

Breathing and CMT

While uncommon, some particularly severe forms of CMT can affect breathing.

BY MICHAEL E. SHY, MD, CMT CLINIC, UNIVERSITY OF IOWA HOSPITAL

We receive a number of questions in our CMT clinic about how Charcot-Marie-Tooth disease affects breathing. CMT affects peripheral nerves called “somatic nerves” that carry motor and sensory information to and from the brain. These include the phrenic nerve that goes to the diaphragm and the intercostal nerves that go to the rib cage. Both the phrenic and intercostal nerves are necessary for these muscles to contract during respiration. When they don’t function, breathing is impaired.

Like many other somatic nerves that go to the arms and legs, the phrenic and intercostal nerves are myelinated, so both the myelin and the axon surrounded by the myelin can be affected by CMT. The question then becomes how severely CMT damages these nerves. The answer depends in part on the specific type of CMT a patient has and how severely CMT affects him or her. The bottom line is that most patients with CMT do not develop clinical evidence of breathing problems even if some abnormalities can be detected on detailed evaluations.

Most Patients

CMT1A, the most common form of CMT, is slowly progressive and has slow nerve conduction velocities. Even though clinical symptoms typically affect the lower legs and hands, all myelinated somatic nerves will have slow nerve conduction velocities. The reason that hands and feet are affected clinically has to do with interactions between abnormal myelin and their axons. These abnormal interactions cause weakness at distal body parts (feet and hands), which are at the furthest ends of the longest nerves. The phrenic or intercostal nerve conduction velocities are also slow in patients with CMT1A; however, partly because these nerves are not as long, patients with CMT1A rarely develop significant respiratory or breathing problems. The same is true for other common types of CMT such as CMTX.

Unusual Patients

Unfortunately, some particularly severe forms of CMT can affect breathing. In these cases, a profound weakness is usually present in infancy or early childhood. As with other neuromuscular diseases such as muscular dystrophy or spinal muscular atrophy, children have in rare cases died because of respiratory failure. Some adults with very severe forms of CMT have also succumbed because of respiratory problems. In these rare cases, patients suffer from what is called “restrictive” lung disease and become unable to breathe without ventilator support. To emphasize, these cases are very rare, but they illustrate that CMT is not always a “mild” or slowly progressive disorder.

Diaphragmatic Impairment and Pulmonary Evaluation

From time to time, particularly in cases of CMT4 or CMT2, patients have developed phrenic nerve abnormalities that result in phrenic nerve impairment so that one-half of the diaphragm becomes paralyzed or doesn’t move. The phrenic nerves are constructed so that one connects to the right side of the diaphragm and the other connects to the left. I have never seen a case that progressed to the point that neither phrenic nerve functioned, although even then a patient would still have intercostal nerves to help with breathing. In situations with phrenic nerve paralysis, patients often ask us about diaphragmatic pacing through electrical stimulation of the nerve. To the best of my knowledge, this has not been shown to work. When we see patients with impaired respiratory function, we have them

evaluated by a pulmonologist (lung specialist) who has experience in neuromuscular diseases including CMT. They typically perform pulmonary function tests (PFTs) and blood tests that can help measure the volume of air patients can move in and out of their lungs, the force they can use to inhale and exhale, and the amount of oxygen that makes it into their blood. Results from these tests provide guidance as to what, if any, therapy is required.

Sleep Apnea

It is increasingly recognized that patients with all types of CMT may develop sleep apnea. Sleep apnea—repetitive pauses in breathing at night—may be caused by obstructions in the upper airway, which may be caused by CMT, although the exact mechanism is unknown. Sleep apnea can result in daytime drowsiness and fatigue. It is typically associated with heavy snoring at night. Sleep apnea can be treated by techniques such as continuous positive airway pressure (CPAP) masks, although these devices can be uncomfortable to wear.

Vocal Cord Paralysis

Some patients, particularly those with CMT2A or CMT4A, have been identified with paralysis of at least one side of their vocal cords. This can make it difficult for them to generate force or loudness when speaking. It can be associated with shortness of breath. We usually have these patients evaluated by ENT (ear, nose and throat) specialists, who are best equipped to evaluate vocal cord function. Artificially building up the vocal cords is a concern in these situations because of the potential for the vocal cord to close the airway. In extreme cases surgical interventions such as tracheostomies may be necessary.

Summary

What I presented above is a summary based on our experience from over 20 years of running CMT clinics. While I believe this information to be correct, many issues concerning breathing in different forms of CMT have yet to be studied in controlled trials. Details of respiratory function in patients with CMT are not yet available, though we are starting to address this in our Inherited Neuropathies Consortium (INC) with support from the CMTA. Over the years, we have performed some studies of pulmonary function tests in patients with CMT1A and these have generally been normal, although we have not looked at changes over time. Clearly, more work needs to be done with this important issue. In the meantime, we also need to encourage patients not to smoke or do any other activities that are harmful to their lungs.