Schwartz Jampel Syndrome : A case report
Le syndrome de Schwartz Jampel : A propos d'une observation

Emna Trabelsi [1,2], Imen Bel Hadj [1,2], Ines Trabelsi [1,2], Khadija Boussetta [1,2]

[1] Hôpital d'Enfants Béchir Hamza, Service de Médecine Infantile B , 1007, Tunis, Tunisie
[2] Université de Tunis El Manar, Faculté de Médecine de Tunis, 1007, Tunis, Tunisie

ABSTRACT :

Schwartz-Jampel Syndrome (SJS) is an extremely rare autosomal recessive genetic disorder, only about 130 cases have been reported worldwide. Affected individuals present with a distinctive craniofacial features, skeletal abnormalities (chondrodysplasia) and persistent muscle stiffness (myotonia), with symptom onset typically occurring from birth to early childhood. This study aims to report a case of SJS. We present the case of a 3-year-old boy born to first-degree consanguineous parents. He was followed in orthopedic care for a congenital right-sided torticollis. He was referred to our department due to concerns about global developmental delay with facial dysmorphism. On physical examination, we found a failure to thrive, a microcephaly, a mask-like face and chest deformed with a carinate appearance. Ocular examination revealed blepharophimosis. Mildly elevated serum levels of creatine phosphokinase (265 U/L) and lactate dehydrogenase (967 U/L) were observed with severe anemia. Pelvic X-ray showed acetabular dysplasia. Brain CT identified mild ventriculomegaly. Neurophysiological investigations demonstrated frequent myotonic discharges with efforts yielding proportionate electromyographic responses despite being difficult to maintain which are typical Schwartz-Jampel syndrome patterns. The patient was treated with carbamazepine. By the time of his last follow-up at 17 years of age, his myotonia had shown slight improvement and the disease course was marked by learning difficulties, ataxic gait, and progressive worsening of skeletal deformities in the legs and elbows. This case of SJS highlights classic features alongside rare findings like neurodevelopmental delay and severe anemia, expanding its clinical spectrum. It underscores the need for multidisciplinary care and early genetic counseling.

Keywords: myotonia, chondrodysplasia, child, dysmorphism

RÉSUMÉ:

Le syndrome de Schwartz-Jampel (SSJ) est une anomalie génétique autosomique récessive très rare, seuls 130 cas ont été décrits dans la littérature à ce jour. Les signes cliniques distinctifs sont une dysmorphie cranio-faciale, des anomalies squelettiques (chondroplasie) et une myotonie. Ces symptômes apparaissent entre la naissance et la petite enfance. L'objectif de notre étude était de décrire les particularités cliniques et évolutives du SSJ à travers une observation clinique. Il s'agit d'un garçon de 3 ans, issu d'un mariage consanguin du premier degree, aux antécédents de suivi en orthopédie infantile pour torticolis congénital. Il nous a été adressé pour un retard du développent psychomoteur associée à une dysmorphie faciale. L'examen a trouvé un retard statural, une microcéphalie, un faciès figé une déformation thoracique en pectus carinatum. L'examen ophtalmologique a note un blépharophimosis. Les créatines phosphokinases et les lactates déshydrogénases étaient élevées associées à une anémie profonde. La radiographie du bassin a révélé une dysplasie acétabulaire. Une ventriculomégalie a été notée au scanner cérébral. L'électromyogramme a montré un tracé de décharges myotoniques typique du SSJ. Le patient a été mis sous carbamazepine avec une amélioration partielle. Le suivi de 17 années a révélé des difficultés scolaires, une ataxie d'aggravation progressive et une aggravation des déformations des membres inférieurs. Cette observation met l'accent sur les anomalies classiques du SSJ ainsi que sur certaines anomalies plus rarement observées comme le retard neuro-développemental et l'anémie. Une prise en charge multidisciplinaire est nécessaire pour améliorer la qualité de vie de ces patients.

Mots clés : myotonie, chondrodysplasie, enfant, dysmorphie

Auteur principal :
Dr Emna Trabelsi
Email : emna.trabelsi@fmt.utm.tn

INTRODUCTION

Schwartz-Jampel Syndrome (SJS) is an extremely rare genetic disorder, affecting fewer than one in a million individuals [1], marked by persistent muscle stiffness (myotonia) and skeletal abnormalities (chondrodysplasia). First described by Schwartz and Jampel in 1962, this autosomal recessive condition stems from mutations in the heparan sulfate proteoglycan 2 (HSPG2) gene which encodes perlecan, a crucial proteoglycan found in the extracellular matrix [2]. Perlecan plays an essential role in regulating muscle contraction, chondrogenesis, cell adhesion, and anchoring acetylcholinesterase at neuromuscular junctions [1]. Dysfunction of this gene leads to impaired secretion of perlecan, resulting in the hallmark features of the syndrome : myotonia and chondrodysplasia. Affected individuals often present with a constellation of distinctive craniofacial features, including narrow palpebral fissures, blepharophimosis, pursed lips, and a mask-like facial expression. Skeletal abnormalities such as dwarfism, pectus carinatum, kyphoscoliosis, and bowed legs are frequently observed, with symptom onset typically occurring from birth to early childhood [3]. Despite being a multisystem condition, Only about 130 cases have been reported worldwide, making research challenging [4]. This study aims to report a case of Schwartz Jampel Syndrome. Alongside this investigation, a comprehensive review of the literature was conducted to collect relevant data on comparable genetic variants, associated clinical phenotypes, and potential pathogenic mechanisms.

CASE PRESENTATION

We present the case of a 3-year-old boy born at term to first-degree consanguineous parents. His birth was via spontaneous vaginal delivery but was complicated by perinatal asphyxia. In early infancy, he was followed in orthopedic care for a congenital right-sided torticollis, which resolved spontaneously. He also underwent pediatric surgery for a right inguinal hernia, successfully repaired at the age of 2. He was referred to our department due to concerns about global developmental delay in the context of notable facial dysmorphism. On physical examination, he exhibited features of failure to thrive, with a height of 79 cm and a body weight of 11 kg. His facial appearance was striking for a microcephaly, a mask-like face, mandibular retrusion, high-arched palate, and low-set hairline and ears. The chest was deformed with a carinate (pigeon chest) appearance, accompanied by kyphoscoliosis. Despite these skeletal abnormalities, joint mobility was within normal limits, and muscle bulk was notably increased in both the upper and lower limbs. Muscle strength and deep tendon reflexes were preserved. Ocular examination revealed blepharophimosis and a trace light reflex bilaterally, with no abnormalities observed in the pupils, lens, or fundus.

Mildly elevated serum levels of creatine phosphokinase (265 U/L) and lactate dehydrogenase (967 U/L) were observed on laboratory testing along with severe anemia attributed to iron deficiency. The remainder of the blood workup was unremarkable. A cervical spine computed tomography revealed hypertrophy and bifid morphology of the C2 vertebral body, along with flattening of the remaining vertebral bodies. Pelvic X-ray showed horizontal orientation of the acetabular roofs associated with acetabular dysplasia. Brain CT identified mild ventriculomegaly without other associated anomalies. Neurophysiological investigations demonstrated findings consistent with a typical Schwartz-Jampel syndrome pattern. Nerve conduction studies showed no evidence of sensory or motor neuropathy. However, frequent myotonic discharges were recorded in both the tibialis anterior and biceps brachii muscles, with efforts yielding proportionate electromyographic responses despite being difficult to maintain (Figure 1).

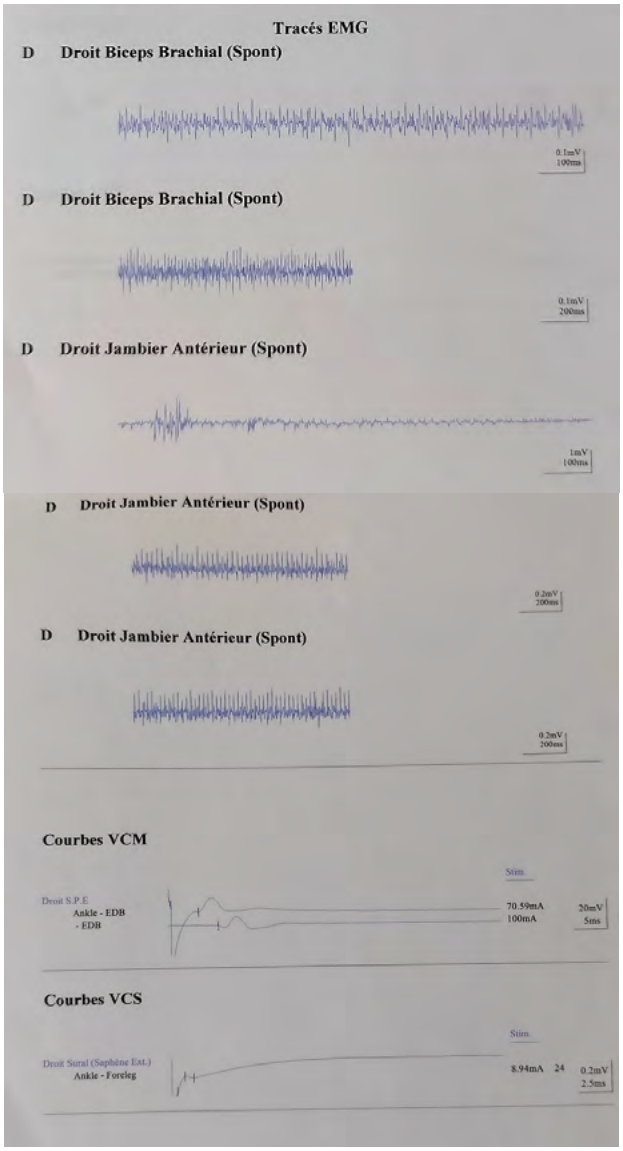

Figure 1 : Electrophysiological studies : electromyography recording frequent myotonic discharges in the tibialis anterior and biceps brachii muscles

The patient was treated with carbamazepine, which provided partial symptomatic relief. By the time of his last follow-up at 17 years of age, his myotonia had shown slight improvement compared to the initial presentation, although it remained persistent. The disease course was later marked by learning difficulties, ataxic gait, and progressive worsening of skeletal deformities in the legs and elbows, eventually requiring corrective orthopedic surgery at the age of 17.

DISCUSSION

Schwartz-Jampel syndrome (SJS) is a rare genetic disorder characterized by a spectrum of musculoskeletal and neuromuscular abnormalities. Three distinct types of SJS have been described—types 1A, 1B, and 2—each varying in clinical severity and age of onset [5]. Types 1A and 1B are caused by mutations in the HSPG2 gene, which encodes perlecan, a large heparan sulfate proteoglycan crucial for skeletal development, neuromuscular junction stability, and vascular integrity. This gene is located on the short arm of chromosome 1 (1p36.1–p34) [6]. Type 1B, a more severe form, typically presents at birth with pronounced skeletal abnormalities, while type 2, currently referred to as Stüve-Wiedemann syndrome, is caused by mutations in the LIFR gene and is associated with short-limb dysplasia and bowing of long bones. Although SJS is most commonly inherited in an autosomal recessive manner, rare autosomal dominant cases have also been documented, likely due to dominantnegative effects of altered perlecan [7].

Our patient displayed the classical triad of SJS: persistent myotonia, chondrodysplasia, and distinctive facial features such as a mask-like facies and mandibular retrusion. These features typically emerge in early childhood and are attributable to perlecan deficiency. In fact, this extracellular matrix protein is composed of five functional domains, and the newly identified mutation affects cysteine residue Cys375 within domain II, a region involved in calcium and Wingless signaling. This mutation likely disrupts a critical disulfide bond, promoting misfolding, ubiquitination, and subsequent degradation of perlecan. The resulting deficiency impairs acetylcholinesterase anchoring at the neuromuscular junction, leading to increased muscle excitability and sustained contraction. These clinical manifestations were confirmed by neurophysiological studies, which showed frequent myotonic discharges in proximal and distal muscles [6]. Additionally, perlecan's role in calcium signaling appears disrupted in this patient. Impairment in calcium dynamics, particularly involving the sarco/endoplasmic reticulum calcium-ATPase and ryanodine receptor 1, may further contribute to the observed muscle pathology and sustained myotonia [7]. Beyond the classic features, our patient also demonstrated several craniofacial anomalies including dental crowding and a narrow maxillary arch, which likely reflect the combined effects of skeletal dysplasia and chronic myotonic activity. These abnormalities not only pose challenges for feeding and oral hygiene but may also predispose affected individuals to pediatric obstructive sleep apnea, an association not widely recognized due to the rarity of SJS but deserving of closer investigation [4]. Two unusual features in this case merit further discussion: global developmental delay and severe anemia. While neurodevelopmental delay has been reported in a few SJS cases, often in association with additional gene mutations such as WWOX and PRMT7 [8], our patient's delay occurred in the absence of known comorbid mutations, raising the possibility of broader phenotypic variability or unrecognized genetic modifiers. The patient's severe anemia, ultimately attributed to iron deficiency, also raises important clinical considerations. Although gastrointestinal bleeding is rarely reported in SJS, one similar case in a young child has been described [9]. Experimental studies in animal models of perlecan deficiency have shown vascular abnormalities including microaneuvrysms, endothelial dysfunction, and tissue hemorrhage . These findings suggest that perlecan plays an underappreciated role in maintaining vascular and mucosal integrity, and its deficiency could plausibly lead to increased bleeding risk, including within the gastrointestinal tract [8].

Electromyography in SJS classically reveals complex repetitive discharges (CRDs) without waxing and waning, consistent with our patient's findings. Although muscle biopsy was not performed, previously reported cases have shown cholinesterase deficiency and denervation, both of which align with the long-duration motor unit action potentials (MUAPs) observed in our patient. Pharmacologically, the patient experienced modest improvement in myotonia with carbamazepine, a response also reported in the literature, suggesting partial symptomatic benefit through modulation of sodium channel activity [10].

CONCLUSION

This case of Schwartz-Jampel syndrome highlights classic features alongside rare findings like neurodevelopmental delay and severe anemia, expanding its clinical spectrum. It underscores the need for multidisciplinary care and early genetic counseling. Ongoing case reports and reviews aim to deepens our understanding of this complex disorder, researchers hope to uncover better diagnostic and treatment strategies and offering hope to families navigating the challenges of SJS.

Aucun conflit d'intérêt à déclarer

REFERENCES

[1] S. Nicole, C.S. Davoine, H. Topaloglu, et al. Perlecan, the major proteoglycan of basement membranes, is altered in patients with

Schwartz-Jampel syndrome (chondrodystrophic myotonia). Nat. Genet,2000; 26 (4): 480–483.

[2] M.C. Farach-Carson, D.D. Carson. Perlecan–a multifunctional extracellular proteoglycan scaffold. Glycobiology, 2007; 17 (9): 897–905

[3] M. Stum, C.S. Davoine, S. Vicart, et al. Spectrum of HSPG2 (Perlecan) mutations in patients with Schwartz-Jampel syndrome. Hum. Mutat, 2006; 27 (11): 1082–1091

[4] Pibulniyom M, Pungchanchaikul P, Assawakawintip T, Peanchitlertkajorn S. Oral findings and craniofacial morphology in a patient with Schwartz-Jampel syndrome and severe obstructive sleep apnea: A case report. Clin Case Rep, 2020 ; 8(12): 2550-2553.

[5] Giedion A, Boltshauser E, Briner J et al. Heterogeneity in Schwartz-Jampel chondrodystrophic myotonia. Eur J Pediatr, 1997; 156(3):214–22

[6] Lin PY, Hung JH, Hsu CK, Chang YT, Sun YT. A Novel Pathogenic HSPG2 Mutation in Schwartz-Jampel Syndrome. Front Neurol, 2021; 12: 1-10

[7] Pei S, Parthasarathy S, Parajuli A, Martinez J, Lv M, Jiang S, et al. Perlecan/Hspg2 deficiency impairs bone's calcium signaling and associated transcriptome in response to mechanical loading. Bone, 2020; 131:1-24

[8] Elahi Vahed I, Tehrani Fateh S, Kamali M, Hashemi-Gorji F, Esmaeilzadeh Z, Sadeghi H, Miryounesi M, Ghasemi MR. Expanding genetic and clinical aspects of Schwartz-Jampel syndrome: A report of two cases with literature review. Mol Genet Metab Rep, 2024; 40: 1-7

[9] I. Polat, P. Karaoglu, U. Yis, S.H. Kurul, Schwartz-Jampel syndrome with gastroduodenal bleeding. J. Pediatr. Neurosci, 2016; 11 (3): 255–257

[10] Topaloglu H, Serdaroglu A, Okan M, Gucuyener K, Topcu M. Improvement of myotonia with carbamazepine in three cases with the Schwartz Jampel syndrome. Neuropediatrics, 1993; 24: 232-4