Collagen VI-CMD

(Ullrich Congenital Muscular Dystrophy through Bethlem Myopathy)

Disclaimer: This summary of Collagen VI-CMD has been written by a lay person affected with Collagen VI-CMD and also represents Cure CMD and the Congenital Muscle Disease International Registry (CMDIR). This summary is not intended to replace the care of your physician(s) or the expert advice of a neurologist or pulmonologist familiar with neuromuscular conditions. All statements are generalizations as documented in people with Collagen VI-CMD and may or may not apply to you. As much of the official documentation for surveillance and care of this disorder has been written for children, this summary applies to affected individuals of all ages. However, it is still beneficial to read through the following publications and share them with your healthcare providers (attached):

1. Consensus Statement on Standard of Care for Congenital Muscular Dystrophies
2. Congenital Muscular Dystrophy (CMD): A Guide for Families
3. Guide to Respiratory Care for Neuromuscular Disorders
4. Natural history of pulmonary function in collagen VI-related myopathies
5. Evidence-based guideline summary: Evaluation, diagnosis, and management of congenital muscular dystrophy
6. The Collagen VI-Related Myopathies: Muscle Meets Its Matrix: The Clinical Spectrum of Disease

Collagen VI-CMD is a congenital muscular dystrophy that elaborates abnormal or deficient Collagen VI, a key extracellular matrix protein. Collagen VI-CMD is characterized by distal hyperlaxity, proximal contractures, scoliosis, skin changes (hyperkeratosis pilaris, keloid formation) and progressive respiratory failure. There is no cardiac involvement other than right-side heart strain that can develop as the result of poorly managed respiratory failure.

Collagen VI-CMD is a spectrum disorder that ranges from mild/late onset (also known as Bethlem Myopathy) to an intermediate phenotype, to severe/early onset (also known as Ullrich Congenital Muscular Dystrophy). Those with the intermediate to mild phenotype typically gain and maintain the ability to walk into adulthood and experience slower disease progression. Individuals with an intermediate to severe phenotype typically never gain the ability to walk or lose the ability to walk in childhood.

The relative prevalence of Collagen VI-CMD is still unknown; however a recent publication out of Italy estimates it at 0.1 per 100,000. Other studies have put it as high as 0.9 per 100,000. The Congenital Muscle Disease International Registry (CMDIR) currently has 285 registrants identified with Collagen VI-CMD ranging in ages from infancy to 72 years.

The primary driver of mortality in Collagen VI-CMD is respiratory insufficiency. Weak intercostal and diaphragm muscles as well as contractures that develop in the joints between the intercostal muscles can cause rigidity in the chest wall. Scoliosis or curvature of the spine can also contribute to respiratory insufficiency. Breathing function and the ability to cough typically declines with age and have been shown to decline faster in people who have lost the ability to walk. Sometimes, the affected individual does not realize their respiratory function is declining; it can happen very slowly over a long period of time. Respiratory insufficiency can be indicated if the affected individual has signs of day time fatigue, morning headaches, irritability, changes in weight, or lack of appetite. These symptoms are most likely the result of CO2 retention due to under (hypo) ventilation.

Surveillance of pulmonary function is vitally important and includes:

1. Pulmonary Function Testing (PFT) measuring Forced Vital Capacity (FVC) and Cough Peak Flow (CPF). An FVC of less than 80% predicted indicates the need for a Sleep Study (PSG) and possible night time non-invasive ventilation (BiPAP). It is important to perform PFTs both sitting and lying down. The impact to the diaphragm will be indicated in the difference in FVC between the sitting and supine positions. This test should be repeated every six months to evaluate the rate of respiratory decline.
2. Sleep Study (Polysomnography) paying particular attention to incidents of apnea and CO2 retention. The presence of CO2 retention indicates under (hypo) ventilation and the need for non-invasive ventilation (BiPAP/ventilator) while sleeping and possibly during waking hours. This test should be repeated annually to evaluate the rate of respiratory decline and to adjust the settings of the BiPAP or ventilator.
3. If the PFT and Sleep Study indicate there has been a possible long term, untreated respiratory issue, an Echocardiogram should be performed to ensure there is no right-side heart strain as a result of prolonged respiratory insufficiency.

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Illness

If the affected individual develops a respiratory illness or infection, their ability to expel mucous can be compromised and their chances for developing atelectasis (compressed lung tissue) or pneumonia are increased. If the oxygen saturation level is below 92%, it is important in these instances to deliver positive air pressure via a cough assist, BiPAP machine or ventilator to increase the volume of air delivered to the lungs. The instinct is often to deliver oxygen, but oxygen alone cannot overcome the issue. A small device called a pulse oximeter can be obtained at your local drug store or online without a prescription for under $25. It is important for everyone affected with a neuromuscular condition to own one so that oxygen saturation, particularly when ill with a respiratory virus or infection, can be monitored.

Individuals affected with any neuromuscular disorder as well as those they come into frequent contact with should get an annual flu shot. The injection version that contains a dead virus rather than the mist version that contains a live virus is recommended for both the affected individual and their families/care givers. The flu shot can take several weeks to take effect so it is important to obtain your flu shot as soon as possible, at the beginning of flu season.

Surgeries and Procedures that Require Anesthesia

Collagen VI-CMD is associated with very specific issues that can be exacerbated by surgeries if everyone on the care team is not well advised. In the past few years, several individuals with Collagen VI-CMD known to Cure CMD have had life threatening complications during surgery as a result of the "difficult airway" associated with this disorder. Some had only mild respiratory insufficiency. It is imperative that potential issues during and after surgeries be communicated to the care team, especially anyone who will be involved with the procedure or aftercare. This includes a pulmonologist familiar with neuromuscular disease, the anesthesiologist assigned to your case, and the hospitalists, nurses, and respiratory therapists who will monitor post-op care.

The following applies to many people with a neuromuscular condition, and specifically Collagen VI-CMD:

- **"Difficult Airway"**
- Small, narrow mouth and throat
- Highly arched palate
- Jaw contractures, neck and shoulder contractures, scoliosis, and "limited range of motion"
- Rigid chest walls with contractures in the joints between intercostal muscles
- Limited diaphragmatic excursion
- Lower lung volumes
- Tendency for osteopenia or osteoporosis, depending on the degree of mobility
- Often unable to lie flat, requiring support beneath any contractures that have developed

These factors can make intubation very difficult, especially in an emergent situation. The anesthesiologist will need a standard intubation plan and backup plan(s) as well as a bedside tracheostomy kit should it become necessary as a last resort.

Extubation (removal of breathing tube) after a procedure should only be done after consideration as to how easily re-intubation can be accomplished should a respiratory crisis occur during post-op recovery. Connection to a BiPAP machine or ventilator should be made immediately after extubation to ensure the delivery of sufficient lung volumes during recovery.

Some other post-op risks healthcare providers should monitor for based on experiences of those with this disorder:

- Atelectasis, pneumothorax, pleural effusion, and hemothorax have been documented in post-operative patients with Collagen VI-CMD
- Pain management must be closely monitored as most pain medications suppress respiratory function
- Hypercapnia or retained CO2 caused by too much oxygen delivery is common: a capnography monitor in line with breathing equipment should be utilized at all times during recovery
- Worsening contractures and muscle loss due to ongoing immobility while in recovery are key factors in the overall decline of health: gentle stretching and movement of limbs should be done several times a day while hospitalized in an effort to preserve easily lost motor function and range of motion

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This document is only a summary of possible complications and the recommended surveillance and care of Collagen VI-CMD. If proper care of this disorder by physicians is not available locally, we recommend that you request an appointment at the National Institutes of Health with Dr. Carsten Bönnemann or Dr. Reghan Foley. Both are pediatric neurologists who specialize in this disorder, and will also see affected adults. Inquires can be made through their genetic counselor:

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National Institute of Neurological Disorders and Stroke Neurogenetics Branch
Neuromuscular and Neurogenetic Disorders of Childhood Section
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For more information or questions about Collagen VI and other CMD disorders:

Web: www.curecmd.org
Web: www.cmdir.org
Facebook: Cure CMD

Email: counselor@cmdir.org

Facebook Support Groups (private, by invitation only):
Ullrich CMD (Intermediate to Severe Collagen VI) Facebook Support Group
Bethlem Myopathy (Mild to Intermediate Collagen VI) Facebook Support group
Cure CMD Support Group