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CASE REPORT

Rehabilitation Challenges in Wolcott–Rallison Syndrome: A Case Report

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ABSTRACT

Wolcott–Rallison syndrome (WRS) is a rare autosomal recessive disorder characterized by the association of permanent neonatal diabetes mellitus, spondylo-epiphyseal dysplasia with growth retardation and early tendency to skeletal fractures. Fewer than 60 cases of this have been described in the literature with variable multisystem clinical manifestations. The functional limitations or rehabilitation management has not been considered in the treatment outline of the recorded cases. This case report documents the functional limitations and rehabilitation challenges in a 15-year-old male child with Wolcott-Rallison syndrome.

Keywords: Rehabilitation challenges, Spondylo-epiphyseal dysplasia, Wolcott–Rallison syndrome.

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INTRODUCTION

In 1972, Wolcott and Rallison described a syndrome in three siblings with a combination of infancy-onset diabetes mellitus and multiple epiphyseal dysplasias which is also known as WRS.[1] It is a rare autosomal recessive disorder that manifests itself in early infancy with symptoms of diabetes mellitus. Fewer than 60 cases of this have been reported in the literature.[2]

Short stature and walking difficulties become evident in the second year of life. These skeletal changes are progressive with age. A patient without any skeletal manifestations at age of 32 years has been documented as well.[3]

There is usually a short trunk, excessive lordosis, a short and broad chest, genu valgum and restriction of range of motion involving different joints. In most cases, affected individuals are from populations in which consanguineous marriages are frequent.[3]

Genetic study for a mutation in eukaryotic translation initiation factor 2-alpha kinase (EIF2AK3) confirms the diagnosis.[2]

WRS has a variable multisystem presentation. Recurrent liver failure and hyperglycemia are the most common initial presentations. The diabetes mellitus onset is before 6 months of age with skeletal dysplasia diagnosed before one or 2 years of age.[2]

The prognosis of this condition is poor and patients generally die at a younger age. Death occurs after multiorgan failure with predominant liver and renal dysfunction. Only three patients have been reported with age of 10 or more at the time of death out of 19 patients reported in a review.[4] Two patients with longer survival have been reported with age 32 years for one and 35 years for other.[3]

The literature available over WRS focuses on aetiopathogenesis, genetic study and skeletal manifestations with no description of functional limitation and rehabilitation. This case report documents a 15-year-old male child with WRS and describes the musculoskeletal manifestations with associated functional limitations affecting the rehabilitation of the patient.

CASE REPORT

A 15-year-old male child was brought by his mother to the outpatient department of physical medicine and rehabilitation at All India Institute of Physical Medicine and Rehabilitation (AIIPMR), Mumbai, Maharashtra with chief complaints of inability to stand and walk since 3 years.

He is 1st order male child born to third-degree cousins at term without any significant perinatal event. He developed respiratory distress on day 2 for which he received 2 weeks of treatment in the intensive care unit (ICU).

He was well until 3 months of age when he presented to the local hospital with recurrent episodes of poor feeding, vomiting, dehydration, and jaundice which was diagnosed as diabetic ketoacidosis. He was diagnosed with insulin dependent diabetes mellitus and treated with insulin since then.

The child had recurrent episodes of jaundice since 6 months of age with frequency 2–3 times every year till 4 years of age with the last episode 3 years back. The patient

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was diagnosed with WRS as his X-ray findings were suggestive of multiple epiphyseal dysplasias with persistent early onset diabetes mellitus. A liver biopsy done at the age of 10 years was suggestive of early changes of cirrhosis.

There is no history of similar or any other illness in the family. The child had a history of delayed gross motor developmental milestones with independent walking at the age of 4 years.

He had a fall 3 years back leading to fracture of right femur shaft which was managed conservatively. As reported by mother he stopped standing and walking since then.

Clinical Examination

Cognitively child was normal. Secondary sexual characters were present. On physical examination child was underweight, undernourished with stunted growth. The child had a short neck, brachydactyly, globular abdomen without any palpable viscera, barrel-shaped chest (Fig. 1). There was half inch symmetrical chest expansion and reduced air entry bilaterally.

On musculoskeletal examination, the child had reduced muscle bulk and normal tone in all four limbs. There was a restriction of shoulder flexion and abduction by 40° and 30°, respectively. Elbow and knee flexion deformity of 10^0 and 35°, respectively on both sides were presented with right-sided genu valgum (Fig. 1).

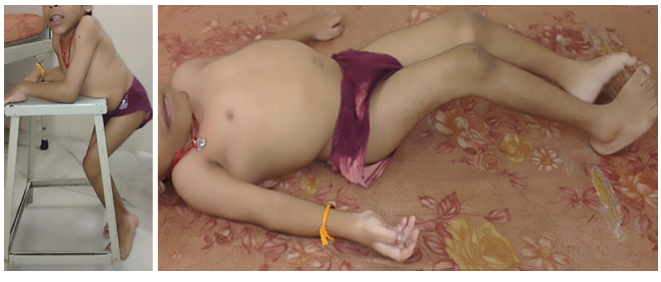

Fig. 1: Clinical findings: child managing to stand with difficulty with maximal support. Short neck, Barrel-shaped chest, brachydactyly, globular abdomen & knee flexion deformity can be seen

There was mediolateral instability at both knee joints and positive telescopy test for both hip joints. Muscle power was grade 4 in all joints of both upper limbs, both hip, ankle and knee joints except knee extension of grade 2 and ankle plantarflexion of grade 3.

Functional Evaluation

Functionally, he had age appropriate hand function with limited overhead activity. He was independent in bathing, grooming, dressing, and eating in sitting posture but dependent for toilet transfers and perineal hygiene.

Mode of indoor ambulation was by crawling or kneeling and outdoors he was carried by mother. He could kneel, do knee walking, and supported squatting. He could climb stairs with support with kneeling and stand with support for 2–3 minutes. He could transfer from lower to the higher height of 18 inches independently.

Investigations

Blood tests revealed anemia, hypocalcemia, raised alkaline phosphatase, HbA_1C 9.6% with fasting and average blood sugar level of 95 mg% and 228.32 mg%, respectively. Thyroid function tests were normal. Urine examination revealed microalbuminuria (32.1 ng/L).

Ultrasound (USG) abdomen was suggestive of the liver span of 10 cm without focal lesion, mild splenomegaly, prominent portal vein, and mild bilateral medical renal disease. X-ray findings (Fig. 2) are as follows:

- X-ray pelvis with both hip joints and lumbosacral spine- platyspondyly, superolateral subluxation of femoral head bilaterally, flat and widened femoral head, shallow acetabulum.
- X-ray both knee: posteromedial bowing of both femur, irregular epiphyses and metaphyses of the femur.
- *X-ray both wrist and hand:* Small dysplastic carpal bones with proximal flaring of metacarpal with short phalanges.

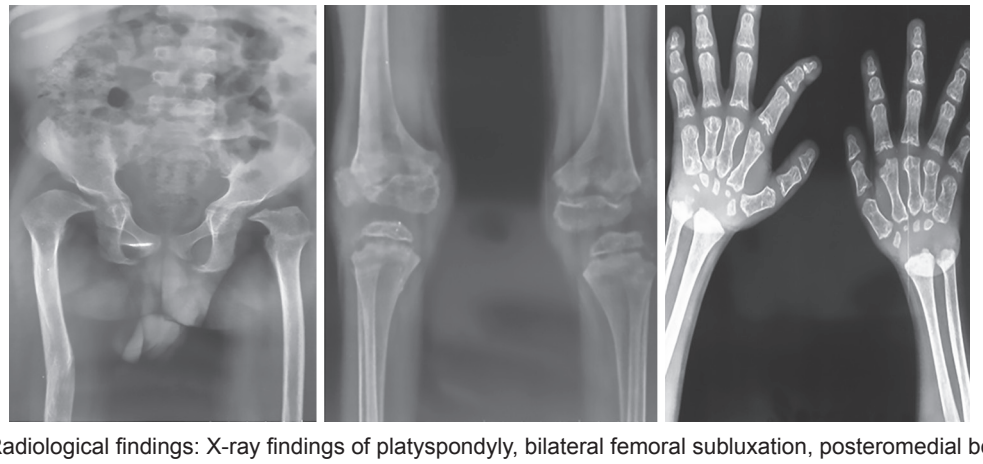

Fig. 2: Radiological findings: X-ray findings of platyspondyly, bilateral femoral subluxation, posteromedial bowing of femur with irregular epiphyses and metaphyses and small dysplastic carpal bones can be seen

Written informed consent of the primary guardian (mother) of the child was taken for the sharing of relevant information and illustrations for this case report.

DISCUSSION

WRS is a rare autosomal recessive disease, characterized by neonatal/early-onset non-autoimmune insulin-requiring diabetes associated with skeletal dysplasia and growth retardation. It is now recognized as the most frequent cause of neonatal/early-onset diabetes in patients with consanguineous parents.[3]

Associated clinical manifestations are frequent episodes of acute liver failure, hypoglycemia, ketoacidosis, renal dysfunction, exocrine pancreas insufficiency, intellectual deficit, hypothyroidism, neutropenia, chances of fracture and recurrent infections.[2]

Close therapeutic monitoring is strictly required for blood sugar levels, liver enzymes, kidney function, and hormonal parameters. The clinical management is mainly concerned about diabetic ketoacidosis, hypoglycemia, hepatic dysfunction and hormonal abnormalities such as hypothyroidism, exocrine insufficiency of the pancreas.[2]

There are less than 60 reported cases with the variable multisystem presentation. The course of the disease is variable due to variable age at onset, severity, and nature of multisystem involvement with a poor prognosis with a life span of a few weeks to 35 years.[2]

There are no cases reported in terms of musculoskeletal manifestations leading to functional impairment of such patients. The reason being a variable clinical presentation, young age at presentation, death before the diagnosis of WRS or inattention by caregivers.

For those patients who are medically stable and following regular treatment, early rehabilitation management should be considered to provide maximum functional independence.

In this case, the child was dependent for his activities of daily living such as overhead activity, transfers, toileting, and perineal hygiene and ambulation. He was dependent for his outdoor ambulation. Manifestations such as restricted shoulder range of motion, deformity of both knee and elbow, subluxation of both hips, muscle weakness, decreased respiratory function were inhibiting factors for effective rehabilitation.

Considering risk involved in anesthesia, the corrective procedures should be avoided. But measures to prevent further deformity and preserve available range and function should be implemented such as proper positioning and static splinting/bracing to prevent further deformity, active or passive range of motion exercises to preserve available range, therapeutic exercises to maintain functional capacity and improve performance. Compensatory strategies for routine activities can be planned based on the patient's functional status. Early identification of the impairments by patient and caregiver education and interdisciplinary approach will help in the implementation of early rehab measures to improve functional independence.

CONCLUSION

Due to the rarity of WRS, many particularities about it remain unknown. By always keeping the prognosis in mind, early rehab interventions should be implemented for such patients not only to improve functional outcome but also to prevent any impairment or deformity and related complications. Close family supervision and professional interdisciplinary approach are required for early and effective rehabilitation in patients with WRS.

REFERENCES

1. Bin-Abbas B, Al-Mulhim A, Al-Ashwal A. Wolcott-Rallison syndrome in two siblings with isolated central hypothyroidism. Am J Med Genet 2002;111(2):187-190.
2. Cécile J, Marc N. Wolcott-Rallison syndrome. Orphanet journal of rare diseases 2010;29;5:1186/1750-1172-5-29.
3. Rubio-Cabezas O, Patch AM, Minton JA, et al. Wolcott-Rallison Syndrome Is the Most Common Genetic Cause of Permanent Neonatal Diabetes in Consanguineous Families. The Journal of Clinical Endocrinology and Metabolism 2009;94(11):4162-4170.
4. Ozbek MN, Senée V, Aydemir S, et al. Wolcott-Rallison syndrome due to the same mutation (W522X) in EIF2AK3 in two unrelated families and review of the literature. Pediatr Diabetes 2010 ;11(4):279-285.