FSHD Masterclass

FSHD Masterclass **Abstracts**

Facioscapulohumeral Muscular Dystrophy (FSHD): Clinical Manifestations

Rabi Tawil, MD

The objectives of this presentation are to familiarize general practitioners, PAs, NPs, and physical therapists with the clinical features of adults with FSHD, how to diagnose the condition, general management, and potential complications. This will be achieved by giving brief background information on the prevalence and genetics of this condition, showing images of the typical physical features of individuals with FSHD, and reviewing the major management issue that occur in this patient population. A survey following the presentation will help assess if the specific learning objectives were met.

Early onset FSHD

Katherine Mathews, MD

This portion of the presentation will focus on the elements of clinical presentation that are more likely to be seen in young children with FSHD. In large families with FSHD, parents and grandparents are often able to recognize subtle features of disease such as sleeping with incomplete eye closure in infancy or early childhood. In the absence of a family history, young children can come to medical attention due to hearing loss, severe retinal disease, or facial weakness. These early onset patients with more severe disease can have more rapid progression of skeletal muscle weakness than patients with more typical onset.

- Learning objective: To be aware of the less-common clinical features seen primarily in young children with FSHD.
- Performance objective: To obtain a thorough FSHD-specific history when a child presents with possible FSHD
- Assessment: Post-conference survey

Facioscapulohumeral Muscular Dystrophy: Genetics, Epigenetics, and Testing

Jacinda Sampson, MD, PhD

In this presentation, the genetics of FSHD1 and FSHD2 will be reviewed. The D4Z4 domain chromosomal structure, the permissive haplotype 4qA role, the role of DNA methylation in gene regulation, and expression of DUX4 will be discussed. Challenges in FSHD1 and FSHD2 genetic testing will be discussed. Detection of FSHD1 contractions will be compared to common genetic testing methodologies such as NextGen sequencing. We will review resources for finding genetic testing labs.

- Learning objectives: To understand the genetic change (deletion) underlying FSHD; to understand what is meant by a permissive haplotype; to understand how FSHD genetic testing is performed.
- Performance objective (tools, resources): To consider FSHD1 testing either prior to, or as a reflex test, with NextGen sequencing neuromuscular test panels when choosing genetic testing; to utilize online resources such as the GeneTestRegistry (GTR) for finding genetic testing labs for FSHD1 or FSHD2
- Assessment: Post-course survey/quiz

Physical Therapy and Exercise

Kate Eichinger, DPT

This session will provide an overview of physical therapy management for individuals with FSHD. In absence of a disease modifying treatment, individuals with FSHD benefit from symptomatic management of their condition. Physical therapy management, while best provided through individualized evaluation and treatment, often addresses common areas including exercise recommendations, use of assistive devices and mobility aids, and orthotics. At the completion of the session, the participant will have an understanding regarding the role of physical therapy and common areas of management for individuals with FSHD and evidence based physical activity and exercise recommendations for individuals with FSHD.

FSHD Swallow and speech concerns

Kiera Berggren, MA/CCC-SLP, MS

This session will provide an overview of orofacial function in FSHD, including the effect on swallow function and speech/communication. The learner will be provided with information regarding orofacial changes in FSHD and their impact on swallow and speech function. After taking the course, the learner will be able to name two changes in swallow function in persons with FSHD with dysphagia and will be able to name two areas of speech impacted by orofacial weakness in persons with FSHD.

Surgical Options in Patients with Symptomatic FSHD

Bassem Elhassan, MD

Understanding the anatomy of the muscles around the scapula, biomechanics of the scapulothoracic articulation, and relation of the scapula to shoulder and arm functions are essential to know how approach and manage patients with symptomatic FSHD. Although scapulothoracic fusion is the classic treatment for advanced muscles atrophy around the scapulothoracic articulation in patients with FSHD, there are additional simpler novel procedures that can also performed and help improve function before performing scapulothoracic fusion.

The learning objectives of this talk are

- To give an overview of the anatomy
- To explain function and biomechanics of the scapulothoracic articulation
- To describe potential surgical options to manage derangement of the scapulothoracic articulation in patients with FSHD.

FSHD – Respiratory Evaluation and Management

Michelle Cao, MD

The aims of the lecture are to discuss the pathophysiology of lung involvement in Facioscapulohumeral muscular dystrophy (FSHD) including respiratory involvement during sleep and in daytime; review the diagnostic criteria and testing for breathing related conditions; and finally, discuss the current treatment options including noninvasive ventilation support. The session incorporates case-base format teaching and learning in order to meet course

objectives. The session will also utilize questionnaires targeted at attendees in order to assess that objectives have been met.

Learning Objectives: Understand the pathophysiology of lung involvement in facioscapulohumeral muscular dystrophy (FSHD); become familiar with the diagnostic criteria and testing for breathing related conditions; develop a treatment plan including noninvasive ventilation support.

Managing Mental Health Issues for FSHD

Kent Drescher, PhD

FSHD is a currently incurable genetic neuromuscular disease that results in lifelong, progressive weakening of skeletal muscle throughout the body. FSHD, produces a wide array of physical problems and additional mental health disease burden. As a genetic disease, FSHD can create family stress around issues of having children, whether and when to get children tested for the disease, and ultimately result in feelings of responsibility or blame directed toward self or others. Caregiving can create relational stresses for the family as well. Stigma about disability, and societal focus on physical appearance can lead to problems with self-esteem and body image. Over time, physical declines steal away many meaningful activities, often generating strong emotional reactions. These challenges add to standard risks for mental health disorders. Effective evidence-based psychological interventions for many mental health problems including anxiety, depression, chronic pain, addiction, and family relationship challenges. Anecdotal evidence suggests some FSHD patients forego regular appointments and stop adhering to clinical recommendations. Mental health interventions for these issues are underutilized. Clinical care for patients with FSHD is enhanced by incorporating evidence-based mental health interventions. This presentation reviews current literature and suggests that evidence-based behavioral treatment can be useful for these issues by enhancing patient psychological flexibility.

Session learning objectives:

- Identify common FSHD mental health challenges
- Review evidence base for mental health interventions in common FSHD problems
- Understand how psychological flexibility can contribute to QoL improvement with FSHD

Molecular pathophysiology, current treatment strategies, and clinical trials

Jeffrey Statland, MD

Facioscapulohumeral muscular dystrophy is one of the most prevalent muscular dystrophies. There are two types: in type 1 deletion of repeated elements on chromosome 4 lead to decreased methylation in the D4Z4 region; in type 2 mutations in chromatin repressors lead to decreased methylation in the same region on chromosome 4. In both the epigenetic change leads to opening of the chromatin structure and expression of a normally suppressed transcription factor called DUX4, which causes disease through a toxic gain of function mechanism. This identifies a target for FSHD specific therapy development. Several strategies are being pursued, and the most advanced try to target or knock-down expression of DUX4. At the same time several efforts are under way to better understand the natural history of FSHD

as measured by strength and motor functional performance to prepare for clinical trials. Here we will review the pathogenic mechanism for FSHD, review several therapeutic approaches in development now, and finally efforts in the field to prepare for clinical trials. At the end of the session we expect learners to be familiar with the genetic cause of FSHD, the proposed pathogenic mechanism, approaches to create disease-targeted therapies, and ongoing efforts towards validating outcome measures and understanding the natural history of FSHD.

FSHD Masterclass **Speaker biographies**

Jamshid Arjomand, PhD. Chief Science Officer at the FSHD Society. A neuroscientist with 15+ years of industry experience, including directing R&D programs using a virtual pharma model through collaboration with academia, contract research organizations and biotech companies.

Rabi Tawil, MD, FAAN, FANA. Professor of Neurology, Professor of Pathology and Laboratory Medicine, University of Rochester Medical Center. Co-Director of MDA Neuromuscular Disease Clinic and Director of the Neuromuscular Pathology Laboratory at the University of Rochester. Fellow, American Academy of Neurology and American Neurological Association, Director, Fields Center for FSHD Research.

Katherine D Mathews, MD, FAAN. Professor of Pediatrics and Neurology and the Vice Chair of Clinical Investigation for the Department of Pediatrics at the University of Iowa Carver College of Medicine. Director of the clinical project at the University of Iowa's Wellstone Muscular Dystrophy Cooperative Research Center, co-PI for the Iowa NeuroNext site and MD STARnet sites. Co-director of the University of Iowa MDA clinic.

Jacinda Sampson, MD, PhD. Clinical Professor of Neurology, Stanford University. Attending neurologist in adult and pediatric Muscular Dystrophy Association clinics. Co-investigator on multiple clinical observational and treatment trials of FSHD with the Stanford Neuromuscular research group. Member of the American Academy of Neurology and the American Society of Human Genetics.

Doris Leung, MD, PhD (Live Q&A panelist). Assistant Professor, Department of Neurology, Johns Hopkins University School of Medicine. Director, Center for Genetic Muscle Disorders, Kennedy Krieger Institute. Board certified: American Board of Psychiatry and Neurology.

Katy Eichinger, PhD, DPT. Assistant Professor in the Neuromuscular Disease Center at the University of Rochester Medical Center. American Board of Physical Therapy Specialties in Neurologic Physical Therapy.

Kiera Berggren, MA/CCC-SLP, MS, is a research speech-language pathologist in the department of neurology at Virginia Commonwealth University (VCU). Member, American Speech-Language-Hearing Association.

Bassem Elhassan, MD. Visiting Professor of Orthopedics Surgery, Mass General Hospital. Program director shoulder fellowship, Co-Chief of Shoulder service. Member of: ASES, AAOS, AAHS, ASSH.

Michelle Cao, MD. Clinical Associate Professor in the Division of Neuromuscular Medicine and Division of Sleep Medicine at the Stanford University School of Medicine. Board certified in Pulmonary Medicine, Critical Care, and Sleep Medicine. Her expertise is in complex sleep-related respiratory disorders and home assisted ventilation for chronic respiratory failure syndromes.

Kent Drescher, MDiv, PhD. Licensed clinical psychologist (retired), National Center for PTSD, VA Palo Alto Healthcare System, Menlo Park CA. Member of Association for Contextual Behavioral Science.

Jeffrey Statland, MD. Associate Professor of Neurology, University of Kansas Medical Center, Kansas City, KS. Co-Director of the Muscular Dystrophy Association Clinics, Co-Director of the FSHD Clinical Trial Research Network. Member: American Academy of Neurology; American Association of neuromuscular & Electrodiagnostic Medicine; and Muscle Study Group Board certified: American Board of Psychiatry and Neurology.

June Kinoshita, Director of Research and Patient Engagement at the FSHD Society. Nonprofit and patient advocacy leader with 30 years' experience in biomedical philanthropy and patient advocacy.