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Becker's Muscular Dystrophy and Orthotopic Heart Transplantation: Perioperative Considerations

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ABSTRACT

Patients with Becker's and Duchenne's muscular dystrophy occasionally have myocardial involvement leading to end-stage heart failure. Heart transplantation is established as an effective therapy. Achieving successful outcomes in this challenging group requires special consideration during the perioperative period to limit preoperative deconditioning, minimize anesthesia complications, and rapidly institute rehabilitation with appropriate precautions. We reviewed our recent experience with Becker's muscular dystrophy patients and discuss the management of perioperative issues specific to this patient group.

INTRODUCTION

Becker's muscular dystrophy (BMD) is one of several types of muscular dystrophies (MDs) that comprise a group of heterogeneous, genetically determined disorders of skeletal muscle that also affect cardiac muscle [Emery 2002]. In the past, the MDs were classified according to clinical symptomatology and genetic inheritance; currently, the classification of these disorders relies on molecular, genetic, and protein biochemical characterization [Emery 2002]. Mutations in the gene encoding the dystrophin-glycoprotein complex are responsible for MD in humans. The dystrophin-glycoprotein complex is necessary for maintaining the functional integrity of the sarcolemma [Petrof 1993]. Dystrophic muscles are predisposed to injury manifested by chronic necrosis and regeneration. In MD, the postsynaptic nicotinic acetylcholine receptors (nAChRs) are expressed as a mixture of fetal- and mature (adult)-type receptors. Fetal nAChRs expression is a consequence of chronic muscle necrosis and regeneration and normally disappears from both synaptic and nonsynaptic muscle membranes. Decreases in dystrophin with a reduction in neuronal nitric oxide synthase in cardiac muscle have been implicated in the pathogenesis of cardiomyopathy [Coral-Vazquez 1999; Stamler 2001].

The incidence of BMD is 1 in 30,000 male births. It is caused by an X-linked recessive mutation causing an abnormal or absent dystrophin protein. The dystrophin in BMD is qualitatively and quantitatively abnormal, whereas in Duchenne's MD (DMD), dystrophin is usually absent [Hoffman 1988]. Patients present with muscle weakness symptoms and muscle atrophy at different stages of development, and the time course and prognosis differ with each syndrome. Symptomatology in BMD is usually milder and has a slower progression. Cardiomyopathy is seen in approximately 15% of patients younger than 16 years and in 75% of patients older than 40 years [Roland 2000]. MD cardiomyopathy rarely progresses to end-stage heart failure [Chrzanowski 2003]. In MD patients affected by end-stage cardiomyopathy, heart transplantation has been shown to yield good long-term results [Donofrio 1989; Rees 1993; Bittner 1995; Finsterer 1999; Leprince 2002; Ruiz-Cano 2003]. The management of patients with MD who present with advanced heart failure requiring transplantation involves careful planning and a multidisciplinary approach to ensure optimal patient outcomes. At our institution, we have successfully transplanted 2 patients with BMD. Review of their perioperative course illustrates a number of issues specific to this patient population.

CASE REPORT

Case 1

Patient 1 is a 28-year-old man who had BMD diagnosed at an early age. He had dilated cardiomyopathy and congestive heart failure diagnosed 7 years prior to transplantation. At the time of referral for cardiac transplantation, his musculoskeletal symptoms were upper and lower extremity weakness in extensor muscles and flexor muscles. At the time of operation, depolarizing muscle relaxants were avoided and inhalational agents were minimized. The patient underwent orthotopic heart transplantation and his postoperative course

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was uneventful. The patient recovered from anesthesia rapidly and was able to be extubated less than 12 hours after surgery. Aggressive in-hospital rehabilitation was instituted following extubation and the patient recovered without a significant decrement in functional status. The patient was able to transfer independently while maintaining sternal precautions. He was discharged to home 2 weeks after surgery and subsequently did well.

Case 2

Patient 2 is a 33-year-old man who also had BMD diagnosed at an early age. The patient had dilated cardiomyopathy and congestive heart failure diagnosed 7 years prior to transplantation. At the time of his transplantation evaluation, the patient's functional status was significantly limited by his BMD. He was unable to climb or descend stairs or walk on uneven surfaces. When rising from a sitting or supine position, the patient would use his upper body and arms to form a tripod as he gradually transferred his weight to his legs. At the time of surgery, depolarizing muscle relaxants and inhalational anesthetics were avoided. The quality of the patient's sternum was noted to be good and was closed using double sternal wires. His postoperative course was complicated by grade 3A rejection requiring pulsed dose methylprednisolone for 3 days with resolution of the rejection episode. Because of the patient's pre-existing musculoskeletal weakness, he required 2-person assistance for all transfers from his bed to maintain sternal precautions. The patient's hospitalization was prolonged in order for him to undergo intensive rehabilitation while adhering to strict sternal precautions. The patient was discharged to a rehabilitation center approximately 1 month after transplantation. He has done well and has recovered to his preoperative functional status.

DISCUSSION

Preoperative Planning

In patients with BMD and DMD who have significant musculoskeletal symptoms, it is difficult to assess the contribution of heart failure to decreasing performance status. In patients with MD, severe muscular weakness may prevent the ability to perform exercise testing to determine maximal oxygen consumption rate, and clinicians may be required to use other measures which are of less predictive value [Haller 1984; Muntoni 2003]. Repeated hospitalizations for heart failure decompensation and the use of inotropic support in these patients leads to muscle wasting and overall worsening in functional status that complicates recovery following transplantation [Conraads 2002]. Early evaluation for heart transplantation should be considered to avoid profound decline in physical performance prior to surgery. Assist devices should also be considered in centers with long transplantation waiting times.

Ethics

Although transplantation in this patient population often raises the question of the ethical and appropriate use of scarce donor organs, it is important to consider several factors in the pretransplantation evaluation. Patients with MD often have developed skeletal muscle impairment for many years before the onset of cardiac symptoms. Whereas the skeletal muscle impairment is mild and slowly progressive, the development of heart failure is often rapid and requires heart transplantation soon after diagnosis. Patients with MD often live past the 5th decade of life, thus their skeletal myopathy is not a complete contraindication to transplantation. Even though we realize that immunosuppression may lead to progression of muscular impairment with an unknown effect on survival and quality of life, patients with MD cardiomyopathy and heart failure have few options. Heart transplantation prolongs survival and improves quality of life without decrement in prognosis. However, it is important to assess the degree of muscular disability and life expectancy before acceptance for cardiac transplantation [Ruiz-Cano 2003].

Anesthesia Considerations

In BMD, the anesthetic implications are related to the presence of the abnormal neuromuscular junction and the increased incidence of malignant hyperthermia (MH) in patients with MD when exposed to succinylcholine and potent volatile inhalational anesthetics. The fetal nAChR demonstrates a reduced sensitivity to competitive antagonists that should render the neuromuscular junction resistant to nondepolarizing neuromuscular blockers (NMB). In fact, the opposite is seen clinically. Patients are more sensitive to nondepolarizing neuromuscular blockade and demonstrate a prolonged effect from just 1 dose of NMB [Ririe 1998].

MH is a clinical syndrome that results from exposure to succinylcholine and/or inhalational anesthetics. Symptoms include a rapidly increasing core body temperature (1°C/5 min), extreme metabolic acidosis, and muscle rigidity. The symptoms are a result of a loss of control of intracellular Ca^{2+} causing a release of unbound Ca^{2+} from storage sites that normally maintain muscle relaxation. Metabolism increases to generate ATP to drive the Ca^{2+} pumps that maintain Ca^{2+} homeostasis. These reactions are exothermic and produce heat.

The anesthesia plan for the patients described above was chosen cautiously to prevent complications such as unnecessary prolongation of NMB and MH. A continuous infusion of propofol and fentanyl with an initial dose of NMB was used throughout both cases, including the time during cardiopulmonary bypass. In addition, intermittent muscle twitch monitoring was done to prevent overdosing of NMB. A total intravenous anesthetic with propofol, opioid analgesia, and an NMB, with or without regional anesthesia, is considered to be a safe and effective technique in patients with MD [Bennun 2000].

Intraoperative Surgical Considerations

Despite significant muscle wasting, there are no specific surgical considerations necessary during transplantation as these patients do not have an inherent connective tissue disorder requiring special care with tissue manipulation. Meticulous sternal closure is critical for patients who will exert increased stress on their sternums with adaptive transfer tech-

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niques. Surgeons should consider the use of double sternal wires or a Robicsek weave at the time of closure.

Postoperative Care

Management of patients with MD after surgery must be focused toward early mobilization and the prevention of physical deconditioning. Daily goals should be focused on minimizing bed rest and inotropic support to prevent muscle wasting. Patients should be promptly weaned from the ventilator once hemodynamic stability is achieved. Patients should be expected to generate vital capacities, tidal volumes, and negative inspiratory forces similar to non-MD patients because axial muscles are usually unaffected by the disease. Prompt weaning of inotropic support as myocardial recovery occurs minimizes muscle wasting.

Postoperatively, patients should begin rehabilitation starting in the intensive care unit with physical therapy consultants. Sternal precautions should be adhered to during physical therapy sessions. This mobilization program should be continued while the patients are in the step-down ward with daily assessment of safety for transfers using strict sternal precautions. Patients must be counseled to use their upper extremities minimally when getting out of bed. Patient transfers with 2-person assistance may be necessary in the early postoperative period. Patients should be considered for rehabilitation center admissions following heart transplantation depending on their functional status.

CONCLUSIONS

Patients with MD and end-stage heart failure benefit from orthotopic heart transplantation. A subset of patients with MD have significant cardiovascular involvement that limits their longevity and quality of life. In these patients, heart transplantation is indicated to restore pre–heart failure functional status. These challenging patients require special consideration to assure optimal outcomes and ethical allocation of scarce donor organs. Once patients require hospitalization for heart failure decompensation despite maximal medical therapy, it is important to consider transplantation to prevent the rapid deconditioning that occurs with bed rest and inotropic support. Preoperative anesthesia consultation should be obtained to address issues of MH and sensitivity to muscle relaxants. During the recovery period, daily care should be focused on early mobilization and intensive rehabilitation. In patients with severe musculoskeletal weakness preoperatively, it may be necessary to prolong hospitalization to provide safe transfers while observing sternal precautions. With attention to these special considerations, patients with BMD and end-stage heart failure can have successful outcomes following heart transplantation.

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