Thymoma and Myotonic Dystrophy: Successful Treatment With Chemotherapy and Radiation*

Case Report and Review of the Literature

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We present the case of a 42-year-old woman with myotonic dystrophy and thymoma. She was treated with combination chemotherapy followed by external beam radiation, and remains in remission 19 months after thymoma was diagnosed. The myotonic dystrophy is unchanged. Only six cases of this nature have been reported in the literature, and this patient is the first to be successfully treated with combined modality therapy. (CHEST 2002; 121:2061–2063)

Key words: positron emission tomography; myotonic dystrophy; thymoma

Abbreviation: PET = positron emission tomography

In 40 to 45% of cases, thymoma is associated with myasthenia gravis or one of several autoimmune and endocrine disorders. The strongest association has been with myasthenia gravis. Association with other myopathies is very rare. We describe in this case report a patient with both myotonic dystrophy and thymoma.

CASE REPORT

A 46-year-old white woman was admitted to the hospital with a 2-week history of dyspnea at rest. Four years earlier, she received a diagnosis of myotonic dystrophy. Two of her sisters have myotonic dystrophy. She was receiving levothyroxine, 100 µg, following partial thyroidectomy for thyroid cancer. The patient was breathless at rest. Jugular veins were distended up to 6 cm above the sternal angle. Breath sounds were decreased, and crackles were heard over both lung bases. She had bilateral symmetrical ptosis, temporal and masseter muscle wasting, distal muscle weakness, and myotonia. Electromyography and nerve conduction study results were consistent with a diagnosis of myotonic dystrophy. Blood counts and serum chemistry levels were within normal limits. Arterial blood gas analysis on 55% oxygen revealed $P_{O_2}$ of 77 mm Hg and $P_{CO_2}$ of 47 min Hg. Chest radiography showed bilateral pleural effusions and cardiomegaly.

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Figure 1. Top: CT scan showing a 6.5 × 8-cm anterior mediastinal mass (thymoma) encasing the superior vena cava and adherent to the aorta and pulmonary artery (arrow). Bottom: CT scan showing a residual 2 × 3-cm anterior mediastinal mass (arrow).
Troponin I level was elevated at 8 ng/mL (normal 0.5–0.7 ng/mL), and ECG showed low-voltage complexes. Echocardiography demonstrated a large pericardial effusion with tamponade physiology. Both atria were enlarged and ventricles dilated with moderate-to-severe global hypokinesis of the left ventricle. Eight hundred fifty milliliters of pericardial fluid was drained by pericardiocentesis. Pleural and pericardial fluid analysis findings were nondiagnostic. The heart failure was managed with digoxin and an angiotensin-converting enzyme inhibitor. A repeat echocardiogram showed only mild global hypokinesis, and multigated equilibrium radionucleotide cineangiography showed a normal ejection fraction. The heart failure and pericardial effusion were attributed to myopericarditis.

A CT scan of the chest (Fig 1, top) showed an invasive 6.5 × 8 cm anterior mediastinal mass encasing the superior vena cava and adherent to the aorta and pulmonary artery. This mass was evident on a positron emission tomographic (PET) scan (Fig 2, top, A to D). Fine-needle aspiration and core biopsy confirmed a diagnosis of invasive thymoma (Masaoka stage III). She was treated with an IV chemotherapeutic regimen consisting of cisplatin, 50 mg/m²; doxorubicin, 50 mg/m²; and cyclophosphamide, 500 mg/m², with amifostine, 1,000 mg. To minimize cardiac toxicity, doxorubicin was administered as a continuous infusion for 96 h rather than as a bolus. Amifostine was added to reduce the risk of cisplatin-induced peripheral neuropathy, which could potentially devastate a person with a preexisting myopathy. A total of six cycles was administered at three weekly intervals. Cardiac function was monitored by serial echocardiography and multigated equilibrium radionucleotide cineangiography that remained normal. Cardiac medications were gradually withdrawn. The tumor shrank approximately 90% after four cycles and plateaued. External beam radiotherapy to the chest followed. A total of 3,900 cGy was administered in 22 fractions (anteroposterior/posteroanterior field), followed by a boost of 900 cGy using oblique fields to avoid the spinal cord and heart. A repeat PET scan (Fig 2, bottom, A to D) on completion of all therapy showed no evidence of the hypermetabolic mass. The patient tolerated the therapy very well and remains in remission 19 months after diagnosis. The myotonic dystrophy is unchanged.

**FIGURE 2.** Top, A to D: PET scan showing a hypermetabolic anterior mediastinal mass, kidneys, and bladder (dark areas). Bottom, A to D: PET scan showing heart and kidneys (dark areas) with no evidence of the hypermetabolic mass. Pre-Rx = before radiotherapy; Post-Rx = after radiotherapy.

**DISCUSSION**

Myasthenia gravis is the neuromuscular disease most commonly associated with thymoma. Approximately 35% of patients with thymoma also have myasthenia gravis, and 15% of individuals with myasthenia gravis have thymoma. In contrast, myotonic dystrophy is very rarely associated with thymoma. To date, there have been only five other cases of thymoma in patients with myotonic dystrophy reported in the literature (Table 1). Myotonic dystrophy (conventional Steinert type or myotonic dystrophy type 1) is a genetic disease linked to chromosome 19 and inherited in an autosomal dominant manner. It is characterized by an excess of trinucleotide (CTG) repeats in the 3’ untranslated region of the myotonin gene. Thymoma is an acquired disorder whose etiopathogenesis is yet unclear. While thousands of cases of thymoma and myotonic dystrophy occur, a survey of the literature reveals only six instances of the two disorders occurring in the same patient. This amounts to a very weak association at best and is more likely to be a coincidence. However, the occurrence of both disorders in the same patient is significant because it presents a management problem.

Patients with myotonic dystrophy frequently have respiratory muscle weakness and cardiomypathy with arrhythmias and heart failure. These factors increase postoperative morbidity and mortality. The only reported patient with myotonic dystrophy and thymoma to undergo thymectomy had a stormy postoperative course that precluded anesthesia and surgery when a maxillary tumor developed several months later. This is important because surgical resection is the mainstay in the treatment of thymoma. Thymectomy ameliorates myasthenia gravis, while there is no evidence of such an outcome in myotonic dystrophy, including our patient. Thus, the increased risk that thymectomy entails has to be seriously considered,
particularly in cases of invasive thymoma where complete resection is technically difficult and hazardous, as in our patient. Hence, chemotherapy was administered and followed up with radiotherapy. The chemotherapeutic regimen used in this patient is considered the current standard and was initiated after normal cardiac function was restored. The increased risk of cardiomyopathy in patients with myotonic dystrophy makes the use of potentially cardiotoxic drugs debatable, but the benefits in this case were believed to outweigh the risks. To further reduce cardiotoxicity, doxorubicin was administered as a continuous infusion over 4 days rather than as a bolus. A PET scan performed at the completion of all therapy showed no evidence of thymoma despite the presence of a residual mass (presumably fibrous tissue) measuring $2 \times 3$ cm on CT scan that has remained stable over 6 months.

Thymoma is best treated by complete surgical resection when feasible. Noninvasive thymoma (Masaoka stage I) is completely resected with a recurrence rate of only 1.5%. No adjuvant therapy is required. Invasive or malignant thymoma (Masaoka stages II, III, and IV) is more difficult to treat. Surgery is still the mainstay with total resection where possible. Radiotherapy and chemotherapy are very useful because thymoma is responsive to both modalities. Adjuvant radiotherapy after complete resection reduces recurrence from nearly 30% to < 10%. After partial resection, radiotherapy often leads to a complete response. Chemotherapy, especially in a neoadjuvant manner, has been employed when surgery is not feasible at diagnosis. Surgical resection and adjuvant radiotherapy follow. When surgery is not possible, a combination of chemotherapy and radiation gives better results than either modality alone.1 In a study of seven patients who achieved a complete response with neoadjuvant chemotherapy, there was no residual tumor at surgery in two patients.4 We were able to achieve a substantial response on the basis of a CT scan and a complete response on the basis of a PET scan. PET scanning in thymoma has been shown to be a sensitive test.6 Thus, although there is a reasonable chance that the residual mass may not contain tumor cells, follow-up has been short and only time will tell since recurrences occur even after 30 years. The number of patients with myotonic dystrophy and thymoma is too small to draw any firm conclusions regarding treatment. We feel that a combined modality approach with chemotherapy and radiation is a safe and reasonable treatment option for these patients.

Table 1—Patients With Thymoma and Myotonic Dystrophy

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Age, yr</th>
<th>Sex</th>
<th>Country</th>
<th>Therapy</th>
<th>Outcome</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>51</td>
<td>Male</td>
<td>Japan²</td>
<td>Radiotherapy, 16 Gy</td>
<td>No response; dead in 4 mo</td>
<td>4 mo</td>
</tr>
<tr>
<td>2</td>
<td>46</td>
<td>Female</td>
<td>Japan¹</td>
<td>None</td>
<td>Died suddenly 4 mo later</td>
<td>4 mo</td>
</tr>
<tr>
<td>3</td>
<td>32</td>
<td>Female</td>
<td>Spain⁴</td>
<td>Radiotherapy, 50 Gy</td>
<td>Complete response</td>
<td>4 yr</td>
</tr>
<tr>
<td>4</td>
<td>64</td>
<td>Female</td>
<td>United States⁵</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
<tr>
<td>5</td>
<td>32</td>
<td>Male</td>
<td>United States⁶</td>
<td>Thymectomy</td>
<td>Complete response; postoperative complications: embolism, pneumonia</td>
<td>Several months</td>
</tr>
<tr>
<td>6</td>
<td>46</td>
<td>Female</td>
<td>United States</td>
<td>Chemotherapy and radiotherapy</td>
<td>Complete response</td>
<td>19 mo</td>
</tr>
</tbody>
</table>

References


Anomalous Collateral from the Coronary Artery to the Affected Lung in a Case of Congenital Absence of the Left Pulmonary Artery

Effect on Coronary Circulation

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A case of congenital absence of the left pulmonary artery, in which perfusion of the affected lung was accomplished via an arterial shunt from the circumflex coronary artery, is discussed. Data from myocardial perfusion scintigraphy showed that myocardial perfusion was unaffected by the existence of the...