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Metastatic Thymoma-Associated Myasthenia Gravis: Favorable Response to Steroid Pulse Therapy Plus Immunosuppressive Agent

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Background: Our study retrospectively reviewed the therapeutic effect of steroid pulse therapy in combination with an immunosuppressive agent in myasthenia gravis (MG) patients with metastatic thymoma.

Material/Methods: MG patients with metastatic thymoma that underwent methylprednisolone pulse therapy plus cyclophosphamide were retrospectively analyzed. Patients initially received methylprednisolone pulse therapy followed by oral methylprednisolone. Cyclophosphamide was prescribed simultaneously at the beginning of treatment. Clinical outcomes, including therapeutic efficacy and adverse effects of MG and thymoma, were assessed.

Results: Twelve patients were recruited. According to histological classification, 4 cases were type B2 thymoma, 3 were type B3, 2 were type B1, and 1 was type AB. After combined treatment for 15 days, both the thymoma and MG responded dramatically to high-dose methylprednisolone plus cyclophosphamide. The symptoms of MG were improved in all patients, with marked improvement in 6 patients and basic remission in 4. Interestingly, complete remission of thymoma was achieved in 5 patients and partial remission in 7 patients. Myasthenic crisis was observed in 1 patient and was relieved after intubation and ventilation. Adverse reactions were observed in 7 patients (58.3%), most commonly infections, and all were resolved without discontinuation of therapy. During the follow-up, all patients were stabilized except for 1 with pleural metastasis who received further treatment and another 1 who died from myasthenic crisis.

Conclusions: The present study in a series of MG patients with metastatic thymoma indicated that steroid pulse therapy in combination with immunosuppressive agents was an effective and well-tolerated for treatment of both metastatic thymoma and MG. Glucocorticoid pulse therapy plus immunosuppressive agents should therefore be considered in MG patients with metastatic thymoma.

MeSH Keywords: Methylprednisolone • Myasthenia Gravis • Thymoma

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Background

Thymoma is an uncommon neoplasm of the thymus, derived from the thymic epithelial cells. More than 90% of patients with thymoma have autoimmune diseases [1]. Myasthenia gravis (MG) is the most common paraneoplastic neurological disorder associated with thymoma. About 30–50% of thymoma patients have been reported to develop MG; while 10–20% of MG patients have thymoma [2,3]. MG with thymoma is particularly associated with autoantibodies against postsynaptic nicotinic acetylcholine receptors (AchR-Abs) [4]. Both thymoma and MG can be treated by surgery. A complete removal of a thymoma may not worsen the prognosis of MG patients [5]. However, mediastinal and pleural recurrence remains a significant clinical problem, especially for patients with advanced and incompletely resected thymoma [6–8]. Surgical treatment of recurrent thymoma is technically challenging and has been reported to be effective in only one-third of patients [6,7]. Even following radical thymoma resection, patients may still suffer from MG, and continuous follow-up and pharmacological treatments are needed for these patients.

Steroids have generally been used for control of MG [9,10]. A growing number of studies have indicated that these drugs are effective in treatment of the patients with advanced or invasive thymoma [11–16]. In patients with MG-associated thymoma, symptoms of both MG and the tumor have been reported to be improved by steroid therapy, particularly in advanced or metastatic cases [17,18]. Immunosuppressive agents such as azathioprine and methylprednisolone have also been used for treatment of invasive thymoma-associated MG, with improved clinical symptoms and reduced tumor volumes [19]. Moreover, combined treatment with steroids and immunosuppressive agents has been suggested to be useful in treatment of invasive thymoma and myasthenic symptoms [20]. However, high-dose steroid pulse therapy carries the risk of worsening MG. Myasthenic crisis has been reported in a patient receiving steroid chemotherapy for advanced thymoma with MG [21]. Unfortunately, almost all these studies are case reports, making it difficult to assess the therapeutic potential of steroids in these patients. In this study, we retrospectively analyzed a series of MG patients with metastatic thymoma that received steroid pulse therapy in combination with immunosuppressive agent therapy.

Material and Methods

Patients

MG patients with metastatic thymoma were reviewed retrospectively. A total of 12 patients who underwent methylprednisolone pulse therapy during January 2013 to January 2016 were identified. The diagnosis of MG was based on clinical symptoms and confirmed by acetylcholine receptor antibody (AChR-Ab) test, neostigmine test, fatigue test, and electromyography tests [22]. The clinical classification of MG was based on Osserman's system [23]. All patients underwent computed tomographic (CT) scanning. Histological diagnosis of thymomas was performed based on the World Health Organization (WHO) histological classification [24]. Clinical and pathologic staging of thymoma was done according to Masaoka staging system [25]. Diagnosis of metastasis was performed by CT scan and/or pathologic analysis. This study was approved by the Ethics Committee of the First Hospital of Shijiazhuang. Informed consent was obtained from all participants.

Treatment of MG patients with metastatic thymoma

As shown in Table 1, 8 MG patients with metastatic thymoma were initially treated according to their clinical conditions, but the symptoms were not improved. The patients were then treated by methylprednisolone pulse therapy plus immunosuppressive agent. Methylprednisolone pulse therapy was begun at 1 g/day and reduced by half every 3 days until reaching 60 mg/day. Oral methylprednisolone at 52 mg/day was then prescribed and the patients were discharged from the hospital. The dose of methylprednisolone was reduced and then tapered slowly on alternate days. The detailed schedules of methylprednisolone therapy are described in Table 2. Cyclophosphamide was given simultaneously at a dose of 100 mg/day and continued for 2 months until the discontinuance of oral methylprednisolone.

Clinical outcome and follow-up

The clinical outcome of MG at discharge and during the follow-up was assessed based on the clinical absolute and relative scoring system [26]. Briefly, the clinical relative score (CRS) was calculated to evaluate the improvement or deterioration of the MG: (1) Clinical remission (CR): CRS ≥95%; (2) Basic remission (BR): 80% ≤CRS <95%; (3) Marked improvement (MI): 50% ≤CRS <80%; (4) Improvement (IM): 25% ≤CRS <50%; and (5) Ineffectiveness (IE): CRS <25%. The total clinical efficiency was based on the number of patients with CRS ≥25% (CR, BR, MI, and IM). A follow-up CT scan was performed to assess the response of the thymoma according to WHO criteria [27]. Complete remission was defined as the disappearance of clinical evidence of active tumors for at least 4 weeks; partial remission (PR) as a minimum 50% reduction in total tumor size for at least 4 weeks; non-response (NR) as less than 50% reduction or more than 25% increase in total tumor size of existing lesions; and progressive disease (PD) as more than 25% increase in any measurable lesions or appearance of new lesion(s). All patients were followed up until the date of death or June 2016, and the activity and progression of the diseases were recorded.

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Table 1. Baseline characteristics of MG patients with mestastic thymoma.

No	Age (years)	Gender	Masaoka stage	WHO type	Age at surgery (years)	Prior treatment		Age of MG onset (years)	MG crisis	Osserman stage
						Surgery	Other therapy (cycles)			
1	48	Male	III	B3	42	Thora-cotomy	RT	42	No	I
2	50	Male	II	B2	48	Thora-coscopy	RT	48	No	IIB
3	26	Female	III	B2	21	Thora-cotomy	RT+TP (4)+GP (6)	21	No	IIB
4	65	Female	N/A	N/A	No	No	DP (2)+RT+IP (2)	64	No	IV
5	52	Female	II	B2	45	Thora-coscopy	RT+CTX+TCM	45	No	IIB
6	28	Male	N/A	AB	24	N/A	No	24	Yes	IIB
7	34	Male	N/A	N/A	No	No	RT	31	Yes	IIB
8	59	Female	III	B1	54	Thora-cotomy	RT+CAP (6)	59	No	IIB
9	48	Male	II	B1	44	Thora-cotomy	No	44	No	IIB
10	61	Male	N/A	B2	59	Thora-coscopy	RT+EP (2)	59	Yes	IV
11	47	Female	II	B3	39	Thora-cotomy	GC+CTX	39	Yes	IIB
12	36	Female	II	B3	30	Thora-cotomy	RT+CTX+TCM	30	No	IV

MG – myasthenia gravis; N/A – not available; RT – radiotherapy; TP – paclitaxel plus cisplatin; GP – gemcitabine plus cisplatin; IP – ifosfamide plus cisplatin; CAP – cyclophosphamide plus adriamycin and cisplatin; EP – etoposide plus cisplatin; GC – glucocorticoid therapy; CTX – cyclophosphamidum; TCM – Traditional Chinese medicine.

Table 2. Schedules of methylprednisolone therapy.

Pulse therapy	Dose
3 days	1 g/day
3 days	0.5 g/day
3 days	0.25 g/day
3 days	0.125 g/day
3 days	60 mg/day
Oral therapy	**Dose (4 mg/tablet)**
Phase I	
3 days	52 mg/day
3 days	44 mg/day
3 days	36 mg/day
3 days	24 mg/day

Oral therapy	Dose (4 mg/tablet)
Phase II	
15 days	24 mg and 20 mg on alternate days
15 days	24 mg and 16 mg on alternate days
15 days	24 mg and 12 mg on alternate days
15 days	24 mg and 8 mg on alternate days
15 days	24 mg and 4 mg on alternate days
15 days	24 mg and 0 mg on alternate days
15 days	20 mg and 0 mg on alternate days
15 days	16 mg and 0 mg on alternate days
15 days	12 mg and 0 mg on alternate days
15 days	8 mg and 0 mg on alternate days
15 days	4 mg and 0 mg on alternate days

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Table 3. Clinical characteristics and therapy of MG patients with mestastic thymoma.

No	Time from surgery to metastasis (months)	Metastasis	WHO type	MG crisis	Initial therapy (Cycle)	GC+ Immunosuppressive agent
1	49	Right cardiophrenic angle	N/A	No	RT	MP+CTX
2	18	Right pleura and interlobular septa	B2	No	–	MP+CTX
3	38	Right lung and diaphragm	B3	No	–	MP+CTX
4	24*	Pleura	N/A	No	–	MP+CTX
5	60	Right pleura	B2	No	RT	MP+CTX
6	48	Pleura	N/A	Yes	DP (1)	MP+CTX
7	38*	Pleura	N/A	Yes	Immune globulin	MP+CTX
8	42	Lower right pleura	B1	No	Docetaxel (?)	MP+CTX
9	36	Right pleura and diaphragm*	N/A	No	DP (3)+RT	MP+CTX
10	26	Chest wall	B2	Yes	RT	MP+CTX
11	62	Chest wall	B3	Yes	RT	MP+CTX
12	65	Anterosuperior mediastinum	B3	No	–	MP+CTX

N/A – not available; MP – methylprednisolone; CTX – cyclophosphamidum; RT – radiotherapy; DP – docetaxel plus cisplatinum.
* Recurrence after further therapy with DP (2)+RT+IP (2). * Time from thymoma diagnosis to metastasis since the patients did not underwent surgery.

Results

The medical records of 12 MG patients with metastatic thymoma who underwent methylprednisolone pulse therapy plus methylprednisolone were reviewed. There were 6 males and 6 females. The median age of the patients was 48 years (range: 26–65 years). Clinical characteristics with regard to thymoma and MG of the patients and prior treatments are summarized in Table 1. Anti-acetylcholine receptor (Anti-AchR-Ab) test results were positive in all but 1 patient. The histologic types of thymoma were B2 in 4 patients, B3 in 3 patients, B1 in 2 patients, and AB in 1 patient. Five patients were at Masaoka stage II, and 3 in stage III. The clinical type of MG was IIB in 8 patients, IV in 3 patients, and I in 1 patient. Nine patients were treated by surgery. The operative approach was thoracotomy in 6 patients and thoracoscopy in 3 patients. Ten patients were further treated by radiotherapy (RT) and/or medication.

All patients showed metastatic tumors under CT scanning. As shown in Table 3, the most common sites of metastases were the pleura, occurring in 5 out of 12 patients. However, biopsies were not performed in some cases; therefore, the exact histological types of their thymomas were not available. The mean time from surgery to local metastasis was 42 months (range: 18–65). Four patients experienced an MG crisis. The patients were initially treated by radiotherapy, docetaxel-based chemotherapy (docetaxel plus cisplatinum or docetaxel alone), and/or immune globulin therapy, without improvement in clinical outcome. Methylprednisolone pulse therapy was then prescribed in combination with an immunosuppressive agent (CTX).

After methylprednisolone pulse plus CTX therapy for 15 days, chest CT showed marked shrinkage of the thymoma in all patients. As shown in Table 4, 5 patients were in complete remission and the remaining 7 patients were in partial remission. With respect to clinical outcome of MG, the symptoms of all patients were resolved, with a remission rate of 100% (CRS ≥25%). The response to MG was MI in 6 cases, BR in 4 cases, CR and IM in 1 case each. During the treatment period, 1 patient developed myasthenic crisis and the symptom was relieved by intubation and ventilation (case no. 5). Adverse effects were observed in 7 patients (58.3%). Infection was the most common one and occurred in 4 patients (3 with pulmonary infection and 1 with gastrointestinal fungal infection). Two patients had elevated alanine transaminase (ALT) levels.

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Table 4. Outcome of MG patients with mestastic thymoma.

No	Response of thymoma	AchR-Ab		MG score		Response of MG	Adverse effects	Follow-up	
		Before	After	Before	After			Progression/ months	Status/ months
1	PR	8.83	6.97	6	1	BR	Steroid diabetes	No	Alive/6
2	CR	13.78	8.12	46	4	BR	Elevated blood lipid	No	Alive/6
3	PR	10.29	1.26	30	6	BR	No	No	Alive/11
4	CR	10.6	15.09	32	18	IM	No	No	Alive/11
5	CR	0.01	0.02	6	0	CR*	No	MG crisis/11	Alive/11
6	CR	11.61	–	56	12	MI	Pulmonary infection, elevated ALT	No	Alive/35
7	PR	7.59	4.81	34	8	MI	Pulmonary infection	No	Alive/13
8	PR	3.84	2.3	24	10	MI	Elevated ALT	Pleural metastasis/20	Alive/20
9	PR	5.89	6.41	14	6	MI	Gastrointestinal fungal infection	No	Alive/12
10	PR	12.5	6.93	50	4	BR	No	MG crisis/18	Die/18
11	PR	12.6	7.8	34	12	MI	No	No	Alive/4
12	CR	8.6	4.3	26	8	MI	Pulmonary infection	No	Alive/18

CR – complete remission; PR – partial remission; CR – complete remission; BR – basic remission; MI – marked improvement; IM – improvement; ALT – aminotransferase.

Steroid diabetes and elevated blood lipid were identified in 1 patient each. All adverse events were resolved without discontinuation of therapy.

The patients were then prescribed oral methylprednisolone and discharged from the hospital. The patients were followed up for 11.5 months (range: 4–35). During the follow-up, 1 patient (case no. 10) died from myasthenic crisis after 18 months of follow-up. Another patient (case no. 8) developed pleural metastasis 20 months later and received further methylprednisolone pulse plus CTX therapy.

Discussion

Steroids and immunosuppressive agents have both been used for treatment of MG and thymoma. The latter is generally prescribed together with steroids to allow tapering the dose of steroids [9]. However, to the best of our knowledge, their use in treatment of MG and thymoma has been reported as case reports in only a few patients with MG-associated thymoma. Therefore, we retrospectively analyzed the therapeutic potential of methylprednisolone pulse plus CTX therapy in a case series of 12 MG patients with metastatic thymoma during January 2013 to January 2016. Our study showed a marked beneficial effect of combined use of high-dose steroid pulse therapy in combination with an immunosuppressive agent in treatment of metastatic thymoma and MG. All metastatic thymomas responded dramatically to methylprednisolone pulse therapy plus CTX. MG symptoms were also found to be successfully resolved, without significant adverse effects.

Glucocorticoids are widely used for treatment of thymoma, especially for advanced or recurrent/metastatic ones [14]. The most dramatic response has been reported in cases of subtype B1 thymoma, which contains numerous lymphocytes [11,28–30]. The mechanism has been suggested to be associated with the apoptotic effects of corticosteroids on the lymphocyte component of the tumors [12,30]. However, it was also reported to act on both neoplastic thymic epithelial cells and lymphocytes [31]. Glucocorticoid receptor (GR) is expressed in all histological types of thymoma, and no significant difference has been identified among the different subtypes [32]. Furthermore, steroid pulse therapy has been reported to induce the apoptosis of both neoplastic thymic epithelial cells and lymphocytes [15,33]. In MG-associated thymoma, MG was found to be significantly more common in type B thymomas, particularly in subtype B1 [34]. Most MG-associated thymomas that

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have been reported to respond to glucocorticoids (alone and combined) were B type [18,20,21,33]. Corroborating the results of these studies, in the present study almost all primary thymomas were classified as type B, although fewer subtype B1 cases were identified. High-dose methylprednisolone pulse therapy plus immunosuppressive agents dramatically reduced the tumor sizes of all patients. Symptoms of MG were also obviously improved, without significant adverse events. Our findings show that glucocorticoids pulse therapy plus immunosuppressive agents is helpful for treatment of metastatic thymoma with MG. Hayashi et al. suggested that high-dose methylprednisolone with chemotherapy was potentially effective for invasive thymoma, regardless of the histological subtypes of thymoma [13]. However, in view of the few cases reported and the few cases of type A thymoma-associated MG in our study, it is hard for us to determine the therapeutic effect of glucocorticoids in different histological types of thymoma associated with MG. Therefore, future studies with a larger number of patients, especially with type A thymoma-associated MG, are needed.

Both MG and thymoma have been suggested to respond well to glucocorticoids and immunosuppressive agent therapy. However, high-dose glucocorticoid pulse therapy has been reported to cause transient exacerbation of MG symptoms [35], which may lead to use of low-dose steroids among patients and physicians [36]. However, according to a double-blind placebo-controlled study, a single intravenous methylprednisolone pulse caused no severe adverse effects in patients with moderate MG [37]. A comparative study of high-dose intravenous methylprednisone with low-dose oral prednisolone in an open-label, randomized trial showed more rapid improvement and fewer adverse effects in the high-dose intravenous methylprednisone group [38]. In MG-associated thymoma, MG crisis has been reported in a patient when chemotherapy, including high-dose methylprednisolone, was prescribed for advanced thymoma [21]. In other case studies of MG-associated thymoma, however, no adverse effects were reported with use of steroids or their combined therapy with immunosuppressive agents [18,33] . Our results showed some adverse effects of methylprednisolone pulse therapy plus immunosuppressive agents, most commonly infections. All adverse effects were well controlled without discontinuation of the treatment. These variations seem to be caused by the different regimens of steroids and immunosuppressive agents used in our study. The combined treatment with 'steroid-sparing' immunosuppressants has been suggested to be helpful for dose-tapering of steroids, which may contribute to the reduced risk of related adverse effects [39]. However, despite these variations, the results of our study show that methylprednisolone pulse therapy plus an immunosuppressive agent was effective and well-tolerated in synchronous treatment of MG and metastatic thymoma, without significant adverse events.

This study has some limitations. Primarily, it was a retrospective study without a control group; therefore, the same diagnostic and therapeutic protocols were not available. In addition, the number of patients recruited was small and it was difficult for us to analyze the risk factors based on this small sample size, and a larger cohort study is needed. Despite these limitations, our study shows therapeutic benefit of methylprednisolone pulse therapy plus immunosuppressive agents in treatment of both MG and metastatic thymoma.

Conclusions

Our study describes a series of MG patients with metastatic thymoma well controlled by methylprednisolone pulse therapy plus immunosuppressive agents (CTX). Our findings suggest that steroid pulse therapy in combination with immunosuppressive agents were effective and well-tolerated in treatment of both metastatic thymoma and MG. Steroid pulse therapy plus immunosuppressive agents should therefore be considered in MG patients with metastatic thymoma for synchronous treatment of both thymoma and MG.

Disclosure

The authors declare no conflicts of interest.

References:

1. Filosso PL, Galassi C, Ruffini E et al: Thymoma and the increased risk of developing extrathymic malignancies: A multicentre study. Eur J Cardiothorac Surg, 2013; 44: 219–24
2. Romi F: Thymoma in myasthenia gravis: From diagnosis to treatment. Autoimmune Dis, 2011; 2011: 474512
3. Marx A, Porubsky S, Belharazem D et al: Thymoma related myasthenia gravis in humans and potential animal models. Exp Neurol, 2015; 270: 55–65
4. Cufi P, Soussan P, Truffault F et al: Thymoma-associated myasthenia gravis: On the search for a pathogen signature. J Autoimmun, 2014; 52: 29–35
5. Romi F, Gilhus N, Varhaug J et al: Disease severity and outcome in thymoma myasthenia gravis: A long-term observation study. Eur J Neurol, 2003; 10: 701–6
6. Lucchi M, Davini F, Ricciardi R et al: Management of pleural recurrence after curative resection of thymoma. J Thorac Cardiovasc Surg, 2009; 137: 1185–89
7. Okumura M, Shiono H, Inoue M et al: Outcome of surgical treatment for recurrent thymic epithelial tumors with reference to world health organization histologic classification system. J Surg Oncol, 2007; 95: 40–44
8. Lucchi M, Basolo F, Mussi A: Surgical treatment of pleural recurrence from thymoma. Eur J Cardiothorac Surg, 2008; 33: 707–11
9. Sathasivam S: Steroids and immunosuppressant drugs in myasthenia gravis. Nat Clin Pract Neurol, 2008; 4: 317–27
10. Group MS: A trial of mycophenolate mofetil with prednisone as initial immunotherapy in myasthenia gravis. Neurology, 2008; 71: 394–99

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11. Barratt S, Puthucheary ZA, Plummeridge M: Complete regression of a thymoma to glucocorticoids, commenced for palliation of symptoms. Eur J Cardiothorac Surg, 2007; 31: 1142–43
12. Tiseo M, Monetti F, Ferrarini M et al: Dramatic responses to therapy in rare tumors CASE 1. Complete remission to corticosteroids in an octreotide-refractory thymoma. J Clin Oncol, 2005; 23: 1578–79
13. Hayashi M, Taira M, Yamawaki I, Ohkawa S-I: High-dose methylprednisolone with chemotherapy for invasive thymoma: A case report. Anticancer Res, 2006; 26: 3645–48
14. Loehrer PJ, Wang W, Johnson DH, Ettinger DS: Octreotide alone or with prednisone in patients with advanced thymoma and thymic carcinoma: An Eastern Cooperative Oncology Group Phase II Trial. J Clin Oncol, 2004; 22: 293–99
15. Kobayashi Y, Fujii Y, Yano M et al: Preoperative steroid pulse therapy for invasive thymoma. Cancer, 2006; 106: 1901–7
16. Ito J, Sekiya M, Miura K et al: Refractory recurrent thymoma successfully treated with long-acting somatostatin analogue and prednisolone. Intern Med, 2009; 48: 1061–64
17. Mizuno T, Hashimoto T, Yamakawa Y et al: A case of a small thymoma associated with myasthenia gravis in which the tumor was reduced by corticosteroid therapy. Nihon Kyobu Geka Gakkai, 1992; 40:975–77
18. Tandan R, Taylor R, DiCostanzo DP et al: Metastasizing thymoma and myasthenia gravis. Favorable response to glucocorticoids after failed chemotherapy and radiation therapy. Cancer, 1990; 65:1286–90
19. Kumagai M, Kondou T, Handa M et al: Treatment of invasive thymoma with myasthenia gravis: A case report responsive to azathioprine and methylprednisolone. Kyobu Geka, 1990; 43: 231–35
20. Miura S, Azuma K, Yamada K et al: Combined treatment with prednisolone and tacrolimus for myasthenia gravis with invasive thymoma. Acta Neurol Belg, 2010; 110: 107
21. Fujiwara A, Inoue M, Kusumoto H et al: Myasthenic crisis caused by preoperative chemotherapy with steroid for advanced thymoma. Ann Thorac Surg, 2015; 99: e11–13
22. Li Z-Y, Bogdos M, Giannopoulos S et al: China guidelines for the diagnosis and treatment of myasthenia gravis. Neuroimmunol Neuroinfammation, 2016; 3: 1–9
23. Li Z-Y, Bogdos M, Giannopoulos S et al: China guidelines for the diagnosis and treatment of myasthenia gravis. 2016
24. Moran CA, Suster S: The World Health Organization (WHO) histologic classification of thymomas: A reanalysis. Curr Treat Options Oncol, 2008; 9(4–6): 288–99
25. Luebke T, Beckurts KT, Wickenhauser C et al: Masaoka staging is of prognostic relevance in type B3/C thymomas. Anticancer Res, 2004; 24: 4113–19
26. Liu G-C, Gao B-L, Yang H-Q et al: The clinical absolute and relative scoring system – A quantitative scale measuring myasthenia gravis severity and outcome used in the traditional Chinese medicine. Complement Ther Med, 2014; 22: 877–86
27. World Health Organization: WHO handbook for reporting results of cancer treatment. 1979
28. Termeer A, Visser F, Mravunac M: Regression of invasive thymoma following corticosteroid therapy. Neth J Med, 2001; 58: 181–84
29. Koshio J, Tsukada H, Nagasawa Y et al: Successful corticosteroid therapy of a recurrent thymoma with pure red cell aplasia. Nihon Kokyuki Gakkai zasshi, 2007; 45: 879–83
30. Palmieri G, Lastoria S, Colao A et al: Successful treatment of a patient with a thymoma and pure red-cell aplasia with octreotide and prednisone. N Engl J Med, 1997; 336: 263–65
31. Funakoshi Y, Shiono H, Inoue M et al: Glucocorticoids induce G1 cell cycle arrest in human neoplastic thymic epithelial cells. J Cancer Res Clin Oncol, 2005; 131: 314–22
32. Mimae T, Tsuta K, Takahashi F et al: Steroid receptor expression in thymomas and thymic carcinomas. Cancer, 2011; 117: 4396–405
33. Yoshida Y, Ueda R, Murakawa T et al: Thymoma hyalinized by steroid therapy in myasthenia gravis. Asian Cardiovasc Thorac Ann, 2012; 20: 479–81
34. Ströbel P, Bauer A, Puppe B et al: Tumor recurrence and survival in patients treated for thymomas and thymic squamous cell carcinomas: A retrospective analysis. J Clin Oncol, 2004; 22: 1501–9
35. Bae JS, Go SM, Kim BJ: Clinical predictors of steroid-induced exacerbation in myasthenia gravis. J Clin Neurosci, 2006; 13: 1006–10
36. Kataoka H, Furiya Y, Ueno S: Complete remission of generalized myasthenia gravis by corticosteroid treatment alone without thymectomy. Case Rep Neurol, 2011; 3: 239–41
37. Lindberg C, Andersen O, Lefvert A: Treatment of myasthenia gravis with methylprednisolone pulse: A double blind study. Acta Neurol Scand, 1998; 97: 370–73
38. Zhang J, Wu H: Effectiveness of steroid treatment in juvenile myasthenia gravis. Chinese Journal of Pediatrics, 1998; 36: 612–14 [in Chinese]
39. Hoffmann S, Kohler S, Ziegler A, Meisel A: Glucocorticoids in myasthenia gravis – if, when, how, and how much? Acta Neurol Scand, 2014; 130: 211–21

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