ELSEVIER

THORACIC

Heart Transplantation in Patients With Emery-Dreifuss Muscular Dystrophy: Case Reports

A. Dell'Amore, L. Botta, S. Martin Suarez, A. Lo Forte, E. Mikus, N. Camurri, L. Ortelli, and G. Arpesella

ABSTRACT

Emery-Dreifuss muscular dystrophy (EDMD) is an hereditary syndrome characterized by slow but progressive locomotor involvement and cardiomyopathy. Cardiac impairment is often the life-limiting feature of the illness. Only a few cases of cardiac transplantation have been reported previously in muscular dystrophy, and only 4 cases of end-stage disease due to EDMD have been treated previously with heart transplantation. Herein we have reported our experince with 2 consecutive patients who underwent heart transplantation for EDMD cardiomyopathy.

EMERY-DREIFUSS MUSCULAR DYSTROPHY (EDMD) is an hereditary neuromuscular disorder manifested by contracture of the elbows, Achilles tendons, and postcervical muscles, with slow, progressive muscle wasting and weakness.[1] Various forms of EDMD have been reported in the literature. The X-linked EDMD gene (Xq28) encodes a ubiquitous protein called Emerin.[2,3] A second less common form is autosomal dominant inheritance disease (AD-EDMD), which involves mutations in the laminin A/C gene on chromosome 1q21.3.[4] The effect on the heart becomes apparent in the teenage years. It is characterized by cardiac conduction defects and infiltration of the myocardium by fibrous and adipose tissue.[5] In contrast to the Duchenne and Becker varieties of muscular dystrophy, locomotor abnormalities are mild and progress slowly. Afterward, cardiac involvement becomes the predominant feature of the disease. Arrhythmias and heart block are often the first signs of myocardial involvement,[5] with evolution toward end-stage cardiomyopathy.[6,7]

Until today only 4 heart transplantations for EDMD have been described in the literature (Table 1).[8–10] Herein we have reported our experience with 2 consecutive patients who underwent cardiac transplantation for X-linked and AD-EDMD–related cardiomyopathy.

PATIENTS AND METHODS

Patient 1

A 51-year-old man was first seen at the age of 32 years when he underwent surgical repair for an Achilles tendon rupture. In 1984 he started warfarin therapy for new onset atrial fibrillation. In 1992 at the age of 43 years he was evaluated for muscular dystrophy, because of progressive muscle wasting and weakness. Muscle biopsy showed chronic myopathic changes. AD-EDMD was diagnosed by DNA testing. In 1999 he had a transient neurologic event with complete recovery. In the last 3 years he was frequently hospitalized for congestive heart failure. The patient was treated with an implantable cardioverter defibrillator (ICD) for runs of

From the Heart and Lung Transplantation Program, S. Orsola-Malpighi University of Bologna, Bologna, Italy.

Address reprint requests to Andrea Dell'Amore, MD, S. Orsola-Malpighi University of Bologna, via Massarenti 9, Bologna, Bo, Italy. E-mail: dellamore76@libero.it

0041-1345/07/$–see front matter
doi:10.1016/j.transproceed.2007.06.076

Table 1. Previous Reported Experience With Heart Transplantation for EDMD

Authors	Publication Date	No. of Patients
Merchut et al[8]	1990	1
Rees et al[9]	1993	1
Kichuck Chrisant et al[10]	2004	2

nonsustained ventricular tachycardia diagnosed on the Holter-ECG. Cardiac evaluation documented progression toward a dilated cardiomyopathy despite maximal medical therapy. The echocardiography reported severe biventricular and atrial dilatation, with an ejection fraction (EF) of 21% associated with severe mitral and tricuspid regurgitation. The patient showed moderate muscle weakness and moderate kyphoscoliosis with need for a walking stick. The patient was listed for heart transplantation. He underwent orthotopic bicaval cardiac transplantation in October 2001 after waiting 14 months. There were no operative complications. The postoperative period was complicated by moderate renal insufficiency and an increase in pancreatic enzymes without clinical symptoms. Heart function was good. He was extubated on the first postoperative day (POD). He started physiotherapy and ambulation on the 2nd POD to prevent muscle weakness and atrophy. He was discharged from the hospital after 2 months in good clinical condition. After 66 months follow-up, the patient is alive and heart function is good without myocardial rejection. No progression of proexisting muscular dystrophy has been diagnosed.

Patient 2

A 47-year-old woman was first seen when she was 15 years old, because she underwent surgical repair of an Achilles tendon rupturé. Muscle contractures and weariness appeared at the age of 29 years when she was screened for muscular dystrophy. Serum creatinine kinase concentrations were increased, and muscle biopsy specimens showed chronic myopathic changes. The genetic evaluation diagnosed an X-linked EDMD. At the age of 40 years she was evaluated for complete heart block with syncope. A bicameral pacemaker was implanted. In the following years she was frequently hospitalized for congestive heart failure despite maximal medical therapy. The echocardiographic evaluation showed a huge right atrial enlargement (8 cm diameter), an EF of 18% with marked biventricular dilatation, and 4+ mitral regurgitation. The patient showed mild muscle weakness and contractures; however, she was completely independent in daily activity. Afterward, we decided to insert her on the waiting list for heart transplantation. She underwent orthotopic bicaval cardiac transplantation in January 2003 after a 4-month wait. There were no intraoperative complications. In the postoperative period heart function was good. Prolonged mechanical ventilatory support was necessary, because of poor respiratory dynamics due to muscle weariness. We administered pressure support ventilation, high-calorie food supplements, antioxidant therapy, and carnitine. The patient was extubated after 76 hours, and an ICU stay of 26 days. She was discharged from the hospital after 3 months in good clinical condition. After 40 months follow-up, she is in good clinical condition with only a mild worsening of muscle contractures.

DISCUSSION

EDMD is a distinctive but heterogeneous neuromuscular disorder whose inheritance is variable and sporadic, including an X-linked, autosomal dominant from (AD-EDMD).[10] The X-linked EDMD involves a mutation of the Emerin gene (Xq28), which codes for an integral nuclear membrane protein.[2] The AD-EDMD form is less common, involving mutation of nuclear membrane proteins called laminins A and C (LMNA gene, 1q21.3).[4] This muscular disorder is manifested by slow, progressive muscle wasting and weakness with typical humeroperoneal distribution and early contractures of the elbows, Achilles tendons, postcervical muscles, and cardiomyopathy.[1] In contrast to Duchenne and Becker muscular dystrophies, locomotor abnormalities are mild and progress slowly. Long-term survival is not unusual; it is limited by the related cardiomyopathy.[6] Frequently cardiac involvement is a predominant feature of the disease. In young adults, this may be the first problem that causes them to present for treatment.[7] Early signs of cardiac impairment are usually conduction defects, atrial or ventricular arrhythmias, and sudden death. Frequently these patients need pacemaker or ICD implantation.[11] Not so rare is the evolution toward dilated cardiomyopathy needing maximal medical therapy.[6,7]

Cardiac involvement in AD-EDMD may differ from X-linked EDMD. Ventricular arrhythmias and dilated cardiomyopathy are more common and occur earlier in AD-EDMD. However, cardiomyopathy is a constant feature of EDMD, limiting long-term survival.[10] In case of end-stage cardiomyopathy, heart transplantation should be considered.

Nowadays to the best of our knowledge only a few cases of EDMD-related cardiomyopathy have been treated with cardiac transplantation (Table 1).[8–10] Herein we have described 2 patients who underwent orthotopic heart transplantation for end-stage cardiomyopathy due to X-linked and AD-EDMD. In the past, both patients underwent surgical repair of Achilles tendon rupture as the first sign of the pathology. During the preoperative evaluation both patients showed mild muscular impairment, characterized by contractures and muscle weariness. In both patients the cardiac evaluation showed end-stage dilated cardiomyopathy despite maximal medical therapy. In regard to the poor prognosis due to heart failure, in contrast to a benign form of muscular dystrophy, we believe that cardiac transplantation was lifesaving in these cases. Both patients underwent successful orthotopic heart transplantation.

After 66 and 40 months follow-up, respectively, the patients showed good heart function without a high grade of rejection. The first patient does not show progression of muscular dystrophy. The second patient has only a mild worsening of the disease; until now, she is still self-sufficient. Neither patient experienced complications related to immunosuppressive therapy (azathioprine, cyclosporine, and steroids). However, these patients must be considered to be at high risk for surgery needing a multidisciplinary approach. Expert neurologists and physiotherapists are essential in the pre- and postoperative periods. Anesthetic evaluation[12] and management with short-acting drugs are useful to allow early extubation, feeding, physical therapy, and mobilization. This approach is fundamental to

avoid atrophy and weakness of the neuromuscular apparatus. A correct nutritional supply and sometimes high-calorie food supplements may be helpful.

In conclusion, EDMD should not be considered a contraindication to heart transplantation. We believe that for these patients cardiac transplantation may be lifesaving, because the cardiomyopathy is often the life-limiting feature of this complex syndrome.

REFERENCES

1. Emery AEH: Emery-Dreifuss syndrome. J Med Genet 26:637, 1989

2. Emery AEH, Dreifuss FE: Unusual type of benign X-linked muscular dystrophy. J Neurol Neurosurg Psychiatry 29:338, 1966

3. Cartegni L, di Barletta MR, Barresi R, et al: Heart-specific localization of Emerin: new insights into Emery-Dreifuss muscular dystrophy. Hum Mol Genet 6:2257, 1997

4. Baur X, Witt TN, Pongratz D, et al: Dominant autosomal humeroperoneal syndrome with early contractures and cardiomyopathy. Klin Wochenschr 237:316, 1990

5. Buckley AE, Dean J, Mahy IR: Cardiac involvement in Emery-Dreifuss muscular dystrophy: a case series. Heart 82:105, 1999

6. Yoshioka M, Saida K, Itagaki Y, et al: Follow-up study of cardiac involvement in Emery-Dreifuss muscular dystrophy. Arch Dis Child 64:713, 1989

7. Bialer MG, McDaniel NL, Kelly TE: Progression of cardiac disease in Emery-Dreifuss muscular dystrophy. Clin Cardiol 14: 411, 1991

8. Merchut MP, Zdonczyk D, Gujrati M: Cardiac transplantation in female Emery-Dreifuss muscular dystrophy. J Neurol 237:316, 1990

9. Rees W, Schuler S, Hummel M, et al: Heart transplantation in patients with muscular dystrophy associated with end-stage cardiomyopathy. J Heart Lung Transplant 12:804, 1993

10. Kichuck Chrisant MR, Drummond-Webb J, Hallowell S, et al: Cardiac transplantation in twins with autosomal dominant Emery-Dreifuss muscular dystrophy. J Heart Lung Transplant 23:496, 2004

11. Walker S, Levy T, Rex S, et al: Biventricular implantable cardioverter defibrillator use in a patient with heart failure and ventricular tachycardia secondary to Emery-Dreifuss syndrome. Europace 1:206, 1999

12. Jensen V: The anaesthetic management of a patient with Emery-Dreifuss muscular dystrophy. Can J Anaesth 43:968, 1996