Multiple Thymoma With Myotonic Dystrophy

A case of multiple thymoma associated with myotonic dystrophy is reported. The patient was a 42-year-old man who had two separate encapsulated thymoma in the anterior mediastinum, at 3 cm in diameter on the right side, and at 4 cm in diameter on the left. Extended thymo-thymomectomy was performed. Microscopically, the tumor in the right thymic lobe was predominantly mixed type, and that in the left predominantly epithelial type. Neuromuscular disease appeared to develop, with severe sputum retention in the larynx and he was referred to neurology at 6 months after surgery. On examination, he presented a characteristic hatchet face, muscle atrophy, muscle weakness, percussion myotonia and grip myotonia, and diagnosis was revised to be multiple thymoma associated with myotonic dystrophy. This association is extremely rare. It is difficult to clarify whether this association was a syndrome or coincidence. (JJTCVS 2001; 49: 457–460)

Key words: thymoma, myotonic dystrophy, multiple, neuromuscular disease

Takashi Hirai, MD, Akira Yamanaka, MD, Toshio Fujimoto, MD, Ayuko Takahashi, MD, Yoshihiro Takayama, MD,* and Koji Yamanaka, MD.*

Many diseases are associated with thymoma, including myasthenia gravis, cancer, pure red cell aplasia, hypogammaglobulinemia, polymyositis, and lupus erythematosus. However, the association of thymoma with myopathies other than myasthenia gravis is extremely rare. Here, we describe a case of multiple thymoma associated with myotonic dystrophy (MD).

Case

A 42-year-old Japanese man was admitted to the Fukui Red Cross Hospital for an evaluation of mediastinal masses. Tumor markers (CEA, CA-19–9, AFP, HCG) were each within normal ranges, and the serum anti-acetylcholine receptor antibody was normal. He had no myasthenic symptoms. His respiratory function was normal. IgG was normal, but IgA and IgM were each low. (IgA 73, IgM 52 mg/dl). A chest X-ray showed bilateral hilar swelling (Fig. 1). A chest CT showed two mediastinal tumors, at 3 cm in diameter on the right side, and at 4 cm in diameter on the left (Fig. 2). He was then diagnosed as having multiple thymoma with low levels of IgA and IgM.

Extended thymo-thymomectomy was performed. Two separate tumors were recognized one in the left thymic lobe and the other in the right thymic lobe. Both tumors were encapsulated (Fig. 3). The histological appearances of the two tumors were different. The tumor in the right thymic lobe was predomi-

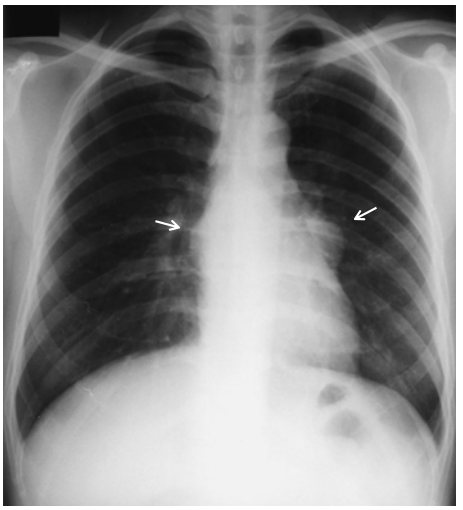


Fig. 1. Chest X-ray.
Chest-X ray showed bilateral hilar swelling. Arrows indicate the tumors.

From the Departments of Chest Surgery and* Neurology, Fukui Red Cross Hospital, Fukui, Japan.
Received for publication October 19, 2000.
Accepted for publication February 22, 2001.
Address for reprints: Takashi Hirai, MD, Department of Chest Surgery, Fukui Red Cross Hospital, 2–4–1 Tsukimi, Fukui 918–8501, Japan.

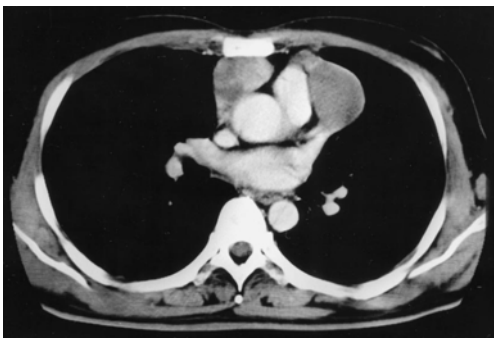


Fig. 2. Chest CT.
Chest CT showed two mediastinal tumors, in the right at 3 cm in diameter, and in the left at 4 cm in diameter.

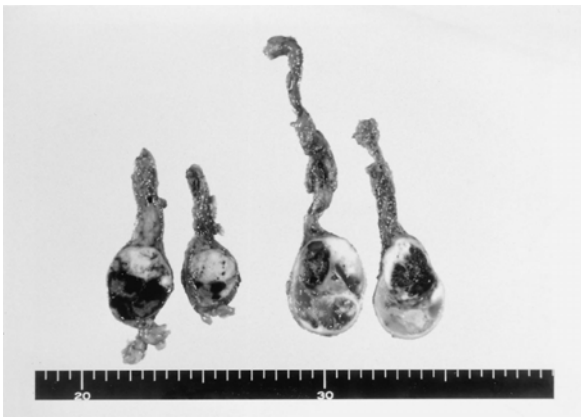
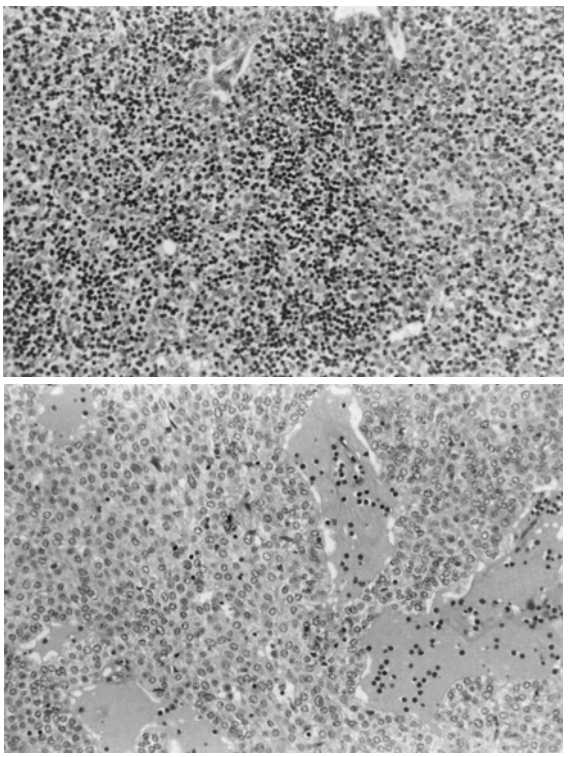


Fig. 3. Macroscopic findings of multiple thymomas.
Two separate tumors were recognized one in the left thymic lobe and the other in the right thymic lobe. Both tumors were encapsulated.



A
B

Fig. 4. Microscopic findings.
The tumor in the right thymic lobe was predominantly mixed type (Fig. 4A) (100 ×). The left tumor was predominantly epithelial type (Fig. 4B) (100 ×).

nantly mixed type, while that in the left was predominantly epithelial type (Fig. 4).

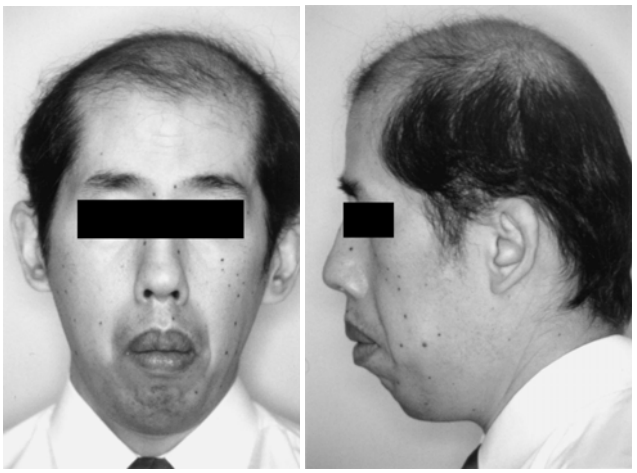
At six months after surgery, he complained of a large amount of sputum in the morning without chest X-ray abnormality, and referred to otorinolaryngology. Neuromuscular disease was suspected because of severe sputum retention in the larynx, and he was consequently referred to neurology. On examination, he presented a characteristic hatchet face, muscle atrophy, muscle weakness, percussion myotonia and grip myotonia, and diagnosed as having myotonic dystrophy. Since childhood he had always mis-swallowed while eating, and ran slowly. He tended to be sleepy all day long. He was unemployed and single. His father had suspected myopathy from a detailed interview. His appearance had a rather dull, expressionless look with sagging jaw and slight ptosis in the eyelids. Atrophy in the temporalis muscle was severe (myotonic face, hatchet face) (Fig. 5). His voice was nasal and monotonous. His grasping power was 3 kg. He presented frontal baldness, cataracts, and dysphagia.

The time of onset of the MD was not clear. In the preoperative period, he had shown no myasthenic symptom, and his respiratory function was normal. However, retrospectively, his typical hatchet face was seen but was not recognized as a sign of MD at that time.

A recurrent tumor was found in the left paracardiac mediastinum at one year and 2 months after surgery, and eight months after the diagnosis of MD. Radiation therapy was performed and complete remission was obtained. He has shown no further recurrent tumor. His muscle atrophy and muscle weakness have become progressively worse.

Discussion

Myotonic dystrophy (MD) is an autosomal dominant hereditary disease characterized by myotonia, muscular wasting of a characteristic pattern, cata-



A|B

Fig. 5. Hatchet face (myotonic face).
He had a rather dull, expressionless face with sagging jaw and slight ptosis in the eyelids. Atrophy of the temporalis muscle was severe.

Table I. *Reported cases of thymoma with myotonic dystrophy in the literature*

Case	*Year*	*Author*	*Age*	*Sex*	*Operation*	*Histology*
1	1969	Goto	51	M	autopsy	spindle
2	1980	Mudge	32	M	thymectomy	
3	1981	Kuroiwa	46	F	autopsy	mixed
4	1981	Carlin	64	F	biopsy	polygonal
5	1989	Ohkubo	42	F	autopsy	lymphocytic
6	1993	Yamamoto	36	M	ext-thymectomy*	mixed
7	Present	Hirai	41	M	ext-thymectomy*	mixed, epithelial

*extended thymectomy.

racts, testicular atrophy, and frontal baldness. Incidence of the disease is 0.5• 5.5 per 100,000. The disease usually begins in early adult life. Myotonia consists of an inability to relax a muscle normally after its contraction. Progressive muscle atrophy, muscle weakness and myotonia are the main symptoms. MD is a multi-systemic disease including the neuromuscular system, the endocrine system, the immune system, and the cardiovascular system. Gait disturbance typically occurs in the 40's. The most common cause of death in MD patients is sudden cardiac arrest.

We have found only 7 cases of MD in association with pathologically confirmed thymoma, in the world literature, including our case (Table I).[1–4] Three of the 7 cases were determined at autopsy. Kuroiwa et al. reported that association of MD and thymoma was probably coincidental.[1] However, MD is indicated as a potential complication in thymoma. It is not clear whether this association is a syndrome or coincidence.

Multiple thymoma is well known, but has seldomly been reported because of its rarity. Bernatz et al. reported that 3 (2.2%) of 138 patients with thymoma had multiple and separate tumors.[5] They did not describe any histological characteristics of multiple thymoma in detail. Jaretzky et al. reported only one case (1.05%) of multiple thymoma among 95 cases of thymoma.[6] Murakawa et al. reviewed 140 patients with thymoma clinically and histopathologically. No patient with multiple thymoma was described in this report.[7]

It is possible that the genesis of multiple thymoma involves both intra-thymic metastasis and multicentric tumors. Nomori et al. reported a case having two separate thymomas in the anterior mediastinum.[8] The two thymomas had similar histological, morphometric and immunohistochemical characteristics. They suggested the possibility of intra-thymic metastasis rather than multicentric tumors. Pescarmona et al.

investigated twenty cases of macroscopically non- neoplastic thymuses obtained from patients with myasthenia gravis histologically.[9] In three cases, multiple foci of microscopic thymoma, 0.2–0.4 mm in diameter, were observed. These findings suggested a possible multifocal origin for multiple thymoma. Okada et al. reported two cases of synchronous multiple thymoma without myasthenia gravis, and the possibility of their being multicentric tumors.[10] In our case, two encapsulated tumors existed in different thymic lobes separately, and they had different histological appearances. In our case, the findings suggest the multiple thymoma to be multicentric tumors rather than due to intra-thymic metastasis.

Murakawa et al. reviewed 140 patients with thymoma, from 43 years of experience.[7] There were 4 incidences of recurrence among 27 Masaoka's Stage I patients who underwent thymomectomy through lateral thoracotomy, before 1976. Since 1976, they adopted extended thymectomy with thymomectomy under median sternotomy as the standard operation for a thymoma even at Stage I. There was no recurrence among the 37 Stage I thymoma patients who underwent the extended resection of the thymus.

From the viewpoint of thymic tissue distribution and possible multiple thymoma, extended thymothymomectomy under median sternotomy can be considered as adequate treatment even for a Stage I thymoma.

Conclusion

We have experienced a case of multiple thymoma associated with myotonic dystrophy. Further accumulation of cases is needed to clarify whether this association is a syndrome or coincidence.

REFERENCES

1. Kuroiwa Y, Yamada A, Ikebe K, Kosaka K, Sugita H, Murakami T. Myotonic dystrophy and thymoma: a necropsy report. J Neurol Neurosurg Psychiatry 1981; 44: 173–5.
2. Carlin L, Biller J. Myotonic dystrophy and thymoma. J Neurol Neurosurg Psychiatry 1981; 44: 852–3.
3. Goto I, Ichimura K, Maruyama T, Yamaguchi T. An autopsy case of myotonic dystrophy with familial diabetes mellitus, mixed tumor of the parotid gland and a thymoma. Fukuoka Act Med 1969; 60: 126–33.
4. Mudge BJ, Tayler PB, Vanderstpek AFL. Perioperative hazards in myotonic dystrophy. Anaesthesia 1980; 35: 492–5.
5. Bernatz PE, Harrison EG, Claget OT. Thymoma: a clinicopathologic study. J Thorac Cardiovasc Surg 1961; 42: 424–44.
6. Jaretzky A, Penn AS, Younger DS, Wolf M, Olarte MR, Lovelace RE, et al. Maximal thymectomy for myasthenia gravis. J Thorac Cardiovasc Surg 1988; 95: 747–57.
7. Murakawa T, Nakajima J, Kohno T, Tanaka M, Matsumoto J, Takeuchi E, et al. Results from surgical treatment for thymoma: 43 years of experience. JJTCVS 2000; 48: 89–95.
8. Nomori H, Kobayashi K, Ishihara T, Suito T, Torikata C. A case of multiple thymoma: the possibility of intra-thymic metastasis. Jpn J Clin Oncol 1990; 20: 209–11.
9. Pescarmona E, Rosati S, Pisacane A, Rendina EA, Venuta F, Baroni CD. Microscopic thymoma: histological evidence of multi-focal cortical and medullary origin. Histopathology 1992; 20: 263–6.
10. Okada M, Tsubota N, Yoshimura M, Miyamoto Y, Sakamoto T. Two cases of synchronous multiple thymoma. Jpn J Surg 1998; 28: 1323–5.