Myotonic Dystrophy FOUNDATION

Consensus-based Care Recommendations for Adults with Myotonic Dystrophy Type 1

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Due to the multisystemic nature of this disease, the studies and rigorous evidence needed to drive the creation of an evidence-based guideline for the clinical care of adult myotonic dystrophy type 1 (DM1) patients are not currently available for all affected body systems and symptoms. In order to improve and standardize care for this disorder now, more than 65 leading myotonic dystrophy (DM) clinicians in Western Europe, the UK, Canada and the US joined in a process started in Spring 2015 and concluded in Spring 2017 to create the Consensus-based Care Recommendations for Adults with Myotonic Dystrophy Type 1. The project was organized and supported by the Myotonic Dystrophy Foundation (MDF).

A complete list of authors and an overview of the process is available in Addendum 1. A complete reading list for each of the study area sections is available in Addendum 2.

The Board of Directors of the American Academy of Neurology formally affirmed the value of the Consensus-based Care Recommendations for Adults with Myotonic Dystrophy Type 1 as an educational tool for neurologists.

An Update Policy has been adopted for this document and will direct a systematic review of literature and appropriate follow up every three years. Myotonic Dystrophy Foundation staff will provide logistical and staff support for the update process.

A Quick Reference Guide extrapolated from the Consensus-based Care Recommendations is available here **https://www.myotonic.org/toolkits-publications**

For more information, visit www.myotonic.org.

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Surgery, anesthesia and pain control

Background

DM1 patients are far more likely than the general population to have adverse reactions to medications used for anesthesia and analgesia, and interactions of the cardiac, respiratory, muscle and central nervous systems in DM1 patients can lead to a variety of untoward responses before, during and after surgery. Serious adverse events have been reported even in patients whose overall DM1 symptoms were mild.

See *MDF's Practical Suggestions for the Anesthetic Management of a Myotonic Dystrophy Patient and Anesthesia Quick Reference Guide* at **https://www.myotonic.org/toolkits-publications**

In addition, behavioral and cognitive abnormalities need careful assessment and management preoperatively (if possible) since these manifestations, along with hypersomnia and preoperative sleep deprivation, can complicate the patient's immediate postoperative care and long term recovery.

Anesthetic risks, as detailed in the MDF anesthesia guidelines referenced above, result from DM effects that include the following:

- Cardiac conduction defects and potentially fatal arrhythmias
- Ventilatory insufficiency and poor airway protection
- Gastrointestinal dysmotility that frequently results in pseudo-obstruction and can lead to aspiration
- Erratic responses to succinylcholine (although DM1 does not increase true malignant hyperthermia reactions, this drug should not be used in DM1 patients because of the risk of masseter spasm and hyperkalemia)
- Prolonged and heightened sensitivity to sedatives and analgesics, resulting in serious complications in the post-anesthesia period. After-anesthesia risk of aspiration and other complications, including delayed onset apnea and respiratory failure, is increased due to the following drug-induced effects:

    a. Reduction in level of consciousness
    b. Exaggerated ventilatory weakness

c. Pharyngeal dysfunction with reduced airway protection
d. Gastrointestinal dysmotility and potential pseudo-obstruction

Recommendations

1. For procedures requiring anesthesia, see *MDF's Practical Suggestions for the Anesthetic Management of a Myotonic Dystrophy Patient and Anesthesia Quick Reference Guide* at **https://www.myotonic.org/toolkits-publications**
2. Monitor during anesthetization for untoward responses and interactions of the cardiac, respiratory, skeletal muscle and central nervous systems before, during and after surgery
3. Monitor for serious adverse events, even if patient's DM1 symptoms are mild
4. Carefully monitor behavioral and cognitive abnormalities preoperatively (if possible); these manifestations, along with hypersomnia and preoperative sleep deprivation, can complicate the patient's immediate postoperative care and long term recovery
5. Note: most serious complications occur in the post-anesthesia period

Life-threatening symptoms

Respiratory management

Background

DM1 patients often have significant breathing problems that can result from muscle weakness of the diaphragm, abdominal and intercostal muscles and myotonia of these muscles, leading to poor ventilatory force and resulting in low blood oxygen and elevated blood carbon dioxide levels. Chronic respiratory impairment is the primary cause of mortality and morbidity in patients with DM1.

Excessive daytime sleepiness (EDS) and respiratory failure are both common in DM1 and both significantly reduce quality of life. Their causes may overlap, but some sources believe that EDS in DM1 is mostly due to primary central nervous system involvement and that respiratory insufficiency or failure is mostly due to respiratory muscle weakness. That said, insufficient air flow during sleep may contribute to disrupted sleep and excessive daytime fatigue, and central nervous system factors may contribute to the breathing difficulties associated with DM1.

Weakness of the inspiratory and expiratory muscles reduces cough effectiveness and impairs clearing of secretions, leading to an increased risk of pulmonary infections and to aspiration of material into the lungs. Weakness of the swallowing muscles can add to the risk of aspiration of food and drink, saliva, nasal secretions and stomach fluids.

General anesthesia and intravenous pain medications, especially opiates, often cause respiratory failure in patients who were previously clinically stable, highlighting the need for careful perioperative management of patients with DM1.

Recommendations

Monitor at baseline and serially.

Look for:

a. Ineffective cough, recurrent pulmonary infections , a Forced Vital Capacity value of less than 50% of predicted normal values or an MIP of less than 60; if present evaluate every 6 months or more frequently for:

   I. History and frequency of chest infections

   II. Respiratory rate, auscultation, assessment of chest wall motion and recruitment of abdominal muscles (as minimum components of a pulmonary exam)

   III. Orthopnea, dyspnea, poor sleep, morning headaches, apnea, fatigue and snoring

Test for:

a. Forced vital capacity (FVC) and forced expiratory volume in one second (FEV1) in the sitting and supine positions if possible; respiratory muscle strength evaluation with the maximum inspiratory pressure (MIP) and maximum expiratory pressure (MEP) in the upright and supine position, nocturnal oximetry and a cough peak expiratory flow every 6 months

b. Prominent snoring, nightly interrupted sleep, an MIP value of less than 60 or an FVC of less than 50 percent of predicted via a sleep study or other respiratory test. In general the threshold for obtaining a sleep study in DM1 patients should be low

c. Clearance capacity and other respiratory assessments prior to surgery; if needed, adaptation to nocturnal noninvasive ventilation or to cough-assist devices should also occur prior to surgery (see Surgery, anesthesia and pain control)

Treat with:

a. Vaccinations for influenza and pneumonia if no contraindications. Patients with respiratory infections should be treated as soon as possible using standard medical therapy, as well as respiratory cough assistance and mechanical ventilation (as needed). Obtain consultations from respiratory therapy and pulmonary medicine groups as needed

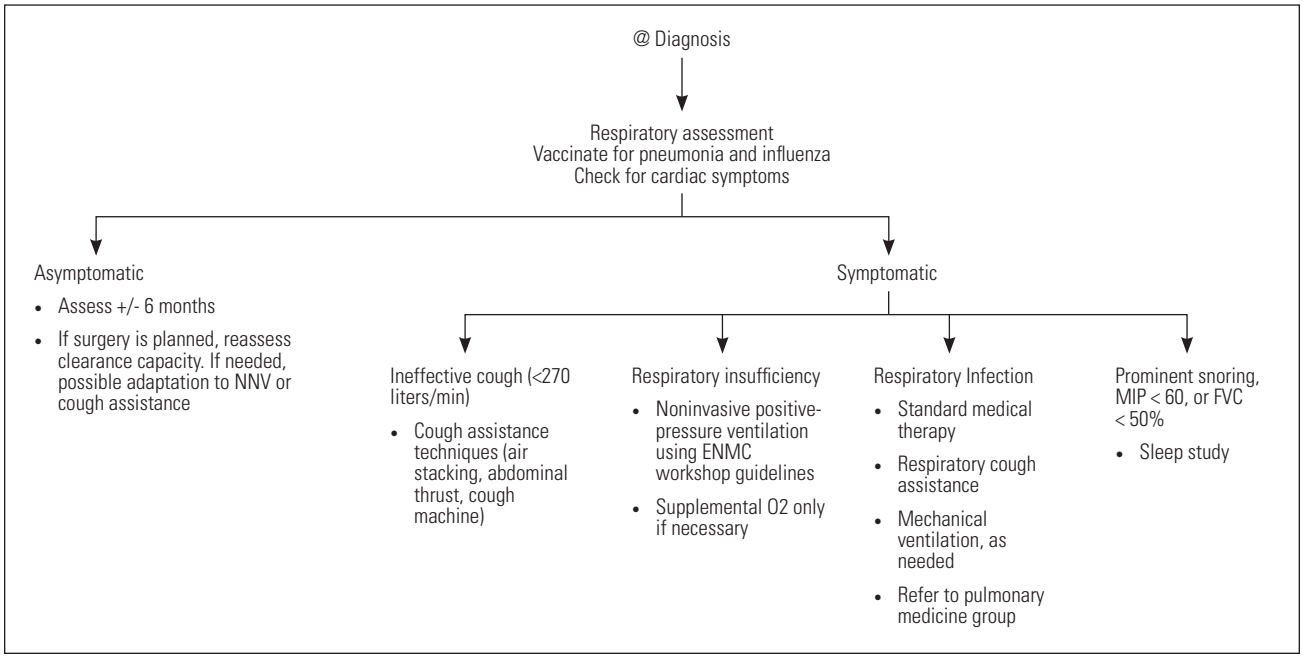
b. Airway clearance and lung volume recruitment techniques (e.g., breath stacking, abdominal thrust, the vest and the mechanical insufflator/exsufflator) for DM1 patients with ineffective cough (cough peak flow of less than 270 liters/minute), and during chest infections and perioperative periods (see Surgery, anesthesia and pain control)

c. Noninvasive positive-pressure ventilation (NIV) for respiratory insufficiency in patients who have respiratory muscle weakness and sleep-related breathing disorders. Some patients will progress to requiring nighttime ventilatory support and full-time ventilation. Noninvasive positive-pressure ventilation should be performed according to the criteria defined in the respiratory consensus ENMC [European Neuromuscular Centre] Workshop (2014-07-21)

d. Supplemental oxygen with caution in conjunction with noninvasive ventilation (see Surgery, anesthesia, and pain control)

e. Emergency medical alert devices prophylactically

Fig. 1 Respiratory Care Recommendations Flowchart



Life-threatening symptoms

Cardiovascular management

Background

DM1-related cardiac pathophysiology, although affecting all myocardial tissue, preferentially targets the cardiac conduction system. Conduction system defects are progressive and, while initially asymptomatic, increase the risk for symptomatic arrhythmias.

Clinical presentations include pre-syncope, syncope, palpitations, dyspnea, chest pain or sudden death from cardiac arrest. Sudden cardiac death is a common cause of death in adults with DM1, second only to respiratory failure. The high incidence of sudden cardiac death underlies the importance of a comprehensive cardiac assessment in order to risk-stratify the DM1 patient.

The evaluation of the severity of cardiac conduction involvement is done by cardiac testing, including the 12-lead electrocardiogram (ECG), long-term ambulatory ECG monitoring, and, for patients at increased risk, an invasive electrophysiological study.

Patients with DM1 are at risk of both bradyarrhythmias and tachyarrhythmias. Pacemakers can be implanted in DM1 patients, either to treat symptomatic bradyarrhythmias or prophylactically in those at high risk for complete heart block.

The most common tachyarrhythmias are atrial fibrillation and atrial flutter, which pose a risk of cardiogenic embolism and stroke. DM1 patients are also at an increased risk of ventricular tachyarrhythmias (tachycardia or fibrillation), a mechanism responsible for cardiac arrest. Implantable cardioverter-defibrillators (ICDs) can be installed in DM1 patients who have survived an episode of a ventricular tachyarrhythmia or, prophylactically, in those at high risk for a ventricular tachyarrhythmia.

Sudden cardiac death has been observed in DM1 patients with pacemakers or ICDs, raising the question of a non-arrhythmia mechanism for this phenomenon.

Imaging studies, including echocardiography, computerized tomography (CT), magnetic resonance (MR), and nuclear imaging can be used to assess the heart's mechanical status, including left ventricular function. Asymptomatic abnormalities are observed in a moderate number of adults with DM1 and are more common in those with conduction system disease.

The development of a dilated, non-ischemic cardiomyopathy is an infrequent but recognized occurrence in adults with DM1. Once a symptomatic dilated cardiomyopathy is present, progression is typically rapid, with congestive heart failure leading to death.

Recommendations

General:

a. Encourage use of emergency medical alert devices

Look for:

a. Palpitations, pre-syncope, syncope, dyspnea and chest pain; if observed direct patient to seek prompt attention

b. Arrhythmias including sinus bradycardia, heart block, atrial fibrillation and flutter, and ventricular tachycardia. Evaluate and treat using ACC (American College of Cardiology)/AHA (American Heart Association)/ESC (European Society of Cardiology) Guidelines for Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death (see **https://www.ncbi.nlm.nih.gov/pubmed/16949478**)

c. Symptom change, abnormal cardiac imaging, abnormal ECG in all DM1 patients; exam should be conducted by cardiologist or electrophysiologist knowledgeable about cardiac manifestations in DM

Test for:

a. Symptoms via a 12-lead ECG should be done at DM1 diagnosis; conduct at diagnosis and approximately annually thereafter

b. Impulse or conduction abnormalities on a standard 12-lead ECG including sinus rate < 50 BPM, PR interval > 200 ms, QRS duration > 100 ms including left or right bundle branch block, left anterior or posterior fascicular block, 2nd or 3rd degree AV block, abnormal Q-waves, atrial tachycardia, fibrillation, or flutter, and ventricular arrhythmias - indicate cardiac involvement

c. Heart failure if abnormal ECG indicative of conduction disease or if other symptoms suggestive of heart failure are present; conduct echocardiograph

Treat with:

a. Serial periodic clinical cardiology evaluations; cardiology consultations are essential in patients with abnormal electrocardiograms and/or cardiac symptoms

b. Consider a primary prevention pacemaker or ICD in a DM1 patient found to be at high risk of cardiac arrest or sudden cardiac death from abnormalities detected via noninvasive or invasive cardiac testing, even in the absence of a guideline-based indication

c. Consider performing cardiac imaging in DM1 patients at diagnosis and every three to five years thereafter, even in the absence of symptoms or abnormalities on cardiac testing

    i. Cardiac imaging modalities other than echocardiography are reasonable alternatives for testing if symptoms being assessed and local expertise warrant

d. Invasive electrophysiology when there is concern about a serious conduction block or arrhythmia because of abnormalities detected via noninvasive cardiac testing

e. Appropriate pharmacological and device therapies based on the ACCF (American College of Cardiology Foundation)/AHA (American Heart Association) Guideline for the Management of Heart Failure (see **https://www.ncbi.nlm.nih.gov/pubmed/23747642**) if heart failure or reduced left ventricular systolic function is present

f. A primary (prophylactic) or secondary (symptomatic) prevention pacemaker or ICD based on the ACC (American College of Cardiology)/AHA (American Heart Association)/HRS (Heart Rhythm Society) Guidelines for Device-based Therapy of Cardiac Rhythm Abnormalities (see **https://www.ncbi.nlm.nih.gov/pubmed/18498951**). This care needs to be under the management of a cardiologist and coordinated with the patient's primary care provider and other consultants as necessary

i. Patient and family preference and the assessment of other risk factors affecting morbidity and mortality should be considered in the decision to implant a pacemaker or ICD in a patient with DM1

g. Ambulatory Holter ECG monitoring – either short-term (24-48 hours) or long-term (30 days or more) – to detect mechanisms of arrhythmias in patients with cardiac symptoms. Periodically repeat such monitoring every 3-5 years if indicated by symptomatic status or if change observed on serial 12-lead ECG

Refer to:

a. A cardiology center experienced in care of DM1 patients with cardiac symptoms, abnormal annual or biennial ECG indicative of cardiac involvement, and DM1 patients over age 40 years without previous cardiac involvement. However, cardiology referral for all DM1 patients is reasonable if part of a multidisciplinary program or if the practitioners providing primary care are unfamiliar with cardiac history, exam, and ECG assessment

b. An anesthesia practitioner, separate from the operating physician, to provide procedural sedation and monitoring for electrophysiology studies and pacemaker or ICD implantation. Perform these cardiology studies and associated anesthesia/sedation in a clinical environment that allows immediate endotracheal intubation and ventilation to be fully prepared to care for those patients who develop post-sedation respiratory insufficiency or respiratory failure (see Surgery, anesthesia and pain control)

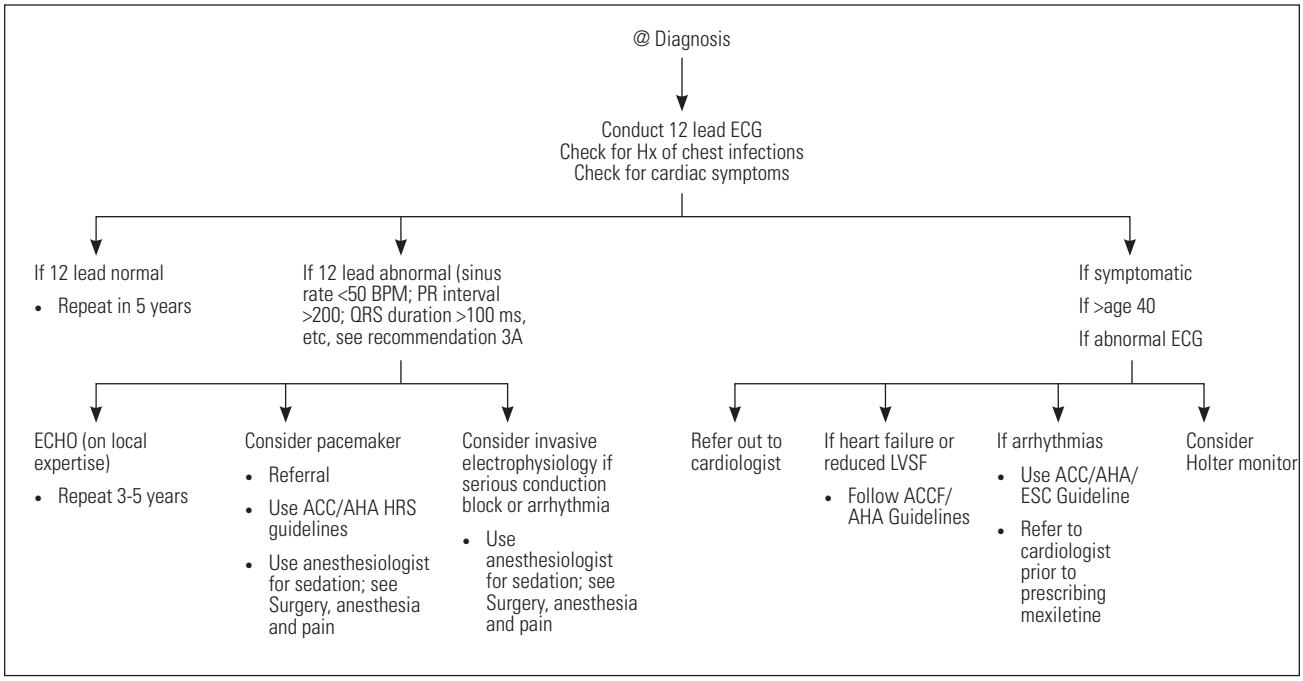
c. The DM clinical experts who developed these recommendations did not reach consensus on the protocol for prescribing and monitoring mexiletine

   Neurologists expert in DM1 care consider mexiletine an effective treatment for myotonia in patients without cardiac abnormalities, particularly congenital and childhood-onset patients. Their recommendation regarding mexiletine and cardiology included obtaining a ECG (electrocardiogram) prior to use, a second follow up ECG within 3 months and serial monitoring

   Cardiologists expert in DM1 care noted that mexiletine is a class 1B anti-arrhythmic that can provide relief for myotonia and sometimes atrial fibrillation. They recommend that the use of any anti-arrhythmic in a DM1 patient begin with a workup to rule out underlying structural or functional abnormalities that may complicate its use. They further recommend monitoring during drug initiation and that mexiletine-related monitoring be conducted by a cardiologist experienced in the treatment of DM1 patients

   For more information see the Cardiac and Myotonia reading lists in Addendum 2.

Fig. 2 Cardiac Care Recommendations Flowchart



Life-threatening symptoms

Pregnancy and obstetrics management

Background

The deleterious effects of DM1 on both smooth and striated muscle can complicate pregnancy, labor and delivery. Added to these maternal complications is the possibility that the baby may have congenital-onset DM1, with severe neonatal complications, including respiratory and swallowing abnormalities. Women with DM1 have a higher than average rate of spontaneous abortion and stillbirth, although most can expect to have a normal vaginal delivery.

Mothers with DM1 are more likely than the general population to experience the following:

- Ectopic pregnancy
- Premature delivery
- Prolonged labor and delivery related to both uterine muscle dysfunction and skeletal muscle weakness
- Postpartum hemorrhage due to inadequate uterine contractions or retained placenta
- Uterine over distention with polyhydramnios (because of impaired swallowing of amniotic fluid by a fetus with congenital DM1), which can lead to preterm labor, inadequate uterine contractions during labor, premature rupture of the membranes or postpartum hemorrhage.
- Untoward reactions to analgesia or anesthesia during labor and delivery
- Diminished ovarian reserve with delayed appearance of human chorionic gonadotropin (HCG) due to gonadal insufficiency

Babies with congenital-onset DM1 may have the following:

- Swallowing difficulties, leading to polyhydramnios during pregnancy and poor feeding at birth, possibly requiring tube feeding
- Respiratory muscle abnormalities, possibly requiring mechanical ventilation at birth
- Poor muscle tone and lack of fetal movement
- Abnormal presentation
- Club foot
- Abnormal accumulation of fluid in the body
- Enlarged ventricles in the brain
- Arthrogryposis

Preimplantation genetic diagnosis can allow selective implantation of unaffected embryos. Prenatal diagnosis by amniocentesis or chorionic villus sampling can allow for termination of an affected pregnancy. It can also prepare the obstetric team for the birth of a DM1- affected baby (see Genetic counseling).

Recommendations

Look for:

a. A patient's reproductive history and DM1-related personal and family history, including current DM1 symptoms

b. Fatigue with more rapid onset than average during labor and increased risk of post-partum hemorrhage (PPH). PPH should be particularly anticipated where there has been a prolonged first or second stage of labor, especially if there has been polyhydramnios

Test for:

a. Preimplantation genetic diagnosis to determine whether the embryo is affected or prenatal genetic diagnosis to determine if the fetus has the DM1 genetic expansion (see Genetic counseling)

Treat with:

a. High-risk obstetrician (Maternal-fetal medicine specialist) for prenatal care and delivery

b. Analgesics or sedating anesthetic drugs should be used extremely carefully because of the high risks associated with these in DM1, particularly during pregnancy, especially during the third trimester and during delivery (see Surgery, anesthesia, and pain control)

c. Emergency medical alert devices

d. Pediatric or neonatal specialist at delivery if the mother is affected with DM1, due to risk of congenital onset when maternally inherited

e. Availability of neonatal intensive care, including possible tube feeding or ventilatory support, for neonates known, or suspected to have DM1

Refer to:

a. Pediatric/neonatal subspecialist, even when the fetus is known to be unaffected by DM1

b. Consulting obstetrician before a decision to induce labor is made

c. Genetic counseling services and family planning services

Severe symptoms

Skeletal muscle weakness and rehabilitation

Background

Skeletal muscle weakness is a major feature of DM1. The weakness, which is associated with a dystrophic process, is bilateral and progresses at the relatively slow rate of 1 to 3 percent per year. With time, it impedes mobility and activities of daily living. In general, flexors weaken more than extensors, and distal muscles weaken before proximal muscles. Substantial proximal weakness is usually a late feature of DM1, although some patients develop shoulder- and hip-girdle weakness early. Back and abdominal muscles are also affected. Bone abnormalities of the skull create elongated facial features and other impacts including jaw and palate abnormalities. Some may require surgical intervention. (See Surgery, anesthesia, and pain).

Typical effects of adult-onset DM1 on skeletal muscle include the following:

- Weakness and atrophy of the jaw and facial muscles, leading to thinning of the facial contour and reduced facial expression
- Weakness of the facial, tongue and palatal muscles, leading to indistinct speech and chewing and swallowing difficulties
- Weakness of the eyelid muscles, leading to drooping of the eyelids (ptosis)
- Neck flexor weakness, causing difficulty raising the head from a surface
- Neck extensor weakness, leading to a dropped head posture and difficulty holding the head up
- Abdominal and spine erectors weakness
- Weakness of the diaphragm and other breathing muscles, causing respiratory symptoms
- Distal upper limb muscle weakness, interfering with dexterity, handwriting and activities of daily living
- Weakness of the foot dorsiflexor muscles, leading to ankle foot drop and subsequent difficulties of balance and walking
- Calf muscle weakness, causing difficulty with jumping or rising up on toes and running
- Impacts to employment and activities of daily living due to loss of ambulation

The combination of weak calf muscles and foot drop can lead to instability of the ankles, difficulty standing still, frequent falls and difficulty with walking and stair climbing. As proximal knee and hip muscles are affected, patients experience greater difficulty rising from a seated position.

Recommendations

Look for:

a. Swallowing and speech difficulties

b. Difficulty with mobility and balance, and falls

c. Impacts to activities of daily living, including self-care

d. Impacts to activities at home, school, work and in the community

e. Need for assistive devices or modifications in the home, school or workplace

f. Evaluate annually through the primary care provider or appropriate specialists, including physical therapists/physiotherapists, occupational therapists, speech/language pathologists, dietitians/nutritionists, social workers, nurses/nurse practitioners, physiatrists and orthopedists, to monitor the above

Treat with:

a. Moderate- or low-intensity aerobic and resistance exercise, minimizing sedentary activities, if possible. Consider a cardiac evaluation prior to starting a new exercise routine

b. Assistive and adaptive devices such as orthoses, braces, canes, walkers, hand-splints, etc.

c. Home and environmental modifications as necessary

Refer to:

a. Appropriate rehab specialist for individual recommendations

Severe symptoms

Skeletal muscle myotonia

Background

Myotonia – sustained muscle contraction and difficulty relaxing muscles – is a hallmark of DM1 and is an aspect of the disease that distinguishes it from other forms of muscular dystrophy. It affects nearly 100 percent of patients with adult-onset DM1. While it is not the most disabling aspect of the disease, myotonia can contribute to muscle stiffness, pain, prolonged hand grip, speech and swallowing difficulties, and GI issues.

Myotonia in DM1 is most prominent in the forearm and finger muscles, where it causes locking of the grip ("grip lock"). It sometimes affects tongue and jaw muscles, leading to difficulty with speech and chewing. Difficulty swallowing can be caused by myotonia of the face, tongue, jaw, esophagus and throat muscles, and myotonia of the respiratory muscles can lead to poor breathing force and low blood oxygen levels.

Clinically detectable myotonia of the ocular muscles is not characteristic of DM-related myotonia, although it is present in other forms of genetic myotonia.

Grip myotonia can be observed by asking the patient to relax his hand after a sustained grip; the hand muscles will typically take a few seconds or more to fully relax. Percussion myotonia can be demonstrated by percussion of specific muscles (usually thenar muscles or the wrist extensor muscles in the forearm) with a tendon reflex hammer which produces a sustained contraction, usually for several seconds or more. Electrical myotonia can also be demonstrated by abnormal, spontaneous muscle fiber discharges seen on a needle electromyogram (EMG).

DM1-associated myotonia is commonly worse in cold weather and is more pronounced after rest. Its improvement with muscle activity is known as the "warm-up" phenomenon. Myotonia in adult-onset DM1 generally declines as weakness increases.

Drugs affecting ion channels, such as mexiletine, have provided significant treatment benefit for some DM1 patients experiencing myotonia. See "Treat with" below for more information.

Recommendations

Look for:

a. Delayed relaxation after grip or percussion and difficulty related to activities of daily life

Treat with:

a. Mexiletine is often recommended for the treatment of myotonia. The DM clinical experts who developed these recommendations did not reach consensus on the protocol for prescribing and monitoring mexiletine

   Neurologists expert in DM1 care consider mexiletine an effective treatment for myotonia in patients without cardiac abnormalities, particularly congenital and childhood-onset patients. Their recommendation regarding mexiletine and cardiology includes obtaining a ECG (electrocardiogram) prior to use, a second follow up ECG within 3 months and serial monitoring. They further recommend that mexiletine be taken with food to avoid dyspepsia and transient 'dizzy feelings' associated with mexiletine treatment. Food extends absorption and lowers the peak level in blood

   Cardiologists expert in DM1 care noted that mexiletine is a class 1B anti-arrhythmic that can provide relief for myotonia and sometimes atrial fibrillation. They recommend that the use of any anti-arrhythmic in a DM1 patient begin with a workup to rule out underlying structural or functional abnormalities that may complicate its use. They further recommend monitoring during drug initiation and that mexiletine-related monitoring be conducted by a cardiologist experienced in the treatment of DM1 patients

   For more information see the Cardiac and Myotonia reading lists in Addendum 2.

Severe symptoms

Ocular management

Background

Major and clinically relevant eye manifestations in DM1 can include the following: cataracts, eyelid ptosis and incomplete eyelid closure, eye movement abnormalities, retinal changes and low intraocular pressure.

Visual impairments in patients with DM1 are most often caused by cataracts. Posterior subcapsular iridescent lens opacities are highly suggestive of DM1 or DM2, although they are not diagnostic. Cataracts in DM1 may progress faster than usual cataracts, and thus patients with DM1 may present with early-onset cataracts. Cataracts before the age of 55 or a family history of premature cataracts suggest a diagnosis of DM1 or DM2 in patients with muscle symptoms.

By direct ophthalmoscopy, the cataracts associated with DM are nonspecific and appear as punctate (dotlike) opacities. By slit-lamp examination, they have a multicolored, iridescent appearance and are located in the posterior lens capsule. Posterior subcapsular iridescent lens opacities represent an initial phase of cataract formation in DM. They are detectable only with slit-lamp examination and are usually found in patients who have not developed visual symptoms.

Glare and blurriness of vision develop as lens opacities progress to stellate (starlike) cataracts and eventually to mature cataracts, which may be indistinguishable from more common types of cataracts. Surgery to remove cataracts in DM1 patients can be performed, but local anesthesia is preferred so that complications associated with general anesthesia in these patients can be avoided (see Surgery, anesthesia and pain control).

Bilateral eyelid ptosis is a frequent feature of DM1. In severe cases, it can obstruct vision and may require surgical or nonsurgical intervention. Weakness of eyelid closure muscles is also a common problem and can cause corneal damage.

Abnormal eye movements can occur in DM1. Saccadic slowing is well documented, but the clinical impact is minimal. Contributing factors are thought to be myotonia of the extraocular muscles and/or central nervous system (CNS) abnormalities. Rebound nystagmus can be seen and may be due to CNS dysfunction. However, these eye movement abnormalities seldom cause visual disturbances.

Retinal changes are also well-documented abnormalities that can occur in DM1. Retinal changes may include pigmentary retinal degeneration, epiretinal membrane and epiretinal fibroplasia. The clinical effects of retinal changes are understudied, with conflicting reports on their effects on visual acuity.

Decreased intraocular pressure can occur and may be due to corneal abnormalities.

Recommendations

Look for:

a. Symptoms of cataracts and other eye manifestations in DM1. Advise patients about safety measures for adjusting to changes in light levels, precautions for driving in the sun and at night related to the effects of the cataracts, and how to protect the cornea, especially if they sleep with the eyes partially open because of weak eyelid closure muscles

Test for:

a. DM1 ocular manifestations via a slit-lamp examination as part of an annual eye exam

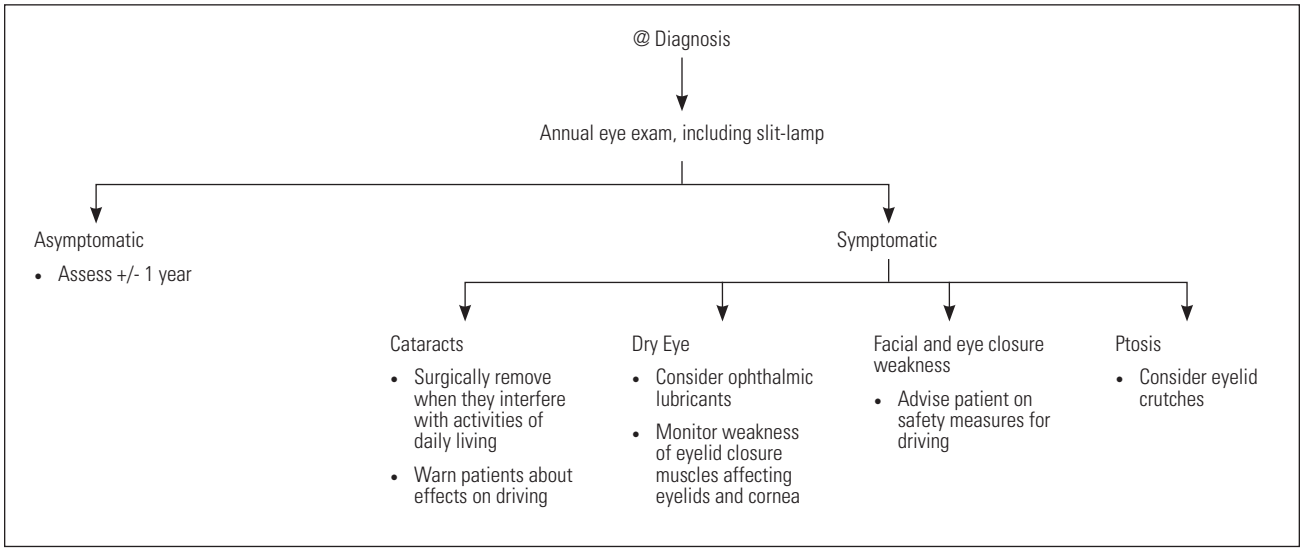
b. Eyelid ptosis; if ptosis becomes severe and interferes with vision, intervention, such as eyelid "crutches" that can be inserted into glasses, may be warranted. Try crutches as a remedy for ptosis before eyelid surgery is considered, due to anesthesia risks and concomitant eye closure weakness

Refer to:

a. Surgical ophthalmologist when cataracts interfere with the ability to meet the needs of daily living and surgical removal of the opaque lens with intraocular lens implantation is indicated. Ensure anesthesia risks are clear to the DM1 patient and surgical team and the long-term efficacy as well as side effects of the surgery are thoroughly vetted with the patient, their family, and other care providers (see Surgery, anesthesia and pain control)

b. Ophthalmologist for regular follow-up re: weakness of eyelid closure. Ophthalmic lubricants for dry eye can be considered

Fig. 3 DM Ocular Recommendations Flowchart



Severe symptoms

Gastrointestinal management

Background

Because the smooth, as well as the skeletal, muscles are involved in DM1, dysfunction along the entire gastrointestinal (GI) tract is common in this disorder. Weakness and myotonia of the smooth muscles occurs. Among the common problems are dysphagia, aspiration, abdominal pain and bloating, especially after eating, slow gastric emptying, gastroesophageal reflux, constipation, diarrhea and "irritable bowel" symptoms, gallstones, dilated colon, which can result in fecal impaction, megacolon and even perforation of the bowel; and anal incontinence. GI symptoms are not only surprisingly common in DM1 but can also be the initial or dominant clinical characteristic. However, these symptoms may be underestimated or ignored by patients.

Recommendations

Look for:

a. Problems with chewing or swallowing, drooling, gastroesophageal reflux, bloating, abdominal pain, frequency and characteristics of bowel movements, diarrhea and fecal incontinence. Careful history should be taken to differentiate oropharyngeal dysphagia from esophageal dysphagia. Esophageal dysphagia sometimes causes chest pain due to acid reflux from the stomach. Food aspiration and resultant pneumonia are a leading cause of death in DM1 patients

b. Involuntary weight loss or weight gain; dysphonia or dysphagia that may indicate pharyngeal muscle weakness; frequent cough and recurrent broncho-pneumopathies that may indicate aspiration; abdominal pain on palpation (generally or in the area of the gallbladder); and abdominal bloating during routine physical exams

c. Physical exams can also include a rectal exam for constipation, including anal sphincter spasm and dyssynergic defecation for symptomatic patients

Test for:

a. Acute abdominal symptoms:

    i. Pseudo-obstruction in addition to mechanical obstruction

    ii. If acute bowel obstruction is considered, CT enterography or MR enterography can distinguish pseudo-obstruction from the surgical emergency of true (mechanical) obstruction.

    iii. In patients with acute abdominal pain, cholecystitis should be excluded

    iv. Patients without mechanical obstruction should be treated conservatively for pseudo-obstruction and/or cholelithiasis

    v. Abdominal x-ray to evaluate abnormal bowel gas or stool, or free abdominal air

b. Abnormal amounts of hydrogen with the glucose breath test. It is abnormal in patients with lactose intolerance and in patients with bacterial overgrowth in their intestine

c. Signs of abnormal bowel gas or stool, or free abdominal air in an abdominal x-ray study

d. Dyssynergic movements, oral and/or pharyngeal weakness, or aspiration using a standard swallowing study or a modified barium swallow evaluation with consultation by a speech therapist

e. Abnormalities in stomach, small bowel, large bowel or gallbladder anatomy with abdominal ultrasound or magnetic resonance imaging (MRI)

f. Lower esophageal function and reflux, gastric emptying, and small bowel anatomy and function using barium upper GI radiographic evaluation

g. Weakness or disordered contraction of esophagus, gastroesophageal sphincter, stomach, small bowel, rectum or anal sphincter using manometry or functional motility testing in patients who do not respond to therapy

h. Abnormal structure or function of pharynx, esophagus, stomach, small intestine or large intestine using endoscopy

i. Cholestasis or hepatic involvement using specific blood tests (serum alkaline phosphatase and bilirubin elevation correlate with cholestasis in DM). Measure GGT levels because elevations of AST and ALT may be due to the skeletal muscle disease from DM1. Cholecystectomy is one of the most common reasons for a DM1 patient to have general anesthesia and neuromuscular blocking agents; extreme care should be taken if general anesthesia is necessary to perform this procedure (see Surgery, anesthesia and pain control)

Early referral for consultation by a gastroenterologist should be considered in patients with refractory symptoms. Care should be taken for those tests requiring anesthesia or sedation (see Surgery, anesthesia and pain control)

Treat with:

Non-pharmacologic treatments for gastrointestinal symptoms:

a. High-fiber diet (15-20 grams per day) for patients with diarrhea or constipation as first response. Increased fiber intake should be undertaken with increased water intake, with the exception of drinks that are high in caffeine and fructose

b. Nutrition consultation for patients with dysphagia, weight loss or weight gain, to assess nutritional adequacy

c. Dysphagia therapy referral, including compensatory strategies and dietary modifications, for patients with oral pharyngeal dysphagia

Potential pharmacologic treatment for gastrointestinal symptoms:

d. Loperamide (Imodium), with care, for diarrhea

e. Gentle laxatives (see below) for constipation. Oils should be avoided. If a patient does not respond to the first- or second-line recommendations below, a referral to a gastrointestinal specialist for anal manometry should be considered

i. First-line therapy recommendations: polyethylene glycol (Miralax), senna (Ex-Lax, Senokot), docusate (Colace) or lactulose (Cholac)

ii. Second-line therapy recommendations: bisacodyl (Dulcolax, Correctol), lubiprostone (Amitiza) or linaclotide (Linzess)

iii. Metoclopramide (Reglan) may be used to reduce the symptoms of gastroparesis, pseudo-obstruction and gastric reflux. Long-term use is not recommended because this drug can cause tardive dyskinesia

iv. If bacterial overgrowth is found on breath testing, treating with antibiotics may reduce diarrhea

f. Enteral feeding (tube feeding) may be required in patients with severe dysphagia, for example, dysphagia that causes weight loss or recurring pneumonia. Tube feeding is not commonly needed in DM1 patients

g. Probiotic regimens (many are over the counter) may be tried under a physicians supervision

DM1 patients should be strongly advised to follow screening guidelines for colon cancer that apply to the general population; epidemiological studies have shown a higher rate of malignancy for this cancer in DM1 patients.

Severe symptoms

Neuropsychiatric management

Background

Specific cognitive deficits are frequently seen in adult-onset DM1 and have also been seen in late-onset DM1, but they are milder than those seen in congenital-onset and childhood-onset DM1. In addition to the primary alteration in brain function thought to be caused by the DM1 genetic mutation, there may be contributions from the disordered sleep patterns or the hormonal or other systemic abnormalities seen in the disorder.

In adult-onset DM1, cognitive and behavioral abnormalities can involve deficits in intelligence, executive function, visual-spatial construction, arithmetic ability, and attention, although the scope and degree of the involvement vary among patients. Lack of executive function can lead to great difficulty planning and organizing one's life, affecting areas such as paying bills, keeping appointments and arranging schedules. Low IQ appears to be a problem of congenital and juvenile onset DM1 although the boundary between true adult-onset cases and late juvenile-onset cases can be difficult to establish.

In addition to the cognitive deficits, personality features such as anxiety, avoidant behavior, apathy, lack of initiative and inactivity have been used to describe DM1 patients. Some studies report high scores on depression scales in DM1. However, depression and apathy may be confused with other aspects of DM1, such as somnolence, fatigue and an inexpressive facial appearance due to facial muscle weakness.

Reduced blood flow in the frontal and temporal lobes of the brain, reduced cerebral volume compared to age-matched controls, and high T2 signal abnormalities in cerebral white matter have been found in patients with DM1, although their relationship to cognitive and behavioral abnormalities is not clear. In addition, studies have shown a unique, abnormal pattern of tau isoform expression in DM1-affected human brains.

The cognitive and personality aspects of DM1 remain relatively uncharacterized, but they can have a significant impact on quality of life for the patient and his or her family. Family members and caregivers of patients with DM1, as well as patients themselves, should be made aware that DM1 is also a "brain disorder" and that thinking and behavior can be affected. Cognitive and personality aspects of DM1 overlap considerably with deficits in psychosocial functioning (see Psychosocial considerations).

Recommendations

Look for:

a. Difficulty organizing and planning, apathy

Test for:

a. Patient's mental health via information from significant others and family members where privacy regulations allow this, as patients with DM1 can have limited insight about their cognition and behavior

b. Psychiatric or behavioral issues and cognitive changes as part of patient's annual exam. A baseline neuropsychological evaluation is recommended, with additional testing to be dictated by the patient's clinical course

Treat with:

a. Psychostimulants if apathy is associated with an impairing level of fatigue or excessive daytime sleepiness (see Excessive daytime sleepiness)

Refer to:

a. Mental health care professional (psychologist or psychiatrist) when the diagnostic impression includes psychiatric or behavioral abnormalities, when feasible, for possible treatment such as medication, couple or family support, or cognitive behavioral therapy

Severe symptoms

Psychosocial management

Background

The complex physical, cognitive and personality aspects of DM1 can seriously interfere with work, schooling, recreation, family and social life. The socioeconomic conditions of DM1-affected patients and families are often compromised because of poor education (related to cognitive impairment), limited employment opportunities, low energy levels, daytime sleepiness, impaired vision, muscle weakness, the likelihood that more than one person in the family may have special needs due to DM1, and the use of alcohol or drugs to manage stress and insomnia.

DM1 patients can have difficulty with many activities of daily living, including those related to personal hygiene, housekeeping, preparing meals, organizing and scheduling, and driving a car. Children of DM1-affected parents may not receive optimal emotional or intellectual support and may sometimes lack even routine care, all of which can be particularly serious if the children themselves have DM1. DM1 patient are vulnerable to social isolation. Caregivers can experience increased burden due to avoidant behavior, renegotiated roles and responsibilities, and the complicated nature of the typical DM health care team. Increased caregiver withdrawal and isolation are common.

Recommendations

Look for:

a. Problems with social circumstances of the patient and family, with special attention to the possibility of child neglect, acute financial need, unsafe driving, or an unsafe or unsanitary home, homelessness and/or abuse. Given the high prevalence of cognitive and or emotional/behavioral issues, as well as physical disability in DM1, physicians and other professionals caring for DM1 patients should provide referrals to appropriate social services, including respite care for caregivers

Refer to:

a. Local support groups and local and international advocacy organizations, such as MDF (see **http://www.myotonic.org**)

Severe symptoms

Excessive daytime sleepiness

Background

Excessive daytime sleepiness (EDS) has been estimated to affect at least 39 percent of patients with DM1, and it often has a major impact on quality of life for the patient and family. EDS can even be the primary and presenting symptom in adult-onset DM1.

As opposed to generalized fatigue, which is also common in DM, hypersomnia causes patients to sleep frequently, and often unpredictably, throughout the day, even if sleep duration during the night has been normal or greater than normal.

EDS in DM1 may result from one or more distinct mechanisms, including behavioral abnormalities, with an erratic sleep schedule and poor sleep hygiene; ventilatory muscle weakness resulting in sleep-related hypoventilation and nonrestorative sleep; airway obstruction due to pharyngeal weakness and obstructive sleep apnea; central nervous system (CNS)-caused alveolar hypoventilation; and CNS-caused hypersomnia due to disordered arousal mechanisms. Its positive response to the psychostimulant drug modafinil (Provigil) in a few studies suggests to some experts that impaired arousal may be the most common cause of EDS in DM1.

Recommendations

Look for:

a. Alcohol and caffeine consumption, medications and sleep habits for their possible contribution to EDS. If poor sleep habits, alcohol or caffeine consumption, or medication side effects are suspected causes of EDS, these factors should be addressed if possible

Test for:

a. EDS via the Epworth Sleepiness Scale or similar scales or sets of questions such as the questions in the MDF Toolkit (**https://www.myotonic.org/toolkits-publications**); prescribe polysomnography as needed

b. Respiratory muscle weakness contributing to EDS in DM1 patients (see Respiratory considerations)

c. Respiratory symptoms, sleep apnea and central hypersomnia during sleep evaluation for EDS

Treat with:

a. Noninvasive positive-pressure ventilation can be considered if a DM1 patient's sleepiness is thought to be related to nocturnal or daytime hypoventilation or sleep apnea. Patients should be referred to pulmonologists who have experience in neuromuscular diseases for consideration of assisted ventilation (see Respiratory considerations)

b. Stimulant therapy with the psychostimulant modafinil (Provigil) can be considered If central hypersomnia is suspected

Refer to:

a. Cognitive behavioral therapy (CBT) or custom training to reduce daytime fatigue or sleepiness

b. Sleep specialist and/or pulmonologist for patients who complain of EDS or score positively on the ESS or other sleepiness scales

Severe symptoms

Endocrine and metabolic

Background

Endocrine and metabolic abnormalities in patients with myotonic dystrophy type 1 (DM1) are well documented. DM1 patients studied over the past 50 years frequently have hyperinsulinemia following glucose ingestion, show glucose and glycated hemoglobin (HbA1c) values typical of prediabetes or impaired glucose tolerance, and have tissue- specific insulin resistance (muscle > fat > liver) due to missplicing of the insulin receptor in these tissues. Clinicians can expect that the frequency of type 1 or type 2 diabetes in patients with DM1 is comparable to that seen in the general population.

Researchers have reported an increased incidence of thyroid, parathyroid and gonadal dysfunction in patients with DM1, along with abnormal blood levels of some adrenal hormones. Abnormalities in the regulation of the hypothalamic-pituitary axis may play a role in these endocrine abnormalities, particularly those involving regulation of thyroid, adrenal and gonadal hormone levels.

Gonadal insufficiency in DM1 contributes to problems of erectile dysfunction, infertility with oligo- and azoospermia in males, and to diminished ovarian reserve with delayed appearance of human chorionic gonadotropin (HCG) in females. Women with DM1 may experience reduced fertility, spontaneous abortion and stillbirth, and they may have a somewhat higher rate of excessively painful and irregular menstruations than the general population. However, not all DM1 patients experience infertility, and women of childbearing age should consult with an OBGYN or primary medical doctor about birth control to avoid unwanted pregnancies.

Clinical and historic reports of alopecia in DM1 are common, but well-controlled, longitudinal studies using age- and gender-matched controls are lacking.

Evidence indicates that liver enzyme alterations are present in many patients with DM1. These alterations are generally not progressive. It is not known whether they represent a primary effect of DM1 on liver cells or are consequence of metabolic derangements, biliary stasis or fatty liver. Insulin resistance is likely to be the major contributing factor to observations of fatty liver and hyperlipidemia, although more research is needed. Biliary stasis is not well studied, but it may be related to smooth-muscle myotonia, weakness or alterations in enterohepatic circulation.

There is some evidence suggesting that there may be abnormal regulation of the renin-angiotensin system and levels of 25-hydroxy vitamin D [25(OH) D], dehydroepiandrosterone (DHEA), interleukin 6 (IL6), tumor necrosis factor alpha (TNF alpha) and insulin-like growth factor 1 (IGF1) in DM1. Adrenal medullary functions may also be altered in the small number of DM1 patients with cardiac arrhythmias suspected of being facilitated by hyperkalemia.

Calcium homeostasis is abnormal in some DM1 patients. This disturbance in homeostasis seems likely to have multiple contributing factors, including parathyroid dysfunction, low levels of vitamin D and nutritional deficiency. The clinical impact of the alterations in calcium homeostasis is unclear.

Recommendations

Look for:

a. Painful or irregular menses in female DM1 patients and refer to OB-GYN specialist as appropriate

b. Reproductive history, fertility/infertility and family planning in male and female DM1 patients; refer to genetic counselor or other specialists as indicated

c. Erectile dysfunction in male DM1 patients; if present consider further workup and medications to treat it, but be careful about the possible cardiac side effects of erectile dysfunction medications for these patients (see Cardiovascular considerations)

Test for:

a. Liver enzymes and bilirubin levels at baseline and then annually. Chronic liver enzyme elevation is commonly seen in DM patients and does not necessarily indicate the need for liver biopsy

b. Thyroid dysfunction in DM1 patients; measure thyroid-stimulating hormone (TSH) and free T4 levels at baseline and every three years. More frequent monitoring is necessary if thyroid dysfunction is suspected

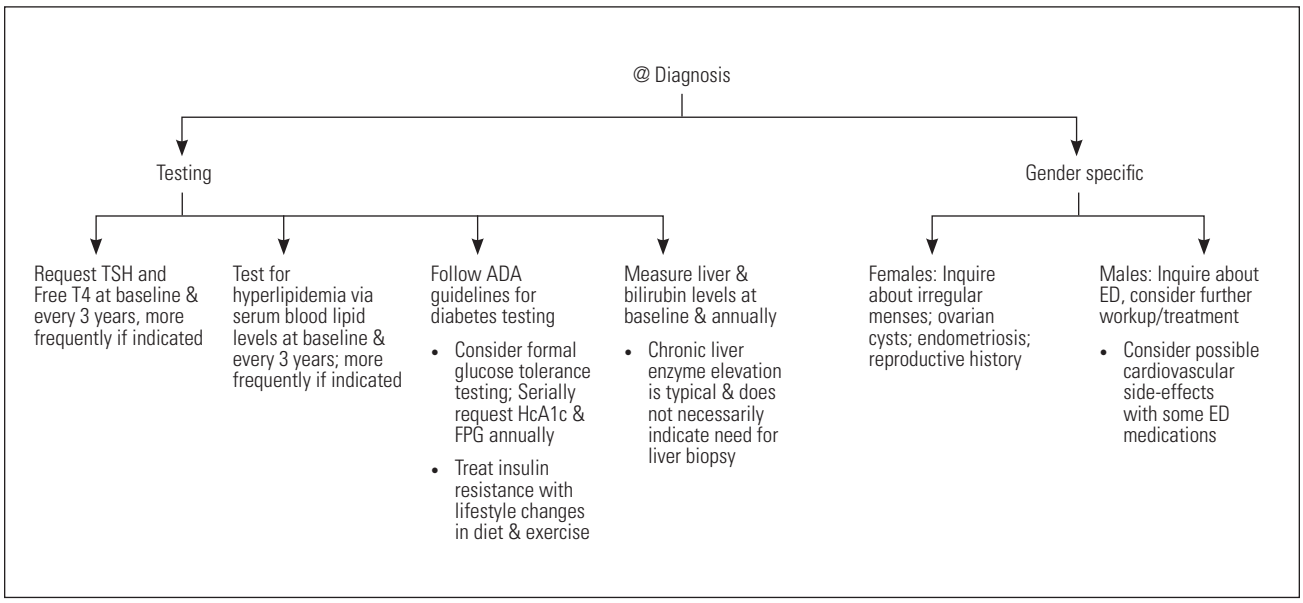
c. Hyperlipidemia via testing for levels of serum lipids at baseline and then every three years, with more frequent testing if hyperlipidemia develops. As the impact of statins on DM1 patients' health is uncertain, clinicians should be monitor patients carefully for muscle-related impacts if these lipid-lowering medications are used

Treat with:

a. Minoxidil (Rogaine) for DM1-associated hair loss

b. Lifestyle changes in diet and exercise and appropriate use of medications to normalize blood glucose and insulin levels for treatment of insulin resistance. Physicians treating DM1 patients should follow criteria from the American Diabetes Association (ADA) at **http://www.diabetes.org** for oral glucose tolerance testing, and request measurements of HbA1c and fasting plasma glucose annually

Fig. 4 DM Endocrine and Metabolic Recommendations Flowchart



Severe symptoms

Tumors

Background

Recent epidemiological studies comparing the risk of malignancies in DM1 patients with the general population have shown that DM1 patients are at increased risk of certain cancers, especially those arising in the ovary, colon, endometrium, brain and thyroid gland. Studies have shown that cancer is a distant third among causes of death in DM1 patients, after respiratory and cardiovascular complications.

DM1 patients are at higher than average risk of developing pilomatrixoma, a rare, usually benign, skin tumor of the hair follicles that only occasionally proves to be malignant. Pilomatrixomas are often found in the skin of the head and neck regions but can appear in other locations. They can be surgically removed.

Recommendations

a. Routinely look for evidence of benign and malignant skin tumors, including pilomatrixomas, and refer patients to surgeons who can safely remove them (see Surgery, anesthesia and pain control). Teach patients to detect pilomatrixomas by feeling for small, hard lumps under the skin and inform patients that these are most often found on the head, especially near the hairline, and on the neck, with some found on the arms, legs or torso

b. Strongly encourage patients to follow cancer screening guidelines that apply to the general population, such as those for colon, breast, testicular and cervical cancers

c. Evaluate suspicious new central nervous system, abdominopelvic and thyroid symptoms and consider the possibility of cancers of the brain, uterus or ovary and thyroid gland

Supplemental considerations

Diagnosis

Background

Making a diagnosis of adult onset myotonic dystrophy type 1 (DM1) usually is not difficult, if the disorder is suspected. However, the path to diagnosis is often complicated by the wide range of body systems involved, the number of different practitioners consulted, and the wide variability in severity of the signs and symptoms of disease. It can take many years for a patient to receive a correct diagnosis of DM1.

The diagnosis of DM1 should be suspected in any patient presenting with at least three of the following:

- Eyelid ptosis
- Distal weakness, primarily of the finger and wrist flexors, without contractures
- Myotonia or "stiffness" of muscles
- Pre-senile cataracts, especially the polychromatic type

The diagnosis of DM1 should be suspected in any patient presenting with any one of the above or a family history and:

- First-degree heart block
- Irritable bowel syndrome (IBS) or elevated liver enzymes
- Gallstones at a young age
- Prolonged recovery or respiratory arrest following an anesthetic
- Insulin resistance or diabetes
- Hypogonadotrophic hypogonadism
- Excessive daytime sleepiness (EDS)
- Mild learning difficulty

If DM1 is suspected, a definitive diagnosis can be made via a genetic test that shows the number of CTG repeats in the 3′ untranslated portion of the dystrophia myotonia protein kinase (DMPK) gene on chromosome 19 is elevated (> 50). CTG repeat numbers between 37 and 50 are considered "premutations," which are capable of expanding into the disease range in subsequent generations.

Recommendations

Look for:

a. Symptoms as listed above

Test for:

a. DM1 via molecular genetic testing as the first line of investigation for any patient suspected of having DM1. Muscle biopsy should no longer be performed as a diagnostic test when there is clear clinical suspicion of DM1. Patients with more than 50 CTG repeats in the 3′ untranslated region of the DMPK gene on chromosome 19 are considered to have DM1. False-negative genetic testing results can occur, even in a family with an established DM1 diagnosis; expert referral is recommended

b. Physical findings suspicious for a diagnosis of DM1 via physical examination with particular emphasis on neuromuscular, cardiovascular and respiratory assessments, and obtain a three generation family history

Refer to:

a. Genetic counseling (see Genetic counseling) for patients who exhibit clinical signs indicative of DM1, for at-risk family members, in order to enable them to make an informed decision about whether to proceed to genetic testing. Such testing should be done through an accredited laboratory experienced in providing DM1 diagnoses (see **genetests.org**). Individuals with 37 to 49 CTG repeats are deemed very unlikely to develop detectable DM1 symptoms. However, such "premutations" can expand into the disease range in subsequent generations, particularly when transmitted by men. Individuals thus identified should be offered genetic counseling (see Genetic counseling) to discuss their risk for transmitting DM1

b. Neuromuscular disease specialist, most likely a neurologist or clinical geneticist with a particular interest in inherited neuromuscular disease, who can facilitate a primary "whole-system" evaluation of the patient, prioritizing additional symptom-specific referrals, and providing ongoing clinical management of the condition

c. Cardiologist if significant cardiac symptoms are detected. Patients suspected of having a diagnosis of DM1 should be immediately advised of the risks of anesthesia and sedation and assessed for possible cardiac complications (See Cardiovascular)

Supplemental considerations

Genetic counseling

Background

DM1 is caused by the expansion of an unstable CTG repeat sequence in an untranslated, but transcribed, portion of the 3' untranslated region of the dystrophia myotonica protein kinase (DMPK) gene located on chromosome 19q13.3.

The normal number of CTG repeats in this region is 5 to 37. Repeat numbers greater than 50 are considered diagnostic of DM1. Occasionally, individuals are identified as inheriting 37 to 49 CTG repeats. Repeats of this length may be encountered in the side branches of known DM1 families, particularly in the older generations, or occasionally by chance in the general population. Individuals with 37 to 49 CTG repeats have not been reported to date to develop detectable DM1 symptoms. However, such "pre-mutations" can expand into the disease range in subsequent generations, particularly when transmitted by men.

While DNA testing, including prenatal and presymptomatic testing, for DM1 is now widely available, there are many potential pitfalls in interpreting the results for the patient and family, making genetic counseling a useful part of the diagnostic process.

A diagnosis of DM1 in one person in a family has implications for other family members, giving rise to questions about whether or not the affected person should tell family members who show no symptoms and then whether or not those family members should be tested. Diagnosis of DM1 in a presymptomatic person (including a child) can have important implications for health monitoring and family planning, but it can also raise the possibility of difficulty in obtaining insurance or encountering prejudice in the workplace.

Recommendations

a. Consider a referral of DM1 patients to genetic counseling services or a neurologist with expertise in DM1, even if the patient does not desire to have children

b. Review pedigree annually. Genetic counseling should be repeated when new information or circumstances change the risks for family members

c. Discuss and convey the complexities of the inheritance patterns observed in this disease, particularly the risk of a minimally affected mother giving birth to a severely affected child, via genetic counseling of DM1-affected families

d. Inform male and female DM1-affected individuals of the possibility of difficulty conceiving and that the difficulty increases with age

e. Help mutation carriers inform their close relatives of the possibility that they may also have inherited the risks and repercussions of DM1, even if they or their children are currently asymptomatic

Supplemental considerations

End of life counseling and management

Background

Awareness of disease progression patterns and the potential for sudden and significant health level changes is of great importance for people with DM1. People with DM1 may be faced with major medical care decisions, including life-sustaining choices, without any prior discussion of these potential scenarios. It is important to offer anticipatory guidance to review what choices and options are available as their disease advances. Options for maintaining nutrition via tube feeding, assisting respiratory function via assisted ventilation (NIV and IV), and preventing cardiac arrhythmias using implanted devices should be discussed.

For some people with DM1, these choices may precede by many years an end-of-life or comfort care situation, while for others, these choices may occur unexpectedly due to a life-threatening event or change in life expectancy. Having these discussions early in the disease and then intermittently throughout the course of care of the person allows the patient, the caregivers and the medical team to have a better awareness of what choices are available and how the choices will affect each person involved. Recognizing the potential for significant caregiver burden and open discussion of this will also help guide decision making.

Recommendations

Physicians and other health professionals caring for DM1 patients should take the following steps toward providing end-of-life care and encouraging advance directives:

a. Recommend the introduction of palliative care at the time of diagnosis and at regular intervals thereafter. Palliative care should be considered as a therapeutic option in the pathway of care to control symptoms, when necessary and not only during the end-of-life stages of disease

b. Introduce shared decision making to patients, so that they develop their own prognostic awareness. Consider that decisions can change throughout, and end-of-life care and respiratory emergency choices need to be rediscussed as the disease progresses because patients can change directions as they get worse

c. Document the durable power of attorney for health care soon after the diagnosis

d. Advise patients that noninvasive ventilation, the presence of pacer or pacer/defibrillator, and nutrition via gastrostomy tube are acceptable parts of hospice care for patients with DM1. It is important that patients are aware that symptoms of respiratory impairment may improve with noninvasive ventilation and this may improve their quality of life; management of dysphagia may reduce the risk of aspiration pneumonia, the main cause of death for these patients; cough-assisted devices may play an important role in secretion management and may avoid choking and reduce the risk of acute respiratory failure

e. Conduct early discussions of advance directives for all patients, especially prior to surgical procedures, childbirth, introduction of assisted ventilation, pacemaker or defibrillator placement, or with any significant medical worsening. Discussions may include living wills, power of attorney documents and other written advance directives

f. Encourage the use of emergency medical alert tools

g. Recommend didactic sessions and ongoing professional relationships involving the palliative care team and the hospice teams in the patients' communities

h. Recognize and address caregiver burden and whether or not the caregiver has DM1, offering respite care or equivalent measures to patients to improve family support

i. Address normal grief on the part of the patient and family, as physical, relational and occupational losses occur, and offer counseling as appropriate

Addendum 1:
Project Overview and List of Authors

Overview

The Consensus-based Care Recommendations for Adults with Myotonic Dystrophy Type 1 was created by a group of over 65 international clinicians with expertise in the care and treatment of people living with myotonic dystrophy type 1. The project included a Steering Committee of 10 and a working group of 58 clinical professionals, with additional support from U.S. Centers for Disease Control and Prevention professionals Dr. Julie Bolen, Team Lead, Epidemiology, and Natalie Street, Health Scientist for Rare Disorders and Health Outcomes. MDF in San Francisco, CA provided project design, development, management and editing support to the project.

The American Academy of Neurology affirms the value of this statement as an educational tool for neurologists.

Acknowledgements

This project, which will significantly improve the information available to clinicians treating DM patients and families living with this disease, would not have been possible without the tireless and long-term commitment made by the international professionals involved in its development. The project extends special thanks for significant additional oversight, guidance, editing and content to Dr. Tetsuo Ashizawa and Dr. Richard Moxley III. The additional feedback and support provided by Dr. Nicholas Johnson, Dr. Giovanni Meola, Dr. Shree Pandya and Dr. Mark Rogers is also deeply appreciated and enhanced the project development process. A full list of authors is available on the next page.

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The Myotonic Dystrophy Foundation team leads included Molly White, Paul Formaker and Pam Lewis. Margaret Wahl, R.N., aggregated of information from the MDF Toolkit and other resources to coordinate the single text procedure document.

Project Methodology

In order to streamline the project timeline and lower cost, MDF developed a custom methodology for creating consensus for this project. The methodology was created by blending the Single Text Procedure and the Nominal Group Technique.

The Single Text Procedure, employing the use of a single document as a starting point to incorporate the input and contributions of stakeholders, began the consensus-building effort. Margaret Wahl, R.N., coordinated the initial document using the following publications as source material:

a) Myotonic Dystrophy Foundation. MDF Toolkit. April 15, 2015 (Toolkit, 2015)

b) Thornton, C. Myotonic dystrophy, Neurologic Clinics. Aug 2014 (Thornton, 2014)

c) Gagnon, C., et al. Integrated care pathway tool for DM1. 2015 (Gagnon, 2015

d) Turner, C., and D. Hilton-Jones. Myotonic dystrophy: diagnosis, management and new therapies (review), Current Opinion in Neurology, Oct 2014 (Turner & Hilton-Jones, 2014)

e) Day, J., Ferschl, M, Gropper, M, Moxley, R., Practical Suggestions for the Anesthetic Management of a Myotonic Dystrophy Patient, 2015 revision

The Steering Committee reviewed and approved the single document, which was then distributed to the Working Group. The Working Group was divided into 8 Study Area Subcommittees addressing 20 specific symptoms or disease areas. Study Area Subcommittee members reviewed and then refined the text via several editing rounds coordinated by MDF, creating a final draft for group consideration and discussion. The Single Text Procedure effort began in Fall 2015 with a kick off meeting at the 2015 MDF Annual Conference in WA, DC, and concluded in April 2016.

The Single Text Procedure was followed by implementation of a two-day project summit involving the Nominal Group Technique. 53 of the 66 Working Group members met in Miami, FL, USA in June 2016 for individual study area subcommittee final discussions and decision-making. Professional facilitators led each of the subcommittee discussions. The final edits developed out of this facilitated discussion were compiled into an updated document that was then shared with the full Working Group.

Working Group members then met in a face-to-face structured meeting led by an experienced facilitator to collect final edits, rank input and suggestions and generate a final draft. In the full Working Group meeting, the facilitator directed a round-robin discussion of each revision or edit created in the subcommittee discussions, and Working Group members offered feedback. All edits were aggregated and each Working Group member then privately rated each proposed edit on a scale of 1-5. Highest-ranking edits were kept, and lower ranking edits were discarded.

The June summit led to additional rounds of refinement in Fall 2016, and the document was finalized for publication submission in Summer 2017. A Quick Reference Guide and flow charts to enhance access and readability were also created at that time.

Addendum 2:
Reading Lists

Surgery, anesthesia, and pain

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The mission of the Myotonic Dystrophy Foundation is to enhance the quality of life of people living with myotonic dystrophy and accelerate research focused on treatments and a cure.

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