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# Type 0 Spinal Muscular Atrophy with Multisystem Involvement

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**Background:** The classical forms of severe Spinal Muscular Atrophy type is well recognized by pediatricians. **Case Characteristics:** A hypotonic neonate with severe respiratory distress at birth. **Observation:** Homozygous absence of exons 7 of the Survival Motor Neuron I gene. **Outcome:** Died 108 days after admission when respiratory support was withdrawn at the request of the parents. **Message:** Spinal Muscular Atrophy should be kept in mind in the differential diagnosis for unexplained severe generalized hypotonia and severe respiratory distress immediately after birth in the neonates.

**Keywords**: *Contracture, Exons 7 Survival Motor Neuron, Hypotonia, Neonate.*

The classical form of severe Spinal Muscular Atrophy (SMA) type 1 (Werdnig-Hoffmann disease) has a very consistent clinical phenotype that is well recognized by pediatricians. We report a case of Type 0 SMA. The other notable features in this case report are a rare multi-systemic presentation of SMA associated with intractable seizures not due to hypoxic ischemic encephalopathy (HIE), asymptomatic congenital heart disease, congenital contracture, spontaneous long bone fracture and osteopenia.

## CASE REPORT

A male neonate was born to a primigravida mother from a non consanguineous marriage by elective cesarean section at 39 wk of gestation. The pregnancy was unremarkable (except for borderline polyhydramnios) and history of reduced fetal movements reduced for one week before delivery. The neonate did not make any respiratory efforts after delivery and had a weak cry requiring intubation and mechanical ventilation at birth, however bradycardia was never noticed. He was ventilator-dependent, hypotonic, alert and responsive to tactile stimuli with absent deep tendon jerks. Extraocular and facial muscles were spared. He had a bell shaped chest and tongue fasciculation. He was noticed to have contractures of wrist and knee joint immediately after birth (***Figs.* 1, 2**). No other dysmorphism or obvious congenital anomalies were noted.

Serum creatine kinase was 110 IU/L. He required sustained mechanical ventilation. Subtle seizures were noticed on day 4 of life, which required multiple antiepileptic drugs and were refractory. The electrolytes and blood sugar levels were normal on multiple occasions. The seizures were not fully controlled with Injectible Phenobarbitone, Sodium Phenytoin, and high dose Inj Midazolam infusion initially. Later on he was started on oral Sodium Valproate and Levetiracetam without sustained seizures control. Transcranial Ultrasonography was unremarkable. Since the baby was

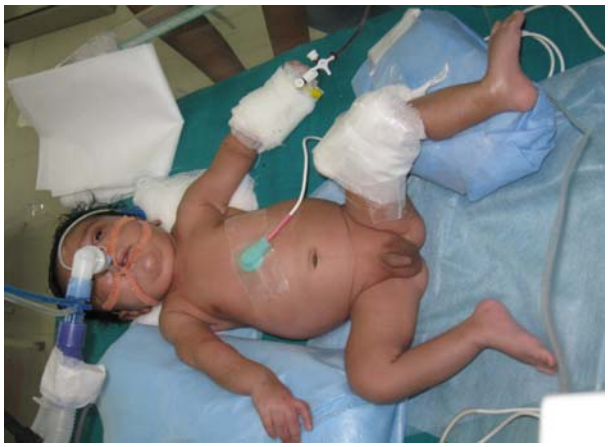

**FIG. 1** *Infant on ventilator with alert expression, pithed frog posture, splinted fracture left femur, bell shaped chest and contracture of wrist and knee joint.*

ventilator- dependent, neuroimaging could not be done. Oral feed was started and escalated to full feed subsequently on day 06. On day 08 of admission he was noticed to have a spontaneous fracture of Lt Femur which was managed by splinting. *X*-Ray of the site revealed a circumferential fracture of mid-shaft of Femur with generalized osteopenia of long bones. He also developed a systolic murmur, clinically small Ventricular Septal Defect (VSD) in 2nd week of life. Echocardiography could not be done. His Molecular genetic analysis revealed the homozygous absence of exons 7 of the Survival Motor Neuron (SMN) I gene. On parental wish despite explaining the prognosis he was continued on prolonged ventilator support and developed ventilator-associated pneumonia, which was managed with broad spectrum antibiotics. He died 108 days after admission when respiratory support was withdrawn at the request of the parents. Genetic counselling of the parents was done.

## DISCUSSION

Type 0 SMA have recently been documented. The presentation is more severe, with a history of diminished fetal movements *in utero,* and presenting at birth with asphyxia and severe weakness. MacLeod, *et al.* [1] first reported five cases of neonatal onset SMA. There is only one previous case report from India [2]. To date, it is not known with certainty whether this subgroup represents a distinct entity or is merely the severe end of the classic SMA type 1. We reported a rare multisystemic presentation of SMA associated with intractable seizures not due to HIE, asymptomatic congenital heart disease (CHD), congenital contracture, spontaneous long bone fracture, and osteopenia. All the above associations are described in different permutation and combination in literature but not in a single patient, as in our case.

SMA presenting with CHD has rarely been reported. However in a study, Rudnik-Schöneborn et al stated that 75% patients with a single *SMN2* copy had congenital SMA with haemodynamically relevant septal defects and suggested that the SMN protein is relevant for normal cardiogenesis [3]. Seizures in case of SMA type 0 are generally described as a consequence of HIE subsequent to birth asphyxia. In our case the infant presented with refractory seizures which were not because of HIE. However a different seizure phenotype has been described with SMA by Dyment, *et al.* [4].

In literature, SMA presenting with congenital contracture have been described in association with Ubiquitin-activating enzyme 1 (UBE1) mutation [5]. The consistent radiographic findings of each infant with neuromuscular disease in study by Rodriguez JI showed multiple diaphyseal or metaphyseal fractures or both, primarily involving the long bones of the upper extremities [6,7]. Eve Vaidla, *et al*. also described both the features of fractures and heart defect in a neonate with SMA in their case report [8].

To conclude, SMA should be kept in mind in the differential diagnosis for unexplained severe generalized hypotonia and severe respiratory distress immediately after birth in the neonates, notably in patients with a bright expression and alert disposition. Various phenotypes of SMA having multisystem involvement are increasingly being described. Whether having a genetic basis or just chance association, still needs to be elucidated.

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