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Review Article

Clinical Overview and Outcome of Stuve-Wiedmann Syndrome: Systematic Review

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Introduction

Stuve-Wiedemann Syndrome (SWS) is a rare genetic condition with autosomic recessive inheritance, characterized by a combination of skeletal changes, (bowing of the lower limb, severe osteoporosis and joint contractures) and dysautonomic disturbances (episodic hyperthermia, frequent respiratory infections, feeding problems), therefore the disease is classified in both groups of skeletal dysplasias (subgroup of bent-bone dysplasias) and ciliary neurotrophic factor (CNTF) pathway related disorders.

- It is caused by mutation in the leukemia inhibitory factor receptor gene (LIFR; 151443) on chromosome 5p13.
- The SWS was first described by Stuve and Wiedemann in 1971 but the disease was recognized as a unique condition since 2000:
- SWS Initially described as lethal in infancy, yet some SWS patients survive into and, beyond adolescence.
- Although motor development is delayed, Cognitive impairment is not a feature.
- SWS is managed on a symptomatic basis since there is no treatment currently available

Objectives and Methods:

To conduct systematic review of clinical aspects of previous reported cases of SWS in order to better delineate the clinical presentation and natural history of SWS and to provide guidance to improve management of SWS patients

Systematic analysis of the medical literature to identify all published clinical cases of SWS using the online database, until January 1st, 2023. The search query was limited with the terms "Stuve- Wiedemann Syndrome". All the publications identified were included and analyzed.

Discussions:

Prevalence

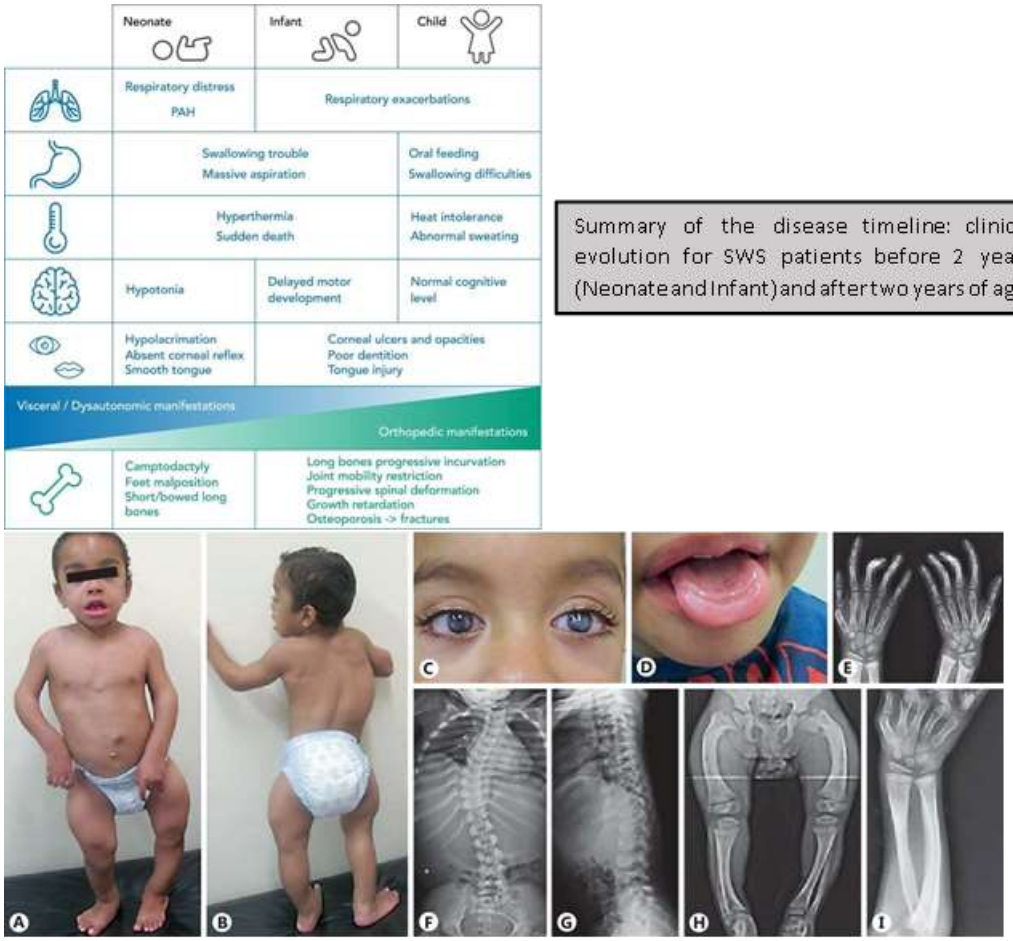
SWS is considered a rare disorder, whose prevalence is unknown.

In the United Arab Emirates population, the prevalence was estimated in 0.52/10,000 births [Al-Gazali et al., 2003.

Clinical Findings and Management

• Clinical presentation of SWS is defined by the association between orthopedic aspects and a pattern of dysautonomia.

• The timeline of the disease is marked by predominant dysautonomic features in infancy with a high mortality rate and prominent orthopedic aspects in childhood with lower risk of life- threatening episodes (Fig.).



Summary of the disease timeline: clinical evolution for SWS patients before 2 years (Neonate and Infant) and after two years of age.

Figure 1

First hallmark of SWS is skeletal dysplasia,

• The individuals affected by SWS present with short and bowed legs associated with joint restrictions, including camptodactyly, feet malposition, and knee and elbow

extension-restricted mobility.

• With age, growth is impaired. There is progressive bowing of the long bones and destruction of the femoral head. Severe spinal deformities arise, along with osteoporosis.

• In order to prevent the progressiveness of the skeletal abnormalities, orthopedic management should start early in the course of the disease.

• Treatment with bisphosphonates, calcium, vitamin D, and/or human growth hormone may be indicated to control osteoporosis and prevent further fractures

Another hallmark of SWS is dysautonomic symptoms.

• Include temperature dysregulation and sweating anomalies. With increased risk for malignant hyperthermia during anesthesia

• Hyperthermic episodes in SWS individuals might be linked to emotional/environmental triggering factors.

• Eye manifestation, There are signs of a reduced corneal reflex and decreased sensation in the eye, with alacrima, and an absent blinking reflex, causing recurrent keratitis with corneal opacities and ulcerations.

• Early protection is mandatory. Frequent follow-up must be done every 3 months.Conservative procedures, such as the use of artificial drops, the use of punctual plug advices or surgical procedure (punctual occlusion) to increase the tear reservoir.

• Smooth tongue appearance with characteristic absence of fungiform papillae.

• Swallowing disorders are probably related to pharyngoesophageal dyskinesia due to an abnormal autonomic control. Nasogastric tube feeding and/or gastrostomy are sometimes required to prevent aspirations and proper feeding.

• Currently, there is no specific treatment for SWS, and management is directed towards the clinical manifestations.

Prenatal abnormalities

• Prenatal skeletal abnormality presented in (80%) patients. The main prenatal ultrasound findings, observed mainly in the second trimester, were mild-to-moderate micromelia and bowing of the lower limb bones.

Conclusions:

• SWS is a rare and severe genetic condition due to pathogenic variants in LIFR gene. Clinical diagnosis criteria includes the association of skeletal involvement with short and bowed long bones, and a dysautonomic pattern,

• Symptoms begin early in life with a high mortality rate in neonates and infants due to dysautonomic involvement. However, in children surviving beyond infancy, mortality rate drops drastically, dysautonomic pattern becomes less severe and orthopaedic aspects are the principal concern with spinal deformations, osteoporosis and increased risk of fractures. Cognitive development is not altered.

• Early, specific and coordinate multidisciplinary care are required to prevent and I manage complications in these patients and provide them with the best quality of life.

• Finally, as a rare disease, SWS requires to be better described through the works of international collaborations to offer care provider dedicated clinical recommendations and better knowledge.

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