial startle disease or congenital stiff-man syndrome was first described by Kirstein and Silfverskiold in 1958.¹ Startle disease is an uncommon hereditary neurological disorder characterized by brief episodes of intense generalized tonic spasms in response to sudden unexpected loud noises or tactile stimulation such as a tap on the tip of nose or shoulder.

Affected neonates suffer from prolonged periods of rigidity, and are at risk for sudden death from apnea or aspiration.^{2,3}

One form, with neonatal onset, can be very severe, characterized by repeated myoclonic jerks and increased muscle tone with life threatening apnea due to contraction of respiratory muscles. Occasionally a baby can die of cardiopulmonary arrest if a tonic episode occurs in sleep, and this can be terminated by life-saving maneuver of forcible flexion of the head and neck toward the trunk.⁴ A neonatal case is presented below.

Case Presentation

A 57-day-old female infant born to consanguineous parents,

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presented with brief jerky movements of all limbs and occasional generalized stiffness secondary to tactile stimulation, which occurred with a frequency of 4-6 times per day since her birth. She was born at term following an uneventful pregnancy. Apgar scores were 6 at the first minute and 9 at the fifth minute respectively; no resuscitation was required. The birth weight was 3100 g.

Physical examination revealed jerking of whole body and exaggerated deep tendon reflexes most noticeable on tapping the dorsum of nose or forehead. No other abnormalities were noted.

The blood cell count, glucose, calcium, serum electrolyte levels, BUN, creatinine, CSF studies, blood gases, and CSF and blood cultures were normal. EEG and head CT scan yielded normal findings.

Episodes of seizure-like and tonic spasms could not be controlled with administration of phenobarbital and phenytoin. Her mother had found that severe generalized stiffness could be stopped promptly by flexing the infant's head toward her trunk. This interesting method was always effective.

Episodic attacks decreased remarkably after starting clonazepam. Her feeding pattern improved, irritability decreased, and spontaneous attacks disappeared.

No other seizure-like episodes and generalized stiffening were noted in the subsequent follow-ups.

Discussion

Startle disease or hyperekplexia is an unusual autosomal dominant neurological disorder that is often confused with epilepsy in the neonatal period. The disorder is categorized into major and minor forms.⁵ The major form is seen in the newborn period when the patient experiences momentary generalized muscular stiffness, hypertonia and an exaggerated startle response. These signs are typically heightened by the slightest stimulus including nose tapping, and disappear with sleep. The muscle stiffness usually returns to normal during the first years of life.⁶ In the minor form the startle response is exaggerated, being more than normal, without any additional symptoms. Excessive startle occurs as a manifestation of tension, fatigue and sleep deprivation in normal people. Familial history was not significant in our case. Diagnosis of hyperekplexia is made by a nose tap test. Tapping the tip of the nose of an unaffected baby will elicit no response, but in hyperekplexia there is an obvious startle response which is repeated each time the nose is tapped. Tactile stimulation, especially nose tapping test, was more provoking than other stimuli (auditory, visual) in our case. The underlying basis for the hyperekplexia is a mutation or change in the gene involved in the

function of neurotransmitter glycine. Glycine is an inhibitory transmitter because it damps down the action of nerve cells, particularly in the spinal cord and brain stem. When glycine receptors are impaired, the nerve cells are too easily excited. C.S.F gamma-amino-butyric acid (GABA) levels were reported to be low in affected patients, and because clonazepam acts through the GABA Type-A receptors, a genetic defect in GABA neurotransmitter receptor is thought to be the cause of this disorder.⁷

Hyperekplexia must be differentiated from other disorders including neonatal tetanus, neonatal drug withdrawal syndrome, Tay-Sach's disease, apneic spells, tonic seizures, spastic quadriplegia, and startle-provoked epileptic seizures (startle epilepsy) that are often due to occult congenital lesion. These seizures are often therapy resistant and the prognosis is generally poor.^{5,7,8}

Clonazepam appears to be the drug of choice (0.05 to 0.1 mg/kg/day) for these patients. No definite guideline exists regarding the duration of therapy but the drug can be tapered slowly once the symptoms subside.⁴ Flexion of infant's head and neck toward the trunk has been found to be the best way of treatment in life-threatening events (severe tonic spasms and apnea).⁹ Development is eventually normal.^{5,10}

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