Case report of prenatal diagnosis of Stüve-Wiedemann Syndrome in a woman with another child affected too

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Summary

Objective: Stüve-Wiedemann Syndrome (SWS; MIM 601 559) is an autosomal-recessive syndrome characterized by myotonia with mask-like face, skeletal dysplasia and intrauterine growth restriction. Other clinical findings are pursed mouth, hypoplastic midface, congenital contractures and muscular hypotonia. We discuss about the importance of prenatal diagnosis in SWS and the possibility of survival after the first year of life in patients suffering from this disease.

Methods: we report a case of Stüve-Wiedemann Syndrome detected by morphological examination in our Operative Unit. Prenatal presumptive diagnosis was given with two-dimensional and 3-D probe, during the second trimester of pregnancy. Caesarean section was performed at 38th week of gestation. Then diagnosis was genetically performed.

Results: at birth, clinical examination was concordant with the ultrasound findings. Genetic analysis also confirmed the presumptive diagnosis. Episodes of respiratory distress and hyperthermia decreased until it disappeared altogether at 1 year of age.

Conclusion: we underline the usefulness of ultrasound study of fetal skeleton in the prenatal diagnosis. It allowed us to do an early detection of birth defects and their appropriate management.

Key words: Stüve-Wiedemann Syndrome, prenatal diagnosis, management, outcome.

Introduction

Stüve-Wiedemann Syndrome (SWS; MIM 601 559) is an autosomal-recessive syndrome characterized by myotonia with mask-like face, skeletal dysplasia and intrauterine growth restriction (IUGR). Stüve and Wiedemann described the first case in 1971 in two sisters with an early lethal outcome (1). Because of the similar clinical and radiological features, SWS and Schwartz-Jampel syndrome type 2 are considered to be a single entity (2). The syndrome is characterized by short stature, bowing of extremities that affects the lower limbs more than the upper limbs, camptodactyly, respiratory distress/apneic spells and hyperthermic episodes frequently associated with feeding/swallowing difficulties. Other clinical findings are pursed mouth, hypoplastic midface, congenital contractures and muscular hypotonia. Associated malformations are rare. SWS is associated with a significant increase in neonatal mortality mainly because of respiratory insufficiency and malignant hyperthermia that is refractory to therapy (3).

The incidence and prevalence of SWS are not estimated, since they were only a few cases in the world. Dagoneau et al. identified that SWS is caused by mutations in the leukemia inhibitory factor receptor (LIFR) gene on chromosome 5p13 (4). Several mutations in this gene were identified in 19 families affected by this syndrome. In families from the United Arab Emirates (UAE), an identical frameshift insertion (653 654T) was identified, indicating a founder effect in this region.

This syndrome had been considered uniformly lethal until Kozlowski and Tenconi reported a boy surviving beyond 3 years (5). Superti-Furga et al. (2) recognized that the reported SWS survivor was caused by mutations in the leukemia inhibitory factor receptor (LIFR) gene on chromosome 5p13 (4). Several mutations in this gene were identified in 19 families affected by this syndrome. In families from the United Arab Emirates (UAE), an identical frameshift insertion (653 654T) was identified, indicating a founder effect in this region.

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A woman of 39 years, G6P5, came to prenatal diagnosis service of our Operating Unit (Gynecology and Obstetrics Unit, the Department of Obstetrics and Gynecology and Radiological Sciences, University of Catania, Italy) for a second trimester ultrasound examination. In her family and personal history, she had nothing to detect with the exception of previous pulmonary tuberculosis infection in 1990, there was no consanguinity with her partner. The obstetric history showed that she had had a first pregnancy with a male fetus, who died after 23 days of life for suspected brain hemorrhage, a second pregnancy with intrauterine death at 28 weeks for unknown cause, two living sons in apparent good health. In 2002 the woman underwent cesarean section with birth of a female fetus, who showed curvature of the lower limbs, respiratory distress and episodes of hyperthermia. The child was followed by the Gaslini Institute of Genoa, where SWS was diagnosed. The diagnosis was genetically confirmed in Paris, through the identification of LIFR (1620-1621 Lins A) (Leukemia Inhibitory Factor Receptor) mutations. The episodes of respiratory distress are gradually decreased until they disappeared completely, while the episodes of termic dysregulation have continued to persist. During the current pregnancy, the patient didn’t carry out laboratory tests until the 23th week. With morphological examination, performed with two-dimensional and 3-D probe, it was revealed a living female fetus with evident anterior bowing and shortening of the lower limbs, mainly femur and tibia (femur 34.2 mm, tibia 31.6 mm, 32.2 mm fibula below the 5th percentile). 

The fetus also showed camptodactyly and an increase in thickness of the coast (Fig. 1). The amniocentesis was performed with the result of a normal 46, XX karyotype. On the basis of these sonographic findings and the positive obstetric history, the presumptive diagnosis of SWS was given. As the legal limit for therapeutic abortion had been exceeded the couple, it was decided to continue the pregnancy. Caesarean section was performed at 38th week of gestation. The weight of the newborn at birth was 3220 g, with a length of 50 cm and head circumference of 33.8 cm. The Apgar score was 4 and 5 respectively at 1 and 5 minutes after birth: for this reason it was necessary to transfer the newborn to a neonatal intensive care unit. At birth, the child had a particular aspect, presenting facial dysmorphism: short neck, small and wrinkled mouth, large eyes, short upturned nose, low-set ears. On clinical examination it was possible to confirm the ultrasound findings, represented by the marked bowing and shortening of the lower limbs, camptodactyly, hyperextension of forefingers and equinovarus feet. External genitalia were normal (Fig. 2). After birth, chest X-rays and lower limbs were performed, which showed a bell-shaped chest and confirmed anterior bowing of the lower limbs, cortical thickening, wide metaphysis and abnormal trabecular pattern. The newborn was rushed to the intensive care unit, because showed episodes of respiratory distress and, later, recurrent episodes of unexplained thermal dysregulation, with changes in temperature between 34 and 39°C, within hours, difficult swallowing, and generalized hypotonia. Despite severe initial conditions the child is now 1 year old and doesn’t show episodes of respiratory distress and thermoregulation while remains a difficulty in swallowing. The definitive diagnosis of Stüve-Wiedemann Syndrome has been made by genetic analysis of molecular type that showed a deletion at the level of LIFR.
gene, which allowed us definitively differentiation from camptomelic and kyphomelic dysplasia. Episodes of respiratory distress and hyperthermia during the first months of life, have decreased until they disappeared altogether, but difficult swallowing remained and episodes of seizures have occurred.

Discussion

Prenatal diagnosis is a crucial moment in pregnancy history. It allows to detect embryonic or fetal diseases for which it’s possible an appropriate treatment, or alternatively it may identify diseases for which, the option of interruption of pregnancy can be chosen. Ultrasound study of fetal skeleton is an important stage of prenatal diagnosis for the possibility of early detection of birth defects.

In our case report, the fetus showed at 23 weeks ultrasound scan, a shortening and anterior bowing of the lower limbs, camptodactyly and increase of ribs thickness. SWS WAS suspected as the family history was positive for this syndrome. The ultrasound examination of this type of bone dysplasia and the identification of its features seems easier after 20 weeks, because abnormalities, such as bowing of the legs, are difficult to evaluate before. There is no treatment available for this syndrome at the moment. Management is symptomatic and includes most importantly prevention of the lung aspirations which are the main cause of death in the first year of life. Care should be taken with the swallowing problems which are the main cause of aspiration (9). Many of the affected children require nasogastric tube feeding and/or gastrostomy at some stages in infancy and well into childhood. Swallowing improves with age and many of the affected children start eating normally by the second or third year. Early protection of the eyes against repeated trauma, including sunlight, is important in the prevention of visual loss. Prevention of injury to the tongue is also important. This is usually carried out by using a special appliance to cover the teeth until the child is old enough to understand how to avoid unintentionally biting the tongue. Progressive skeletal abnormalities are usually managed by physiotherapy and orthopedic correction. Other features like fracture of the bones and hyperthermia should be recognized and treated early (10).

Conclusion

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References


Figure 2. Marked bowing and shortening of the lower limbs. Normal external genitalia.