Original Research Article

Thymectomy in children with juvenile myasthenia gravis: Is it recommended?

Abstract:

Objective:

Juvenile myasthenia gravis (JMG) is a rare disease with possible severe forms. Thymectomy is supported by many authors particularly in generalised forms with positive acetyholine receptor antibody (AchR- Ab). The aim of our study was to discuss the indication and the outcome of thymectomy in seven children with JMG.

Methods:

We performed a retrospective study of medical files of patients with JMG hospitalised in our pediatric surgery department for thymectomy. Explorations performed for all patients were acetyholine receptor antibody (AchR-Ab), Chest x-ray, CT-Scan and MRI.

Thymectomy was indicated on presence of anomalies on CT-Scan or MRI and realised either via thoracotomy or video-assisted thoracoscopy.

Results:

Our results confirmed the benefit of thymectomy in JMG, because remission was obtained in three cases with clinical improvement for the three other patients. One patient couldn't be evaluated because of non adherence to medical treatment.

Conclusion:

We conclude that thymectomy is well tolerated by children and should be indicated in case of JMG with thymic anomalies in imaging explorations. We recommend VAT as gold standard way for thymectomy in children.

Key words: Juvenile myastenia gravis, Thymectomy, children, thoracoscopy.

Introduction:

Juvenile myasthenia gravis (JMG) is a rare auto-immune disorder of neuromuscular transmission caused by production of antibodies against components of postsynaptic membrane of the neuro-muscular junction (1). Young patients may present severe forms with generalised muscle weakness with or without respiratory insufficiency. Specific treatment is needed including immunosuppressive therapy and thymectomy particularly in presence of thymus abnormalities (1-3). The aim of our study is to discuss indication and outcome of thymectomy in children with JMG.

Patients and Methods:

We performed a retrospective study of medical files of patients with JMG hospitalised in our pediatric surgery department for thymectomy.

Diagnosis of JMG was established in pediatric departments based on combination of clinical symptoms and positive pyridostigmine test. Disease severity was established according to Osserman Classification. Explorations performed for all patients were acetyholine receptor antibody (AchR-Ab), Chest x-ray, CT-Scan and MRI.

All patients received medical treatment which consists of pyridostigmine and corticotherapy.

Thymectomy was indicated on presence of anomalies on CT-Scan or MRI and realised either via thoracotomy or video-assisted thoracoscopy (VAT) introduced in 2009 in our department.

Results:

Five patients (table) were included, 1 male and 4 females with sex ratio of 0.25. Mean age was 7.7 years (2.5 to 14 years old). Four patients had a generalised JMG and one had only ocular myasthenia (OMG). Only one patient was AchR-Ab positive. Prior to thymectomy, disease severity was graded as I for one patient, IIa for two patients and IIb for two other patients.

Mediastinal enlargement was noticed on chest x ray of two patients (Fig1). CT-scan showed presence of eventual thymoma (Fig2) in three cases, thymus hypertrophy in two other cases.

A complete thymectomy (Fig3) was indicated for all the patients. It was realised via antero-lateral thoracotomy in three cases and via VAT in two cases.

The initial post operative course was complicated by a pneumthorax in one case, related to pleural breach which was successfully managed by assisted mechanical ventilation and pleural drainage (case 2).

On microscopic examination, showed a follicular hyperplasia in 3 cases (Fig4-5) and it was normal for the remaining case.

Four patients experienced an improvement after thymectomy, with complete remission in one case (case1) which was AchR-Ab positive. Medical treatment was decreased for three patients and stopped in one case. One patient couldn’t be evaluated because of non adherence to medical treatment.

Discussion:

Management of JMG has been initially adopted from adult patients. Whereas, recent studies showed that JMG is different in presentation and the course of the disease, particularly the group of prepubertal children (3-5).

Actually, children with JMG exhibit higher rates of remission than adults. This includes spontaneous remission and remission following a period of drug therapy. Prepubertal children have the highest rates of spontaneous remission (2, 6).

Therapeutic strategies for JMG have been established. Medical treatment as first line therapy consists of pyridostigmine associated to steroids and long term immunosuppression in generalised muscular weakness and moderate to severe bulbar symptoms or respiration insufficiency. Plasmapheresis can be indicated in severe forms (1).

All of our patients received pyridostigmine, associated to steroids in two cases and steroids with immunosuppression in one case.

Because of the presumed role of the thymus in the pathogenesis of myasthenia gravis, thymectomy is a recognised aspect of management. Thymectomy may remove germinal centres and disrupt antibody diversification (2, 7). Childhood thymectomy leads to a premature immunosenescence, mimicking changes expected after physiological thymus involution in the eldery with loss of thymic function (8).

More patients with thymic hyperplasia achieved remission compared to patients with normal thymus (2). In our series, four patients had thymic hyperplasia, one of them showed a complete remission after surgery.

In JMG thymic hyperplasia is evident in 83% of patients and in 3.8% thymoma could be detected (1, 9).

Although the outcome of thymectomy has not been evaluated with randomised studies in children, some case series have suggested that remission rate following thymectomy in JMG is higher than the remission rate with or without medical treatment (3, 10).

Thymectomy is followed by improvement in most cases: remission rate was higher in children after thymectomy than in the group of spontaneous evolution (1, 7, 10, 11-13).

Remission is also higher if thymectomy is performed within the first year after onset (1, 6, 12, 14- 15).

More recent review of children including prepubertal patients, also suggested increased remission rates after thymectomy (2, 12, 14, 16).

Thymectomy is recommended as early as possible in case of generalised weakness (1).

Current evidence suggests that thymectomy should not be indicated in Musk-positive disease as it is unclear whether it confers any benefit (3, 17-19). In our patients Musk-antibodies were not practiced.

Thymectomy in pure OMG remains controversial. Whereas OMG is not life threatening, patients may be dependent on long term immunosuppressant medications, including corticosteroids with the resultant side effects which can be substantial in children. Thymectomy has been performed in refractory cases (2).

A variety of surgical methods for thymectomy have been described: full or partial sternotomy, thoracoscopic or transcervical approaches (2, 20-21).

Many authors recommend transsternal approach in children to prevent incomplete removal of all thymic tissue, which may lead to poor outcome (3, 22).

Less invasive techniques such as VAT thymectomy are now resulting in comparable remission rates following thymectomy in adult MG (3, 23).

Della Marina et al recommend thoracoscopic techniques but these are restricted to specialised centres (1).

Kolski HK et al (24) has applied VAT to a group of juvenile patients for thymectomy and compared it to a similar group of six patients (in terms of age and clinical severity) operated via a median transternal approach. He concluded that VAT thymectomies are comparably effective to transsternal procedures in treating generalised JMG and can be safely performed in children as young as 20 months of age. In addition, VAT surgery is less invasive and significantly shortens the postoperative hospital stay, and has superior cosmetic results.

In our series, thymectomy was performed via antero-lateral thoracotomy in three cases. Thoracotomy was practiced by our surgical team because they mastered it better than sternotomy. VAT was introduced recently and served to treat the two other cases.

A larger series with a randomised controlled study is necessary to compare results of these two methods.

Conclusion:

We conclude that thymectomy in JMG is a well tolerated surgery in children. It is associated to a relatively significant remission and clinical improvement rates particularly in positive AchR-Ab patients. Early surgery for children with JMG and in whom imaging explorations showed thymic anomalies is highly recommended. We recommend VAT as gold standard way for thymectomy in children.

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184 **Figure legends:**

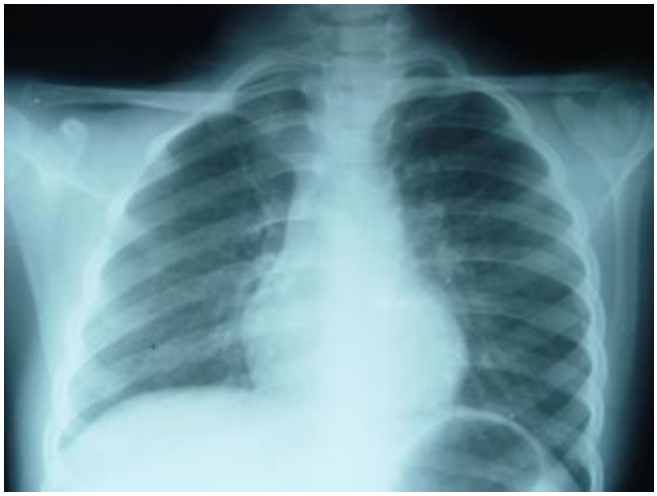
185 Fig1: Chest x-ray: Mediastinal enlargement.

186 Fig2: Mediastinal CT-scan: shows the presence of a thymoma.

187 Fig3: Complete thymectomy.

188 Fig4: Thymic hyperplasia (H&E, original magnification x200)

189 Fig5: Thymic hyperplasia (H&E, original magnification x400)

190 

191 Fig1. Chest x ray

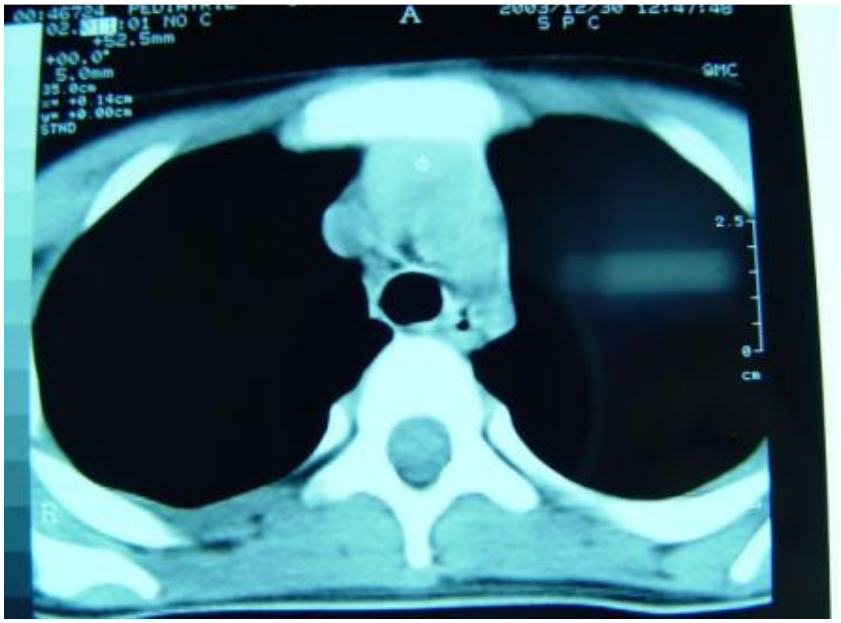


Fig2. CT Scan

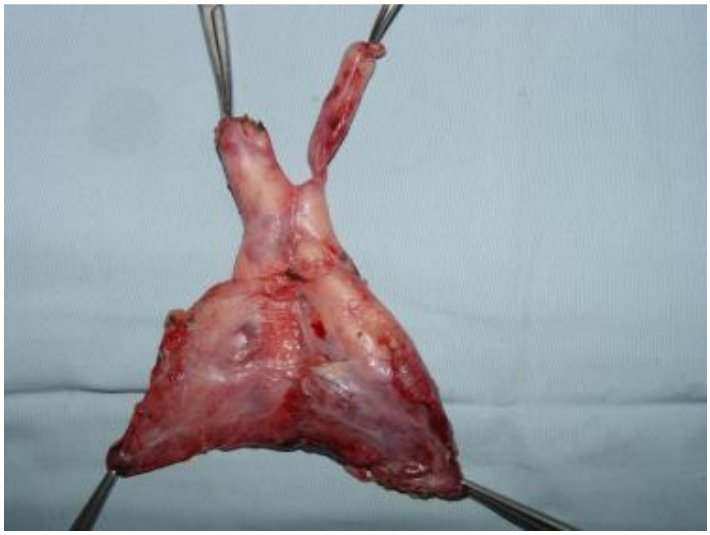


Fig3. Thymectomy

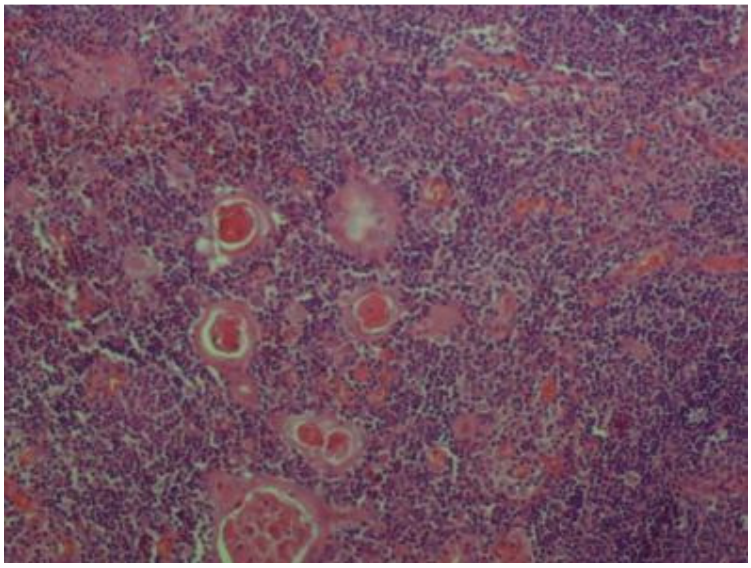


Fig.4 Histology.Thymic hyperplasia (H&E, original magnification x200)

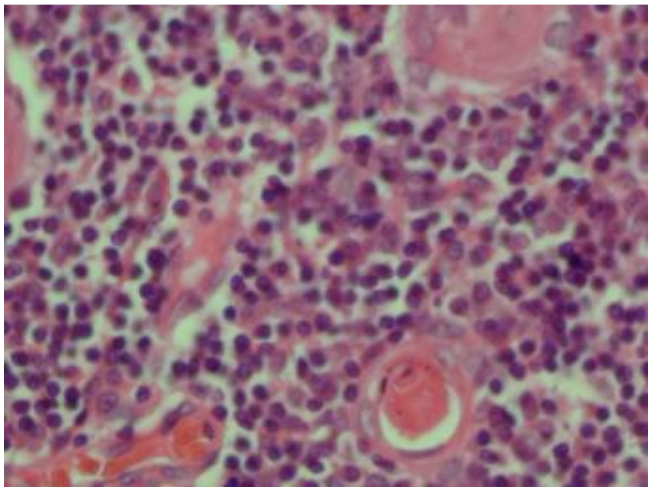


Fig.5 Histology.Thymic hyperplasia (H&E, original magnification x400)

Table : data about the five patients with JMG

Case	Age (year)	sex	Osserman classification	AchR-Ab	Imaging CT-Scan+/-MRI	Medical treatment Tablets/day	Surgery	Histology	Evolution/ Medical treatment Tablets/day
1	14	M	IIb	Positive	Thymoma	Pyridostigmine 6	Thoracotomy	Hyperplasia	Remission/No

2	2.5	F	IIa	Negative	Hypertrophy	Pyridostigmine 6	Thoracotomy	Hyperplasia	Improvement /yes 3
3	9	F	IIa	Negative	Thymoma	Pyridostigmine 3	Thoracotomy	Hyperplasia	Improvement/yes 2
4	10	F	IIb	Negative	Thymoma	Pyridostigmine 4	VAT	Normal	No improvement+ Non adherence to medical treatment
5	3	F	I	Negative	Hypertrophy	Pyridostigmine 3	VAT	Hyperplasia	Improvement/yes 2

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