Thymolipomas in association with myasthenia gravis

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Thymolipomas are rare, benign thymic lesions (2%-9% of thymic tumors), consisting of adipose tissue inside the thymus, which is slow growing¹ and has scarce local and systemic manifestations (50% diagnosed in routine radiologic studies).² Myasthenia gravis (MG) is generally associated with and present in up to 30% of thymomas.¹ However, association with thymolipomas is uncommon, with just 15 cases reported in the English-speaking literature (Medline 1967-August 2000).²⁻¹⁴

We report 3 new cases of this uncommon association and review the literature.

Clinical Summary

Two patients were women, and one was a man. The clinical presentation was general weakness, which increased during the course of the day. The patients had vertical diplopia and weakness of jaw movement. Two patients had dysphagia, more noticeably after eating, and one had dysphonia during conversations, which improved with rest.

In the 3 patients the physical exploration revealed a steady loss of strength on repeated movement, and the edrophony test results were positive. In 2 patients the antiacetylcholine receptor and anti-striated muscle antibody levels were positive. Chest radiography was within normal limits. Mediastinal computed tomography showed no abnormalities in 1 patient. In the other 2 patients the computed tomograms showed a lesion at the thymus that was compatible with a diagnosis of thymoma. Electromyography with repetitive nerve stimulation, done in 2 patients, revealed a decrease of more than 20% in 1 patient and more than 15% in the other patient.

The treatment was implemented with anticholinesterases (pyridostigmine, 60 mg/6 hours) and steroids (prednisone, 60 mg/d), which failed to achieve total remission of the symptoms in 2 patients. The patients underwent thymectomy which extended to the whole of the mediastinal fat. Histologic study revealed thy-

molipomas. During the postoperative period, 1 patient had a venous thrombosis that required anticoagulation.

After the operation, the MG symptoms improved partially, and the MG was controlled with small doses of corticosteroids and, in 2 patients, with small doses of anticholinesterases. Twelve months after the thymectomy, 1 patient had dyspnea, and treatment was reimplemented with pyridostigmine (60 mg/8 hours) and prednisone (20 mg/d), requiring hospital admission. Currently, 10 years after the operation, the patient's clinical symptoms are partially controlled with this medication. In the other patients currently, after 9 and 10 years, the symptoms are being partially controlled with pyridostigmine (30 mg/8 hours) and prednisone (15 mg/d).

Comment

The association of MG with thymolipomas is uncommon, and it is regarded by some authors as a simple epiphenomenon, although the fact that symptoms regress in most patients after thymectomy suggests that there is a relationship. The pathogenesis of thymolipoma is not clear, and there are currently 4 theories.^{2,9} One of the theories considers that the thymolipoma is a fatty involution of a thymoma, and therefore the thymolipomas would be true thymomas. Furthermore, the coexistence of thymolipoma with MG, other autoimmune diseases, or neoplastic conditions suggests that thymoma and thymolipoma are at least related tumors.

The patients with thymolipoma and MG differ from patients without MG in 2 ways: (1) thymolipomas with MG appear in older patients (20-30 years vs 40-50 years)¹² and (2) mean thymolipoma weights are lower in patients with MG (100 g vs 1000 g). This can be explained because thymolipomas without MG are usually diagnosed when they are large.⁹

Treatment for MG is initially medical, with anticholinesterases and corticosteroids and occasionally plasmapheresis. The surgical treatment of MG consists of thymectomy, which can be performed through a vertical sternotomy or cervicotomy; the former is recommended because it makes it easier to extend the thymectomy to the whole of the mediastinal fat, even with removal of both mediastinal pleurae. Extended thymectomy is currently the recommended treatment for MG.

Follow-up data are not easily interpretable because the reported postoperative periods are short, although thymectomy always leads to improvement (Table 1). However, a relapse of MG occurred in 4 (26.7%) of the 15 published cases²⁻¹⁴ but with such short follow-up periods in most cases that it is impossible to assess the long-term results. Our series has a long follow-up period (>9 years). Two of the patients have shown a marked improvement, and the third, despite occasional relapses of MG, has also shown improvement. Only one of the patients, presented by Pan and colleagues,⁶ had total remission of the MG after thymectomy.

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TABLE 1. Cases of thymolipomas with MG reported in the English-speaking literature

Case No.	Author	Age (y)	Sex	Preoperative evolution	Thymolipoma weight	Postoperative evolution	Relapse	Follow-up time
1	Reintgen and colleagues ³	60	Male	1 y	100 g	Improvement	No	3 mo
2	Otto and colleagues ⁴	56	Male	4 y	93 g	Improvement	Yes (3 wk)	1 mo
3	Mikkelsen ⁵	61	Male	29 mo	65 g	Improvement	Yes (7 mo)	8 mo
4	Pan and colleagues ⁶	62	Female	7 mo	90 g	Complete remission	No	24 mo
5	Pan and colleagues ⁶	54	Female	6 y	—	Improvement	Yes (2 mo)	18 mo
6	Olanow and colleagues ⁷	62	?	16 mo	—	Improvement	No	40 mo
7	Alfaro ⁸	31	Male	10 y	10 g	Improvement	No	6 mo
8	Le Marc'hadour and colleagues ⁹	52	Male	2 y	185 g	Improvement	No	18 mo
9	Moran and colleagues ²	—	—	—	—	—	—	—
10	Moran and colleagues ²	—	—	—	—	—	—	—
11	Toyama and colleagues ¹⁰	48	Male	2 mo	680 g	Improvement	Yes (—)	—
12	Sirpal and colleagues ¹¹	60	Female	—	—	Improvement	—	—
13	Verbist and colleagues ¹²	29	Male	4 y	340 g	Improvement	No	2 mo
14	Takamori and colleagues ¹³	29	Female	—	—	Improvement	—	—
15	Hayashi and colleagues ¹⁴	29	Female	—	—	Improvement	—	—
16	Our series	58	Female	7 mo	45 g	Improvement	Yes (12 mo)	10 y
17	Our series	63	Female	6 mo	60 g	Improvement	No	10 y
18	Our series	59	Male	2 y	70 g	Improvement	No	9 y

Although thymectomy does not usually resolve the clinical features of MG associated with thymolipoma, it does considerably improve symptoms and allows them to be controlled with a smaller dose of anticholinesterases and corticosteroids.

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