CASE REPORT

Adrenocorticotropic Hormone Induced Status Dystonicus in a Child with West Syndrome

Jasmine Singh[1], Roosy Aulakh[2]

Abstract

Dystonia is a movement disorder characterized by involuntary sustained or intermittent muscle contraction causing repetitive twisting movements and abnormal postures. Status dystonicus (SD) is an enigmatic disease of cryptic etiology. We hereby report a child with West syndrome (WS) who went on to develop SD following intramuscular adrenocorticotropic hormone (ACTH) injection. An 11-month-old male child presented with complaints of flexor spasms for 2 months. The diagnosis of WS was confirmed by electroencephalography (EEG), which showed hypsarrhythmia. Intramuscular ACTH was added, and oral trihexyphenidyl was started for dystonia. On day 7 of ACTH, the child developed frequent opisthotonic posturing. Management protocol for grade IV SD was initiated. Administration of N-terminal of ACTH in rat locus coeruleus has been shown to produce human dystonia-like movement and abnormal posturing.

Keywords: Adrenocorticotropic hormone, Status dystonicus, West syndrome.

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Introduction

Dystonia is a movement disorder characterized by involuntary sustained or intermittent muscle contraction causing repetitive twisting movements, abnormal postures, or both.[1] Status dystonicus also known as dystonic storm is currently defined as "increasingly frequent and severe episodes of generalized dystonia", which necessitate urgent hospital admission.[2] Though SD is a medical emergency with high morbidity and mortality, it is frequently under-recognized and under-treated, necessitating the spread of awareness of this disease entity among pediatricians.

West syndrome, a form of epileptic encephalopathy characterized by flexor or extensor spasms and hypsarrhythmia on EEG, is frequently seen in children with perinatal cerebral insult. This form of WS following hypoxic-ischemic encephalopathy is termed as symptomatic WS. Intramuscular ACTH is the standard therapy for treating spasms in WS. Adrenocorticotropic hormone is known to cause hyperglycemia and hypertension, however, precipitation of SD has not been previously reported with its use. There have been some data showing the occurrence of dystonia-like movement disorder in animal models following the administration of ACTH. The present case describes a child with WS who developed SD following intramuscular ACTH injection.

Case Report

Eleven-month-old male children presented with complaints of flexor type of epileptic spasms for 2 months. The child was having around 10–15 volleys per spell and around 4 spells per day. The child was born at term gestation via non-consanguineous marriage. There was a history of birth asphyxia followed by mechanical ventilation for a period of 5 days. The child had global developmental delay with partial neck holding, no babbling, and no social smile. Also, an intermittent increase in the tone of both lower limbs more than upper limbs was noted on examination which increased with stimulation and disappeared during sleep pointing towards dystonia. An MRI brain had been done, which showed T2/Fluid attenuated inversion recovery sequence (FLAIR) periventricular white matter hyperintensity along with hyperintensities in basal ganglia and thalamus, suggestive of sequelae of perinatal hypoxic insult (Fig. 1). The diagnosis of WS was confirmed by EEG which showed hypsarrhythmia. The child

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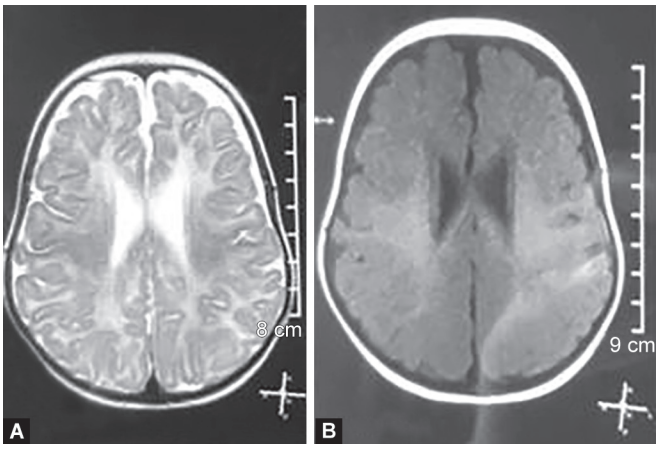

Figs 1A and B: MRI T2/FLAIR images showing periventricular white matter hyperintensity along with hyperintensities in basal ganglia and thalamus

was already receiving valproate for 1 month, initially at a dose of 30 mg/kg/day and then gradually increased to 50 mg/kg/day with no decrease in frequency of spasms. Intramuscular ACTH was added at 20 units per day, and oral trihexyphenidyl was started for dystonia. A good response was noted with decrease in spasm frequency to 4 volleys per day by day 5 and no spasms by day 6 of ACTH. Subjective improvement in activity was also noted by the mother. On day 7 of ACTH, the child developed frequent opisthotonic posturing. The Burke-Fahn-Marsden Dystonia Rating Score[3] increased from 13 at baseline to 30 during the episode. Management protocol for grade IV SD was initiated, and the child was shifted to pediatric intensive care unit, put on round-the-clock analgesics and antipyretics, tetrabenazine was added, and the dose of trihexyphenidyl increased. Secondary causes such as infections were ruled by sending complete blood count, C-reactive protein, blood, and urine cultures. The investigations were normal, and cultures came to be sterile. However, child continued to have persistent opisthotonic posturing and had to be sedated with chloral hydrate followed by Benzodiazepine infusion. Midazolam infusion was started at 1 μg/kg/min and gradually hiked to achieve resolution of dystonia. The dose had to be increased to a maximum of 4 μg/kg/min. In the absence of any other recognizable trigger, we considered to possibility of the event being precipitated by ACTH and it was withheld. The dramatic response was noted to omission of ACTH. The dystonia gradually responded over the next week, and child was slowly weaned off sedatives.

Discussion

Status dystonicus, or dystonic storm, is a life-threatening emergency marked by development of increasingly frequent or continuous severe episodes of generalized dystonic spasms.[2] Being a rarely reported and underdiagnosed condition, the etiology of SD has not been clearly defined, although a few triggers have been recognized, like pain, surgery, fever, infection and calculi, gastroesophageal reflux disease, constipation, abrupt initiation, abrupt withdrawal, or change in medications, including dopamine receptor blockers, haloperidol, lithium, benzodiazepine, baclofen, tetrabenazine, and clonazepam.[4–6] Dystonic storm usually occurs in patients who are already known to have dystonia though rarely de novo presentation has been documented. A single sporadic case of SD in a child with familial idiopathic hypothyroidism has been reported from India.[7] There is no consensus definition of SD as to the number of episodes/severity of dystonia required to be categorized into SD. The common differentials include neuroleptic malignant syndrome, serotonin syndrome, malignant hyperthermia, paroxysmal autonomic instability with dystonia, and acute dystonic reactions.[8] Even with therapy, mortality rates up to 10% have been reported.[9]

Administration of N-terminal of ACTH in rat locus coeruleus has been shown to produce human dystonia-like movement and abnormal posturing.[10] In Segawa disease, a form of dystonia with diurnal variation, the periods of excessive dystonia coincide with excess ACTH. The stress or trauma-induced exacerbation of dystonia has been attributed to excess of ACTH during these conditions. The effectiveness of anticholinergics against dystonia has been attributed to suppression of ACTH released caused by them. In a recent case report, ACTH has also been shown to precipitate SD when used for treatment for epileptic spasms in patients of Leigh syndrome.[11]

Given the possibility of precipitation of SD with ACTH, it needs to be used cautiously for the treatment of epileptic spasms in children with dystonic cerebral palsy as observed in this particular case. In absence of standard diagnostic criteria for SD, high clinical suspicion and regular monitoring can help establish a diagnosis early. Prompt intensive care management, removal of suspected trigger, and appropriate use of anti-dystonia medications and sedatives can result in a favorable outcome.

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