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Atypical Hypotonia-Dominant Infantile Presentation of Genetically Confirmed Schwartz-Jampel Syndrome: A Case Report

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Case Report

Keywords: Schwartz–Jampel syndrome, Genetic, Rehabilitation, Early Intervention

Posted Date: March 18th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-9101955/v1

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Additional Declarations: The authors declare no competing interests.

Abstract

Background

Schwartz–Jampel syndrome (SJS) is an ultra-rare autosomal recessive disorder caused by mutations in the *HSPG2* gene, which encodes the extracellular matrix protein perlecan. The condition is classically characterized by the triad of myotonia, skeletal dysplasia, and distinctive facial dysmorphism. Most patients with SJS type 1 develop symptoms during early childhood, primarily presenting with progressive muscle stiffness and skeletal abnormalities. However, atypical infantile presentations may occur, which can delay diagnosis. This case report describes an unusual hypotonia-dominant presentation of genetically confirmed SJS type 1 in a toddler and highlights the role of early physiotherapy intervention in improving functional motor outcome.

Case presentation

A 2-year-6-month-old girl born to non-consanguineous parents presented with global developmental delay and dysmorphic features. The child was delivered at term via lower segment cesarean section due to absent fetal movements. Neonatal history included jaundice, feeding difficulty, laryngeal stridor and patent ductus arteriosus. At four months, evaluation for absent neck control revealed facial dysmorphism including blepharophimosis and bilateral ptosis, narrow auditory canals and a sacral pit. Echocardiography later revealed atrial septal defect. Genetic testing identified a homozygous mutation in exon 1 of HSPG2 gene, confirming Schwartz- Jampel syndrome type 1. Unlike the typical presentation dominated by myotonia, the child demonstrated predominant hypotonia during infancy.

Intervention

Physiotherapy based on Neurodevelopmental Treatment (NDT) principles was initiated at 10 months of age. The rehabilitation program included prone extension exercises using a therapy ball, bridging with support, dynamic sitting balance training on a Swiss ball, balance board sitting, lower-limb weight-bearing activities, supported standing with reach tasks, whole-body vibration therapy, and tilt-table standing with ankle-foot orthoses.

Outcomes

Gradual improvement in motor milestones was observed. The child achieved neck control at 11 months, rolling at 15 months, supported sitting by 18 months followed by independent sitting, and supported standing at 27 months. Despite persistent hypotonia and poor truncal control, the child demonstrated voluntary grasping and functional interaction with objects.

Conclusion

This case highlights an atypical infantile presentation of SJS type 1 characterized predominantly by hypotonia rather than myotonia. Early genetic diagnosis and timely physiotherapy intervention may facilitate improved motor development and functional outcomes in children with this rare disorder.

INTRODUCTION

Schwartz-Jampel syndrome is a rare autosomal recessive disorder, affecting fewer than one in a million people worldwide. It manifests primarily through muscle stiffness, known as myotonia, alongside chondrodysplasia—a condition involving abnormal cartilage development. Schwartz-Jampel syndrome (SJS) is etiologically linked to loss-of-function mutations within the HSPG2 gene, a large genomic locus encompassing 97 exons. This gene encodes the core protein of perlecan, a multifaceted heparan sulfate proteoglycan essential for extracellular matrix integrity and neuromuscular function[1].

Perlecan, a key heparan sulfate proteoglycan and major constituent of basement membranes, underlies a spectrum of dysplasia and syndromes when mutated. Null mutations in its encoding gene give rise to dyssegmental dysplasia, Silverman-Hand maker type, whereas other allelic variants manifest as dyssegmental dysplasia, Rolland-Desbuquois type, or Schwartz-Jampel syndrome (SJS).Perlecan is a modular, multi-domain protein structured into five distinct regions. It engages in critical protein complexes with extracellular matrix constituents, including fibulins, nidogens, fibronectin, collagen IV, platelet-derived growth factors, and fibroblast growth factors. Notably, among the 48 reported Schwartz-Jampel syndrome (SJS)-causing mutations, five that involve single amino acid substitutions localize to region 3 of perlecan[2].

The Schwartz-Jampel syndrome is characterized by a triad of stiffness, facial dysmorphism and skeletal abnormalities.It is broadly classified into three types. Type 1A typically presents within the first three years of life, featuring mild skeletal abnormalities. Type 1B manifests at birth with severe skeletal involvement. Type 2, also known as Stuve-Wiedemann syndrome, represents the most severe form and is incompatible with life [3].This disorder manifests with short stature, osteochondrodysplasia, myotonia, and a distinctive facial appearance featuring a "fixed" expression, blepharophimosis, pursed lips, and occasionally low-set ears and myopia. Skeletal anomalies encompass kyphoscoliosis, platyspondyly with coronal vertebral clefts, metaphyseal and epiphyseal dysplasia, and joint contractures[4].Dysmorphic features are often evident at birth. Muscle weakness leads to delayed motor development, while progressive muscle stiffness worsens with age, impairing gait primarily through restricted knee flexion[5].

This report describes a child with genetically confirmed SJS type 1 presenting withpredominant hypotonia during infancy and documents the motor development progress following early physiotherapy intervention.

PATIENT INFORMATION

2-year 6-month-old girl child of normal, unrelated parents presented with global developmental delay and multiple dysmorphic features. There was no relevant family history of congenital anomalies, neuromuscular disorders or consanguinity. The pregnancy was full-term via lower segment cesarean section due to the absent fetal movement. Intraoperatively, the placenta was found to be inflamed. The infant cried immediately after birth but exhibited jaundice, feeding difficulties, and laryngeal stridor. Sucking reflex was poor, necessitating admission to the NICU for 5 days. Patent ductus arteriosus was diagnosed via neonatal echocardiography.

CLINICAL FINDINGS

At 4 months, parents sought evaluation for absent neck control. Examination revealed narrow external auditory canals, sacral pit, and facial dysmorphism prompting ophthalmology consult.Audiological evaluation yielded normal results. Subsequently, renal function tests, prompted by the presence of a sacral pit, were also unremarkable.In case of ophthalmology assessment, blepharophimosis was noted, more pronounce in the left eye than right along with bilateral ptosis**(Image 1)**. The echocardiography showed progression to Atrial Septal Defect.Given the constellation of multisystem findings without family history, gene test was recommended and performed. Targeted genetic testing identified a homozygous mutation in exon 1 of the HSPG2 gene, consistent with autosomal recessive inheritance of Schwartz- Jampel syndrome type 1 (SJS1). Parental carrier testing was initiated but results remain pending at the time of reporting.

Neurological examination demonstrated generalized hypotonia with poor truncal stability. Deep tendon reflexes are preserved. There were no joint contractures or fixed skeletal deformities at the time of evaluation.

At the most recent assessment, the child demonstrated:

- Persistent hypotonia
- Truncal instability
- Knee hyperextension during supported standing
- Voluntary grasping and object manipulation
- Delayed speech with poor Oro-motor control

Outcome measures such as Gross Motor Function Measure (GMFM-88) and Pediatric Berg Balance scale are also measured.The gross motor function measure (GMFM-88) score was 40% that is level 3 or 4, which indicate moderate gross motor delay. With a score of 14 out of 56 on the pediatric berg balance scale, the child’s balance was impaired and there is high risk of fall.

Image 1

blepharophimosis and ptosis of eyes

TIMELINE

Table 1
timeline of age and the clinical events

AGE	CLINICAL EVENT
Birth	Jaundice, feeding difficulty, laryngeal stridor
4 months	Evaluation of absent neck control
10 months	Physiotherapy initiated
11 months	Neck control achieved
15 months	Rolling achieved
18 months	Sitting with support
20 months	Independent sitting
27 months	Supported standing

DIAGNOSTIC ASSESSMENT

- Audiological assessment was normal. Renal function testing was performed because of the sacral pit and showed normal findings.
- Echocardiography later demonstrated progression to atrial septal defect.
- Given the presence of multiple dysmorphic features and developmental delay, genetic testing was performed. Molecular analysis identified a homozygous pathogenic mutation in HSPG2 gene, confirming the diagnosis of Schwartz- Jampel syndrome type 1.
- Parental carrier testing was recommended.

INTERVENTION

Neurodevelopmental Treatment (NDT) is a hands-on therapy to improve mobility and function in individuals with neurological impairments. It targets motor control deficits to promote greater independence in daily activities through individualized interventions.

The rehabilitation program focused on:

- Facilitating postural control
- Improving trunk stability

- Promoting weight-bearing through the lower limbs
- Enhancing balance and motor coordination

Table 2
Specific tailored intervention for child having Schwartz- Jampel syndrome

Intervention	Therapeutic goal	Clinical rationale	Dosage /protocol	Expected outcome
Prone extension on therapy ball[6]	Improve extensor muscle activation& head control	Facilitates anti-gravity postural activation and trunk extension	10 repetitions with 15 seconds hold, 2 sets	Improved head control and trunk extension
Bridging with support[7]	Strengthens pelvic stabilizers & trunk muscles	Enhances core stability& prepares for sitting&standing	10 repetitions, 2 sets	Improved pelvic stability& trunk control
Sitting on therapy ball (anti-rotation)	Improve dynamic sitting balance	Activate trunk stabilizers and improves postural reactions	10 repetitions, 2 sets	Better trunk control during sitting
Swiss ball dynamic balance exercise	Improve equilibrium responses and trunk coordination	Provides controlled perturbations to enhance balance reactions	3–5 minutes per sessions	Improved balance and postural adjustments
Balance board sitting	Enhance postural stability and trunk activation	Encourages active postural correction during unstable sitting	3–5 minute per session	Improved sitting balance
Lower limb weight-bearing exercises	Promote joint stability and lower limb activation	Gradual loading helps to develop anti-gravitycontrol and bone strength	5 minutes for each limb	Improved lower limb stability
Supported standing with reaching activities[8]	Facilitates upright posture and functional motor control	Encourages weight transfer and postural alignment	10 repetitions of reaching tasks, 2 sets	Improved standing tolerance
Whole body vibration therapy[9, 10, 11]	Enhance neuromuscular activation and muscle recruitment	Mechanical vibration may stimulatemuscle spindle activation	10 minutes per session	Improved muscle activation and balance
Tilt-table standing with ankle foot orthoses	Promote gradual weight-bearing and upright posture	Helps to prevent contractures and improves postural alignment	10 minutes per session	Increased standing tolerance

Sessions were conducted regularly under physiotherapy supervision.

DISCUSSION

First documented by Schwartz and Jampel in 1962, this rare condition—also termed myotonic chondrodystrophy—is characterized by congenital blepharophimosis, distinctive facial features, muscle stiffness (myotonia), and progressive joint deformities. It is a rare autosomal recessive disorder arising from mutations in the HSPG2 gene on chromosome 1p34-36, which encodes the perlecan protein —a key basement membrane heparan sulfate proteoglycan. These genetic alterations disrupt perlecan function, leading to impaired cartilage development and aberrant neuromuscular transmission[12].The disorder typically presents with skeletal dysplasia and persistent myotonia, while cognition and lifespan are generally preserved. To date, only around 150 cases have been reported worldwide[13].

Giedion proposed a preliminary classification of Schwartz-Jampel syndrome (SJS) into three subtypes: type 1A, typically diagnosed in childhood and featuring moderate skeletal dysplasia, aligning with the original descriptions by Schwartz, Jampel, and Aberfeld; type 1B, resembling type 1A but evident from birth with more severe bone dysplasia akin to Kniest dysplasia; and type 2, presenting neonatally with heightened mortality and skeletal changes suggestive of Pyle disease. Notably, genetic analysis in a family with two affected siblings with SJS type 2 yielded evidence against linkage to chromosome 1p36-34[14].

Most patients with Schwartz-Jampel syndrome type 1 (SJS1) become symptomatic between the ages of 3 and 10 years, exhibiting a characteristic phenotype that includes short stature, mask-like facies, epicanthic folds, receding chin, upturned nose, long philtrum, short neck, pinched facial appearance, low-set ears, high-arched palate, prominent musculature, and a high-pitched voice. Diagnostic hallmarks encompass this distinctive facial morphology, muscle hypertrophy, and continuous muscle fiber activity on electromyography. Affected individuals often display slow, deliberate movements with semi-flexed arms, toe-walking, restricted mouth opening, mild kyphosis, joint contractures (particularly at the elbows, spine, and pelvis), metaphyseal widening, lumbar lordosis, and reduced range of motion in major joints, alongside potential complications such as hydrocephalus, carpal tunnel syndrome, myelopathy, recurrent infections, laryngeal stridor, and, in rare instances, mild intellectual impairment [15].Compared to existing literature, this toddler's presentation shares core SJS1A features per Giedion classification: blepharophimosis/ptosis (82–100% prevalence), facial dysmorphism, and delayed motor milestones, but diverges with prominent early hypotonia over myotonia—reported in ~ 30% of infantile cases before stiffness predominates. Prenatal/perinatal clues like reduced fetal movements, inflamed placenta, laryngeal stridor, and transient PDA/ASD echo multisystem perlecan roles in placental vascularity and cardiac septation, seen in 10–20% of SJS cohorts, while sacral pit and narrow auditory canals reflect skeletal dysplasia precursors absent in milder reviews.

Nerve conduction studies in Schwartz-Jampel syndrome type 1 (SJS1) typically remain normal. Needle electromyography, however, reveals continuous muscle fiber activity at rest, characterized by high-frequency spontaneous repetitive potentials that persist even during sleep and general anesthesia. These discharges often resemble myotonic potentials but lack the characteristic waxing and waning amplitude. Muscle biopsy findings are generally nonspecific, showing mild myopathic changes. Radiographic evaluation of the spine commonly demonstrates kyphosis along with other skeletal

deformities. The distinctive combination of facial dysmorphism, skeletal deformities, muscle stiffness with contractures, and myotonic discharges lacking waxing-waning patterns on electromyography is pathognomonic for Schwartz-Jampel syndrome (SJS), minimizing diagnostic confusion with other entities. Nearly all documented cases in the literature have relied on these characteristic clinical and electrophysiological features for diagnosis. Differential considerations encompass disorders of muscle cramping and stiffness (e.g., stiff person syndrome, Isaacs syndrome), myotonic conditions (e.g., congenital myotonic dystrophy, myotonic dystrophy type 1, myotonia congenita, Para myotonia congenita), muscular dystrophies (e.g., Becker and Duchenne dystrophies, congenital muscular dystrophy), congenital myopathies, channelopathies, mucopolysaccharidoses (e.g., Morquio syndrome), Ehlers-Danlos syndrome, malignant hyperthermia susceptibility, blepharospasm, and Stuve-Wiedemann syndrome[16].

Treatment for Schwartz-Jampel syndrome (SJS) varies by symptom severity and may involve noninvasive pharmacotherapy with muscle relaxants or antiepileptics, or more invasive interventions. While traditional muscle relaxants such as baclofen offer limited benefit, antiepileptic agents—particularly carbamazepine (CBZ)—provide substantial relief from myotonia and stiffness. CBZ also offers neuroprotective effects against the relatively frequent epileptic seizures observed in this population. Pharmacologic approaches, however, have constrained efficacy, proving most effective in early-diagnosed, milder cases. In patients with greater disease burden, surgical options become essential. Local botulinum toxin A injections yield transient symptom alleviation in facial and mimic muscles, showing particular promise in less severe presentations or as adjuncts to systemic medications and orthopedic surgery. To date, no standardized surgical protocols exist specifically for managing SJS manifestations[17].

It is important to note that the present report describes the clinical course of a single patient, and therefore causal relationships between the physiotherapy intervention and motor improvement cannot be definitively established. Developmental maturation may also contribute to milestone acquisition. Nevertheless, the temporal association between rehabilitation intervention and functional progress highlights the potential value of early physiotherapy as part of a multidisciplinary management strategy for children with Schwartz-Jampel syndrome.

Further studies involving larger case series and longitudinal follow-up are required to better understand the natural history of motor development in Schwartz-Jampel syndrome and to establish evidence-based rehabilitation protocols. Given the rarity of the disorder, detailed case reports describing clinical presentation, rehabilitation strategies, and functional outcomes remain valuable contributions to the literature.

CONCLUSION

This case illustrates Schwartz-Jampel syndrome type 1 presenting atypically in infancy with hypotonia, dysmorphic features, and cardiac anomalies rather than predominant myotonia, emphasizing the need

for genetic testing in unexplained developmental delay syndromes. It also emphasizes how early physiotherapy enabled progressive motor gains.

Declarations

The parent of the child provided written informed consent to participate in research and publish the findings including images and videos

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Figures



Figure 1

Image 1: blepharophimosis and ptosis of eyes