Bethlem Myopathy (Collagen VI-Related Dystrophies): A Retrospective Cohort Study on Musculoskeletal Pathologies and Clinical Course

Rachel Sanislo Silverstein[1], Daniel Wang, Lee Haruno[2], Tim Lotze, Allison C Scott, Scott B Rosenfeld
[1]Texas Children's Hospital, [2]Cedars-Sinai Medical Center

INTRODUCTION:

Collagen VI related myopathies with a pathologic variant in the *COL6A1, COL6A2,* and *COL6A3* manifest as a phenotypic continuum of rare disorders ranging from mild Bethlem myopathy to severe Ullrich congenital muscular dystrophy. Patients have a variable ability to ambulate due to early onset muscle weakness, proximal joint contractures and distal joint laxity. Our purpose was to elaborate on concomitant orthopedic manifestations, potential management strategies, and patient outcomes.

METHODS:

A retrospective cohort study was conducted with 23 patients from two pediatric institutions with a confirmed diagnosis of Bethlem myopathy. Charts were reviewed for demographic data, age of disease presentation and diagnosis, *COL6* genotype, diagnosis method, ambulation status, need for assistance, musculoskeletal abnormalities, other systemic co-morbidities, advanced imaging and screening diagnostics, previous surgical interventions, and progression of disease.

RESULTS:

The mean age was 11.65 years (range 3 to 19 years old). Mean age at initial presentation with symptoms was 4.18 years old, whereas diagnosis was delayed until 8.22 years old. The time period between initial presentation and diagnosis was on average 4.09 years. 10 patients were diagnosed by genetic testing and muscle biopsy, 12 patients were diagnosed by genetic testing only, and one patient was diagnosed only by muscle biopsy. Muscle weakness was the most common presenting symptom (65.2%) and 73.9% of patients required some use of assistive or mobility devices such as braces, walkers, or wheelchairs. Seven (30.4%) patients were diagnosed with scoliosis, four (57.1%) patients required operative intervention with fusion for their scoliosis. Ten (43.5%) patients were found to have acetabular dysplasia, one (10%) patient required open reduction of a dislocated hip, one (10%) required closed reduction with hip spica application, and one (10%) required bilateral periacetabular osteotomies for instability. 21 (91.3%) patients developed foot and ankle deformities such as hindfoot varus, equinovarus, cavus, and pes planus. Seven (33.3%) patients underwent a posteromedial-lateral equinovarus releases and six (28.6%) required an Achilles tendon lengthening. Twenty (86.9%) patients had muscle tendon contractures, the most common locations: ankle (55%) and the elbow (40%).

DISCUSSION AND CONCLUSION:

Although physical manifestations have been considered to be less severe than those of the similarly presenting but more common neuropathies and myopathies including Charcot-Marie-Tooth and Duchenne muscular dystrophy, BM does lead to progressive musculoskeletal deformity and disability. Its relative rarity makes it less familiar to providers and likely contributes to delay in diagnosis. Scoliosis, hip dysplasia, and equinus and varus ankle deformities are the most common musculoskeletal deformities. Physicians and surgeons should appropriately counsel patients and families about the clinical course of this disorder its impact on patient quality of life.