Journal of Pediatric Surgery 55 (2020) 1850–1853

Contents lists available at ScienceDirect

Journal of Pediatric Surgery

journal homepage: www.elsevier.com/locate/jpedsurg

Open versus thoracoscopic thymectomy for juvenile myasthenia gravis

S Christopher Derderian [a], D Dean Potter [b], Samiksha Bansal [a], Phillip G Rowse [c], David A Partrick [a,*]

[a] Department of Pediatric Surgery, Children's Hospital Colorado, Aurora, CO
[b] Division of Pediatric Surgery, Mayo Clinic, Rochester, MN
[c] Department of Cardiothoracic Surgery, Mayo Clinic, Rochester, MN

ARTICLE INFO

Article history:
Received 22 July 2019
Received in revised form 1 November 2019
Accepted 19 November 2019

Key words:
Juvenile myasthenia gravis
Myasthenia gravis
Thymectomy
Thymoma
Thoracoscopic thymectomy

ABSTRACT

Background: Juvenile myasthenia gravis (JMG) is an antibody mediated autoimmune disorder that manifests as progressive voluntary muscle weakness and fatigue. In medically refractory cases, thymectomy has been shown to abrogate symptoms and reduce glucocorticoid dependence. While transcervical or transsternal incisions have been the traditional approach, adult trends now favor thoracoscopic thymectomy. Little data exist to support this approach in children.
Methods: A retrospective review of all patients younger than 20 years of age who underwent a thymectomy for JMG at two pediatric institutions between 2001 and 2018 was performed. Children were divided into either an open (transcervical or transsternal) or thoracoscopic group and baseline characteristics, perioperative, and postoperative outcomes were compared.
Results: Thirty-four thymectomies were performed during the 18-year study period; 18 via an open and 16 via a thoracoscopic approach. The operative time was shorter for open procedures compared thoracoscopic ones (108 ± 49 and 145 ± 43 min, respectively, $p = 0.025$). Thoracoscopic thymectomy was associated with less intraoperative blood loss (5.5 ± 6.0 vs 55 ± 67 ml, $p = 0.007$), decreased duration of postoperative intravenous narcotic use (5.0 ± 1.5 vs 20 ± 23 h, $p = 0.018$), and a shorter length of hospitalization (1.7 ± 1.0 vs 2.7 ± 1.1 days, $p = 0.009$). No perioperative complication occurred in either group. Clinical improvement was reported in 94% of children in both groups.
Conclusions: Thoracoscopic thymectomy in children is a safe and effective surgical technique for the treatment of JMG. Increased acceptance of this minimally invasive approach by children, families, and referring neurologists may enable earlier surgical intervention.
Type of study: Clinical research paper.
Level of evidence: III

Myasthenia gravis affects one in 50,000 individuals of whom 10%–25% are children or adolescents [1,2]. As an organ specific autoimmune disorder, it is characterized by the production of antibodies directed against postsynaptic nicotinic acetylcholine receptors (AChR) on voluntary muscles. Blockade of these receptors results in progressive voluntary muscle weakness and fatigue. Patient history and clinical examination are heavily relied upon to make the diagnosis; however, adjunctive tests including an immune assay for serum AChR antibodies are frequently obtained [3]. Additional tests employed when the diagnosis remains in question include single fiber electromyography and the Tensilon test, which is performed by administering edrophonium to promote accumulation of acetylcholine at the post-synaptic AChR and, in the setting of myasthenia gravis, it results in improvement in muscle strength [3].

Disease severity can be classified according to the Osserman classification: I — extraocular muscle involvement including ptosis and diplopia; IIa — mild generalized muscle weakness in which ocular muscles and minimal bulbar and skeletal muscle are involved; IIb — moderate generalized muscle weakness with progressive onset of symptoms and weakness; III — acute onset of symptoms within six months of diagnosis including severe bulbar and skeletal muscle and respiratory muscle weakness; and V — severe late myasthenia gravis with disease progression for two or more years [4].

First line therapy for myasthenia gravis is an acetylcholinesterase inhibitor. Among patients who fail to respond to an acetylcholinesterase inhibitor, immunosuppressants such as steroids are initiated with the goal to taper the dose over time. For patients who are unable to be weaned from steroids or suffer from frequent relapses in symptoms, steroid-sparing immunosuppressants such as azathioprine, mycophenolate, or methotrexate are often started. If these do not adequately alleviate symptoms, additional adjunctive immunosuppressants including tacrolimus, ciclosporin, rituximab, and cyclophosphamide may be considered. For acute exacerbations, symptomatic improvement has been observed with rapid immunotherapies include plasma exchange and intravenous immune globulin [5]. Depending on the immunosuppressive agent

* Corresponding author at: Department of Pediatric Surgery, Children's Hospital Colorado, 13123, East 16th Ave, Aurora, CO 80045. Tel.: +1 720 777 6174.
E-mail address: david.partrick@childrenscolorado.org (D.A. Partrick).

https://doi.org/10.1016/j.jpedsurg.2019.11.013
0022-3468/

prescribed, debilitating side effects may include increased susceptibility to infections, mood instability, weight gain, nausea, and diarrhea.

Surgery is indicated in medically refractory disease with the goal of promoting disease remission (i.e. resolution of symptoms). If not achieved, symptomatic improvement and/or steroid dose reduction is often accomplished. In order to gauge the responsiveness to surgical thymectomy, the DeFilippi classification has been proposed. This classification is divided into five categories with class I defined as complete remission with no medication requirement, class II as asymptomatic with a decreased medication requirement, class III as improved symptoms with a decreased medications requirement, class IV as no change in symptoms or medication requirement, and class V as progression of symptoms [6].

Since the first report of a therapeutic thymectomy by Alfred Blalock in 1939, followed by a series from his colleagues in 1945, suggesting remission after thymectomy [7,8], this treatment modality has played a central role in the management of medically refractory disease. Compared to adult myasthenia gravis, rates of remission and clinical improvement after thymectomy in juvenile myasthenia gravis (JMG) are substantially higher, suggesting that early intervention may be more effective [9,10].

Traditionally, thymectomies have been performed through open techniques, including a complete or partial median sternotomy, a transcervical incision, or a combination of the two. Additionally, some surgeons use a hybrid strategy combining open and thoracoscopic techniques [11,12]. In recent years, several adult studies have advocated for complete thoracoscopic thymectomy [13–15]. This approach has also been performed in children with favorable outcomes supported by small case series [16–18]. As the goal is complete resection while minimizing risk to the patient, the optimal surgical approach for children is still debated. Thus, in this study, we compare open to thoracoscopic thymectomy for JMG to determine if a difference in perioperative and postoperative outcomes exists.

1. Methods

After obtaining Institutional Review Board approval, records of all children younger than 20 years of age, who underwent thymectomy between September 2001 and December 2018 at two geographically separate academic institutions were reviewed. Patients were identified using ICD-9 and ICD-10 codes for myasthenia gravis or thymoma as well as procedural codes for thymectomy and thymic tumor resection. Patients were divided into an open (transcervical, transsternal, or thoracoscopic-assisted) or thoracoscopic group. Patient records were abstracted from the electronic medical record to analyze demographic data, disease severity, prescribed medications, time between diagnosis and thymectomy, as well as operative details and postoperative outcomes.

The diagnosis of JMG was based on a compatible history, physical examination, electromyography findings, evidence of circulatory AChR antibodies and/or response to anticholinergic agents (Tensilon test). The severity of preoperative disease was graded according to the Osserman criteria as described above [4]. Patients with JMG were considered surgical candidates in cases of medically refractory disease agreed upon by both the neurologist and surgeon. Postoperative DeFilippi classification was used to describe the clinical effectiveness of thymectomy [6]. Univariate analyses included Fisher's exact test and Student t-test. A p-value of <0.05 was considered statistically significant.

1.1. Surgical technique

Thoracoscopic thymectomies were performed under general anesthesia through the left chest in all but one case. To approach the thymus from the left hemithorax, the patient was placed in a modified right lateral thoracotomy position with the head elevated 30° as has been previously described by Kogut et al. [19]. The left lung was collapsed either using a selective right lung ventilation strategy or more commonly by a CO_2 insufflation of 5 mmHg pressure. Three 5-mm ports were placed in the left hemithorax including a camera port along the anterior axillary line within the fourth intercostal space. The parietal pleura was incised to expose the lateral border of the left lobe of the thymus. Using a combination of sharp and blunt dissection, the inferior horn of the left lobe of thymus was freed from the pericardium first followed by the sternum anteriorly, keeping the phrenic nerve under direct visualization to avoid injury as this could potentially exacerbate baseline weakness. Electrocautery was also minimized. Dissection was then carried out in an inferior to superior fashion, staying close to the gland. Ligasure (Medtronic, Boulder, CO) was used to divide small vessels draining the gland along the brachiocephalic vein. Mobilization of the gland was then continued into the thoracic inlet, dissecting the gland completely off of surrounding mediastinal fat and removing it entirety through one of the 5-mm ports. Postoperatively, patients were managed on the floor. Chest tube drainage was at the discretion of operating surgeon although most were removed intraoperatively if no evidence of an air leak or excessive drainage was apparent. Patients resumed their preoperative medications immediately after surgery.

2. Results

A total of 34 children underwent a thymectomy for the treatment of JMG at the two institutions over the 18-year study period. Eighteen patients underwent an open thymectomy (six transsternal, six transcervical, and six thoracoscopic-assisted transcervical) and 16 underwent a thoracoscopic thymectomy. All but one open procedure occurred between 2001 and 2009 and all thoracoscopic ones occurred between 2010 and 2018. A partial sternotomy was performed in one of the transcervical cases owing to gland extension into the chest. No thoracoscopic thymectomy required conversion to an open procedure; however, two early cases required bilateral thoracoscopy. Other than age, for which the open group was older than the thoracoscopic one, demographics, baseline diagnostic results, and prescribed medications were similar between groups. No significant differences from time of diagnosis to surgery and Osserman stages between the groups were observed (Table 1).

The operative time for an open thymectomy was shorter than that of a thoracoscopic one (108 ± 43 min versus 145 ± 43 min respectively, $p = 0.025$, Table 2). Operative time for thoracoscopic thymectomy did not decrease over the study period, presumably owing to integral trainee involvement. Intraoperative blood loss was 10-fold less in the thoracoscopic group (5.5 ± 6.0 vs 55 ± 67 ml, $p = 0.007$, Table 2). No patient in either group required an intraoperative or postoperative blood transfusion. Seven children had a chest tube placed that remained in place postoperatively — six were removed on postoperative day one and one on postoperative day two. Among those who underwent an open thymectomy, a chest tube was placed following a transsternal approach in one case and a thoracoscopic assisted transcervical approach in two cases.

Postoperatively, no patient required ventilator support or suffered a major complication. The duration of intravenous narcotic use was fourfold shorter in the thoracoscopic group compared to the open group (5.0 ± 1.5 vs 20 ± 23 h, respectively, $p = 0.018$, Table 2). Those who underwent a thoracoscopic thymectomy were in the hospital one day less than those who underwent an open thymectomy (2.7 ± 1.1 vs 1.7 ± 1.0 days, $p = 0.009$). Clinical improvement, defined by a DeFilippi score of I-III, was observed in all but two children. Seven of the 17 children (41%) who were on a glucocorticoid preoperatively were able to discontinue it by their most recent follow-up visit. In 12 children (35%), complete remission was evident at this time point. There were no differences in clinical improvement or remission rates between the groups (Table 2).

In a separate analysis, which was independent of the surgical technique, pathologic findings were compared to clinical outcomes. Among the 34 pathology specimens evaluated, no thymomas were

Table 1
Demographic and preoperative characteristics of the cohort

Variable	Open thymectomy ($n = 18$)	Thoracoscopic thymectomy ($n = 16$)	P-value
Age (years)	15.6 ± 4.4	11.9 ± 4.3	0.021
Female gender (%)	14 (78%)	8 (50%)	0.151
Positive Tensilon Test	4 (22%)	3 (19%)	1.00
Positive AChR Ab	17 (94%)	15 (94%)	1.00
MG consistent EMG	14 (100%)[4]	11 (100%)[5]	1.00
MG consistent PE	18 (100%)	16 (100%)	1.00
Preop duration of symptoms (months)	10.3 ± 8.8	10.7 ± 7.1	0.878
Preop Cholinesterase Inhibitor	18 (100%)	16 (100%)	1.00
Preop glucocorticoid	9 (50%)	8 (50%)	1.00
Osserman staging (%)			0.173
Stage I	0 (0%)	0 (0%)	
Stage IIa	6 (35%)	2 (14%)	
Stage IIb	11 (61%)	10 (63%)	
Stage III	1 (6%)	4 (29%)	

Legend: Superscripts denote absence of test result in which case this value was removed from the total number to calculate percentages. AChR Ab, Acetylcholine receptor antibody; MG, myasthenia gravis; EMG, electromyography; PE, physical exam; Preop, preoperative.

identified. Thymic hyperplasia was reported in 28 (82%) cases and normal thymic tissue in 6 (18%) cases. The presence or absence of thymic hyperplasia was not predictive of clinical improvement or remission (Table 3). To determine if preoperative or pathologic findings could be used to predict whether surgery would result in disease remission, defined by achieving a DeFilippi score of I, we compared gender, age at diagnoses, preoperative Tensilon test results, presences of AChR antibodies, preoperative Osserman classification, age at surgery, time between diagnoses and thymectomy, surgical approach (open versus thoracoscopic), operative time, weight of thymus, and presence of hyperplasia on pathology and found no significant differences between groups.

3. Discussion

To our knowledge, this is the largest study comparing open and thoracoscopic thymectomy for JMG. We found that clinical improvement and remission rates were similar between approaches. Given the decreased intraoperative blood loss, shortened duration of intravenous narcotic use, reduced hospital length of stay, and presumed improved cosmesis, our findings support the adaptation of thoracoscopic thymectomy to treat medically refractory JMG.

Thymectomy for JMG is thought to reduce circulating autoantibodies and result in clinical improvement in 75%–90% of cases and disease remission in 30%–50% of cases, results markedly superior to adult outcomes [16,20,21]. Furthermore, it has been observed that rates of clinical improvement and remission are similar between children who undergo thoracoscopic and open thymectomy [14,22], and our results further support these findings. Thus, in addition to conventional arguments supporting minimally invasive strategies (e.g. decreased pain and shorter hospitalization), our results, with follow-up beyond four years, support the notion that long-term outcomes are not inferior to traditional open thymectomies.

With the broad implementation of enhanced recovery after surgery (ERAS) across multiple surgical subspecialties, including pediatric surgery, this multidisciplinary patient-centered approach has led to reduced opioid requirements, shorter hospitalizations, and expedited return to normal activities [23–25]. A central tenet of ERAS is minimally invasive surgery. While the current study reports outcomes prior to the implementation of ERAS, both study sites currently have ERAS protocols in development for thymectomies with the expectation that a standardized perioperative approach, implementing regional anesthetic measures and applying multimodal patient-centered strategies, will promote even shorter hospitalizations and opioid requirements.

Greater than 80% of children diagnosed with JMG ultimately undergo a thymectomy; however, the optimal timing remains unclear [26]. Based on case series in the pediatric literature, the average time between diagnosis and thymectomy is approximately one year [14,27,28]. Consequently, these children may be on high-dose glucocorticoids for months and in some cases years prior to surgery. Not only does this disrupt the hypothalamic–pituitary–adrenal axis, but specifically in children with JMG, the prednisone dose has been shown to negatively correlate with bone age and linear growth [29]. While a sternotomy or cervical scar in a child is undesirable and a possible reason to delay thymectomy, the advantage of a thoracoscopic approach is that it only requires three subcentimeter stab incisions along the lateral chest wall. Thus, with a less invasive surgical option, thymectomy should be considered earlier in the disease course to reduce or even eliminate glucocorticoid exposure.

In a systematic review compiling data from 16 retrospective studies including nearly 400 pathologic specimens, Madenci et al. found that 85% of pathologic thymic specimens had hyperplastic thymic tissue, while 9% had normal thymic tissue, and only 6% had evidence of a thymoma [21]. We found that thymic hyperplasia was also more common than normal thymic tissue, evident in 82% of our specimens. While thymomas are present in approximately 30% of adults with myasthenia gravis [30], they are extremely rare in children and over our 18 year experience, we did not find any in our pathologic specimens [31,32]. Historically, we routinely obtained a preoperative thoracic computed tomography (CT) to look for a thymoma, but this is likely unnecessary given the rarity and the fact that it did not change the surgical approach. As such, we have eliminated chest CT from our routine preoperative surgical workup. If cross-sectional imaging is indicated, we favor

Table 2
Perioperative and postoperative outcomes.

Variable	Open thymectomy ($n = 18$)	Thoracoscopic thymectomy ($n = 16$)	P-value
Operative time (min)	108 ± 49	145 ± 43	0.025
Intraoperative blood loss (ml)	55 ± 67	5.5 ± 6.0	0.007
Chest tube placement	3 (17%)	4 (25%)	0.682
Postoperative duration of IV narcotic requirement (h)	20 ± 23[1]	5.0 ± 1.5[2]	0.018
Length of stay (days)	2.7 ± 1.1	1.7 ± 1.0	0.009
Follow up (months)	43 (25, 76)	39 (28, 53)	0.840
DeFilippi Classification			0.977
(I) Remission, off medications	6 (35%)	6 (38%)	
(II) Asymptomatic, reduced medications	4 (22%)	4 (25%)	
(III) Improved, on medications	6 (35%)	5 (31%)	
(IV) No change	1 (6%)	1 (6%)	
(V) Worse	0 (0%)	0 (0%)	
Lost to follow up	1 (6%)	0 (0%)	
Mortality	0	0	1.00

Legend: Min, minute; ml, milliliter; IV, intravenous; h, hours. Data reported as mean ± standard deviation or *n* (%) except for follow up which is reported as median (interquartile range).

Table 3
Correlation between pathologic assessment and clinical outcomes.

	Thymic Hyperplasia ($n = 28$)	Normal Thymic Tissue ($n = 6$)[a]	P-value
Remission	11 (39%)	1 (17%)	0.389
Clinical Improvement	26 (93%)	5 (100%)	1.00
Unchanged/Symptom Progression	2 (7%)	0 (0%)	1.00
Follow-up (months)	44 (25, 76)	41 (15, 98)	0.834

Legend: Children in remission were also considered to have clinical improvement and included in both the remission and clinical improvement row. Data reported as mean ± standard deviation or n (%) except for follow up which is reported as median (interquartile range).
[a] One child with normal thymic tissue was lost to follow up and excluded from analysis.

magnetic resonance imaging (MRI), a modality that provides similar predictive value for detecting a thymoma than CT and avoids the risk of radiation [33].

There are multiple limitations to this study. Although our cohort included 34 thymectomies over an 18-year period at two academic institutions, the rarity of this condition limited our power. Additionally, the open group was essentially a historical control group as thoracoscopic thymectomy is our current preferred approach. Consequently, it is possible that management strategies have evolved over time; however, the number of children who were on glucocorticoids was not different between the two time points. Ideally, a prospective analysis comparing open to thoracoscopic thymectomy would be more convincing, but given results suggesting equivalent rates of clinical improvement and remission, better perioperative outcomes, and presumed superior cosmesis, such a study is unlikely to be performed.

Our comparative case series demonstrates that thoracoscopic thymectomy in children is feasible, safe, and an effective surgical option in treatment of JMG. Additionally, we found that thoracoscopic thymectomy correlated significantly with reduced need of postoperative intravenous narcotic and earlier hospital dismissal. Most importantly, clinical improvement and remission rates appear equivalent to open techniques. We postulate that an increase in acceptance of thoracoscopic thymectomy over traditional open approaches will enable earlier surgical intervention and decrease the need for long-term glucocorticoids use.

References

[1] Lakhoo K, Fonseca JD, Rodda J, et al. Thymectomy in black children with juvenile myasthenia gravis. Pediatr Surg Int 1997;12(2/3):113–5.
[2] Morita MP, Gabbai AA, Oliveira AS, et al. Myasthenia gravis in children: analysis of 18 patients. Arq Neuropsiquiatr 2001;59(3-B):681–5.
[3] Benatar M. A systematic review of diagnostic studies in myasthenia gravis. Neuromuscul Disord 2006;16(7):459–67.
[4] Osserman KE, Genkins G. Studies in myasthenia gravis: review of a twenty-year experience in over 1200 patients. Mt Sinai J Med 1971;38(6):497–537.
[5] Sanders DB, Wolfe GI, Benatar M, et al. International consensus guidance for management of myasthenia gravis: executive summary. Neurology 2016 Jul;87(4):419–25.
[6] DeFilippi VJ, Richman DP, Ferguson MK. Transcervical thymectomy for myasthenia gravis. Ann Thorac Surg 1994;57(1):194–7.
[7] Blalock A, Mason MF, Morgan HJ, et al. Myasthenia gravis and tumors of the thymic region: report of a case in which the tumor was removed. Ann Surg 1939;110(4):544–61.
[8] Blalock A, Harvey AM, Ford FR. The treatment of myasthenia gravis by removal of the thymus gland. Preliminary report JAMA 1945;127:1089–96.
[9] Andrews PI, Massey JM, Howard Jr JF, et al. Race, sex, and puberty influence onset, severity, and outcome in juvenile myasthenia gravis. Neurology 1994;44(7):1208–14.
[10] Finnis MF, Jayawant S. Juvenile myasthenia gravis: a paediatric perspective. Autoimmune Dis 2011;2011:404101.
[11] Yeh CM, Chen HC, Chou CM, et al. Hybrid combination of small subxiphoid incision and thoracoscopic thymectomy for juvenile myasthenia gravis. J Pediatr Surg 2011;46(4):780–3.
[12] Zieliński M, Kuzdzał J, Szlubowski A, et al. Transcervical-subxiphoidvideothoracoscopic "maximal" thymectomy—operative technique and early results. Ann Thorac Surg 2004 Aug;78(2):404–9.
[13] Ersen E, Kilic B, Kara HV, et al. Comparative study of video-assisted thoracoscopic surgery versus open thymectomy for thymoma and myasthenia gravis. Wideochir Inne Tech Maloinwazyjne 2018;13(3):376–82.
[14] Mack MJ, Landreneau RJ, Yim AP, et al. Results of video-assisted thymectomy in patients with myasthenia gravis. J Thorac Cardiovasc Surg 1996;112(5):1352–9 [discussion 9-60].
[15] Raza A, Woo E. Video-assisted thoracoscopic surgery versus sternotomy in thymectomy for thymoma and myasthenia gravis. Ann Cardiothorac Surg 2016;5(1):33–7.
[16] Ashfaq A, Bernes SM, Weidler EM, et al. Outcomes of thoracoscopic thymectomy in patients with juvenile myasthenia gravis. J Pediatr Surg 2016;51(7):1078–83.
[17] Goldstein SD, Culbertson NT, Garrett D, et al. Thymectomy for myasthenia gravis in children: a comparison of open and thoracoscopic approaches. J Pediatr Surg 2015;50(1):92–7.
[18] Kim AG, Upah SA. Brandsema JF. Blinman TA. Thoracoscopic thymectomy for juvenile myasthenia gravis. Pediatr Surg Int: Yum SW; 2019.
[19] Kogut KA, Bufo AJ, Rothenberg SS, et al. Thoracoscopic thymectomy for myasthenia gravis in children. J Pediatr Surg 2000;35(11):1576–7.
[20] Kaufman AJ, Palatt J, Sivak M, et al. Thymectomy for myasthenia gravis: complete stable remission and associated prognostic factors in over 1000 cases. Semin Thorac Cardiovasc Surg 2016;28(2):561–8.
[21] Madenci AL, Li GZ, Weil BR, et al. The role of thymectomy in the treatment of juvenile myasthenia gravis: a systematic review. Pediatr Surg Int 2017;33(6):683–94.
[22] Wagner AJ, Cortes RA, Strober J, et al. Long-term follow-up after thymectomy for myasthenia gravis: thoracoscopic vs open. J Pediatr Surg 2006;41(1):50–4 discussion −4.
[23] Short HL, Taylor N, Thakore M, et al. Implementation of an enhanced recovery protocol in pediatric colorectal surgery. J Pediatr Surg 2018;53(4):688–92.
[24] Rove KO, Brockel MA, Saltzman AF, et al. Prospective study of enhanced recovery after surgery protocol in children undergoing reconstructive operations. J Pediatr Urol 2018 Jun;14(3):252.e1–9.
[25] Basse L, Raskov HH, Hjort Jakobsen D, et al. Accelerated postoperative recovery programme after colonic resection improves physical performance. pulmonary function and body composition Br J Surg 2002;89(4):446–53.
[26] Jastrzebska A, Jastrzebski M, Ryniewicz B, et al. Treatment outcome in juvenile-onset myasthenia gravis. Muscle Nerve 2019;59(5):549–54.
[27] Hennessey IA, Long AM, Hughes I, et al. Thymectomy for inducing remission in juvenile myasthenia gravis. Pediatr Surg Int 2011;27(6):591–4.
[28] Christison-Lagay E, Dharia B, Vajsar J, et al. Efficacy and safety of thoracoscopic thymectomy in the treatment of juvenile myasthenia gravis. Pediatr Surg Int 2013;29(6):583–6.
[29] Wang H, Su Z, Luo C, et al. The effect of steroid treatment and thymectomy on bone age and height development in juvenile myasthenia gravis. Neurol Sci 2013;34(12):2173–80.
[30] Okumura M, Shiono H, Minami M, et al. Clinical and pathological aspects of thymic epithelial tumors. Gen Thorac Cardiovasc Surg 2008;56(1):10–6.
[31] Nikolic DM, Nikolic AV, Lavrnic DV, et al. Childhood-onset myasthenia gravis with thymoma. Pediatr Neurol 2012;46(5):329–31.
[32] Fonseca AL, Ozgediz DE, Christison-Lagay ER, et al. Pediatric thymomas: report of two cases and comprehensive review of the literature. Pediatr Surg Int 2014;30(3):275–86.