CASE REPORTS

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Thymectomy immediately after myasthenic crisis

Timektomija neposredno po završetku miastenične krize

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Abstract

Introduction. Myasthenic crisis (MC) refers to rapid progression of myasthenic weakness accompanied by ventilatory and bulbar dysfunction. Since there is no single standard accepted in the treatment of every patient in myasthenic crisis, we report our experience in the treatment of such a patient. **Case report.** We report a 22-year-old male patient with clinical, pharmacological, neurophysiological, and immunological diagnosis of seropositive generalized myasthenia gravis (MG) of unstable course. During the first 6 months of his disease, three deteriorations were registered, and the last one developed into a myasthenic crisis. The patient was intubated. Previous anticholinergic and imunosuppresive therapies were withdrawn, and he was treated with plasma exchange and human immunoglobulins during the crisis. After thymectomy, performed 3 weeks after extubation, the patient was stable. **Conclusion.** Progress in treatment of MC over the last few decades has dramatically improved its prognosis. Thymectomy is useful in the prevention of MC recurrence.

Key words:
myasthenia gravis; diagnosis; thymectomy; critical illness; treatment outcome.

Apstrakt

Uvod. Miastenična kriza dovodi do brze progresije miastenične slabosti koja je udružena sa respiratornom i bulbarnom disfunkcijom. Kako nije strogo prihvaćen nijedan standard u lečenju svih bolesnika u krizi, u radu smo prikazali naša iskustva u lečenju jednog takvog bolesnika. **Prikaz bolesnika.** U radu je prikazan bolesnik, star 22 godine, sa klinički, farmakološki i imunološki dijagnostikovanom seropozitivnom generalizovanom miastenijom gravis nestabilnog toka. Tokom prvih 6 meseci bolesti registrovana su tri pogoršanja, dok se poslednje razvilo u miasteničnu krizu. Bolesnik je intubiran, ranija antiholinesterazna i imunosupresivna terapija su korigovane, a on je, tokom krize, lečen izmenama plazme i humanim imunoglobulinima. Posle timektomije, izvršene 3 sedmice posle ekstubacije, bolesnik je bio stabilan. **Zaključak.** Napredak u lečenju miastenične krize tokom poslednjih decenija dramatično je poboljšao prognozu miastenične krize. Timektomija je korisna u prevenciji ponavljanih miasteničnih kriza.

Ključne reči:
miastenia gravis; dijagnoza; timektomija; kritična stanja; lečenje, ishod.

Introduction

Myasthenic crisis (MC) is one of the most urgent conditions in neurology. The definition of MC is best formulated by a group of experts for myasthenia gravis (MG) who defined it as a condition in which the patient is vitally threatened by rapid progression of the disease, ventilatory and bulbar dysfunction [1]. Therefore, respiratory insufficiency accompanied by exacerbation of the disease is a sufficient criterion for the diagnosis of MC in patients with MG.

Myasthenic crisis is the state of delayed postoperative extubation for more than 24 hours after the operation because of respiratory failure in patients with MG [2]. Since there is no single standard accepted in the treatment of every MG patient because of heterogenity of the disorder.

According to individual approach to each patient with MG, we report our experience with a MG patient in crisis.

Case report

The patient, a 22-year-old male, experienced the first manifestation of the disease early in 2016. It was a transient episode of double vision, and the disease was not identified at that time. The patient had syndromic diagnosis, and was treated with parenteral corticosteroids for three days, with complete recovery from neurological deficit.

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A year and a half later, the ambiguities followed by semiptosis, speech difficulties, and weakness in the proximal arm muscles, manifested unprovoked.

At that time, a clinical, pharmacological, neurophysiological and immunological diagnosis of seropositive (acetylcholine receptor antibody 5.8 nmol/L) and generalized MG was established.

After initiation of corticosteroid therapy, the patient experienced a deepening of myasthenic weakness, primarily in the form of oculo-bulbar dysfunction. Because of that, we performed a series of five plasma exchange (PE) therapies instead. Thereupon, the patient achieved a complete but short remission. The planned thymectomy was not performed. Over the next two and a half months, there was a development of more pronounced weakness in eyelids, a transient episode of dysphagia and difficulty chewing, as well as neck muscles weakness.

An increase in oral dosage of corticosteroids and pyridostigmine bromde (Mestinon®) resulted in some improvement, but without complete recovery. However, after the next series of five additional PE, the neurological deficit withdrew again for a short time. Two months later, in February of 2018, there was again an increase in generalized weakness, but this time with occasional suffocation, mostly at night.

The patient was hospitalized in February of 2018, when two PEs were performed, with a significant but incomplete recovery. PE was suspended because the patient became febrile (38.8°C). An antibiotic and antipyretic therapy was administered, and haemoculture was taken. After initial improvement, existing weakness of cervical musculature increased. The patient also experienced difficulty in swallowing and speaking, weakness of eye muscles, and episodes of shortness of breath, together with increased secretion in the nose and the mouth, and a decrease in saturation (PCO_2 41 mmHg/51 mmHg PO_2), because the patient was intubated.

It was concluded that it was a MC and an anticholinergic therapy was suspended, but a parenteral corticosteroid therapy and intravenous human immunoglobulin (IVIg) therapy at a dose of 0.4 g/kg body weight was started and continued for 5 consecutive days.

The patient was intubated for in the next 10 days when was regularly monitored for vital parameters. Laboratory blood and urine tests were performed. After stabilization of his general condition and normalization of muscle strength, the patient was extubated.

The patient had a transient episode of strabismus and nasal speech lasting two days, a week after he was extubated, which spontaneously resolved. Thymectomy was performed three weeks after extubation via video-assisted thoracoscopic surgery (VATS), with previous antibiotic preparation and a one-day administration of IVIg.

The surgery was completed without complications. The patient was able to breathe spontaneously immediately after the surgery. His vital parameters were stable and his neurologic status was almost normal, with no significant muscle weakness and persistent fatigue.

Histopathological examination pointed to hyperplasia of the thymus. In the next 6 months, the patient experienced no clinical deterioration.

Discussion

We present a patient with an unstable preoperative course of MG. Initiation of corticosteroid therapy precipitated myasthenia-related increase in weakness and it was the reason for PE therapy, with temporary effects. Infectious syndrome appeared third: the most difficult deterioration of the disease, accompanied by respiratory failure in MC. According to the literature [3], about one-fifth of patients with MG experience crisis during their life, usually within the first year of illness. The interval from disease onset to first MC was in the range 0.5–60 months (median interval 6 months), and most of them (60.6%) experienced recurrent (≥ 2) episodes. Most of these patients were acetylcholine receptor antibody-positive (72.7%). Similar to the above, our patient had seropositive generalized MG, and he developed MC within one year since the onset of clear symptoms of the disorder.

Among the precipitating factors for a MC, cited in the literature (infections and sepsis, surgical procedures, initiation of treatment with corticosteroids or rapid tapering of it, exposure to drugs that may increase myasthenic weakness, pregnancy, reaction to iodinated contrast), infection is the most common [2, 4]. In our patient, initiation of corticosteroid therapy was accompanied by increasing weaknesses, and infectious episodes precipitated MC in his case.

The authors do not agree on cholinesterase inhibitors and MC; according to some, they are recommended in the crisis [5], while most are of the opinion that they should be discontinued [6, 7]. Cholinesterase inhibitors were discontinued in our patient during artificial ventilation, and we believe that in this way it is easier to repair acetylcholine receptors of skeletal muscles, and to provide a better response to the cholinesterase inhibitors upon their re-introduction.

All authors agree that MG patients need PE, IVIg, corticosteroids, immunosuppressants (especially azathioprine), and lately, a monoclonal antibody therapy with rituximab as an additional treatment for MC has also been suggested [8]. Plasma exchange during an MC was significantly associated with early extubation [3] as PE can rapidly eliminate the pathological autoantibodies. We used PE as a superior immunomodulatory therapy in the case of our patient, but it had to be replaced with IVIg because of his fever.

Although guidelines for extubation in patients without MG are clear (vital capacity ≥ 15 mL/kg, maximal inspiratory pressure ≤ 20 cm H_2O, expiratory pressure > 40 cm H_2O, and tidal volume ≥ 5 mL/kg) [9] there is a lack of strict criteria concerning when and how to safely extubate patients in MC because of their fluctuating weakness. The decision to extubate MG patients relies mostly on the clinical judgment of the neurologist. Our patient was extubated at the moment when muscular power tests for all of his skeletal muscles that could be assessed yielded good results. The decision proved right because clinical remission was maintained after extubation.

Duration of ventilation during a MC is an important indicator of treatment efficacy: early extubation is defined as ventilation support for < 7 days; prolonged ventilation is defined as the requirement for mechanical ventilation for > 15 days [10]. A third of patients with MC achieved early extubation (≤ 7 days), and only a quarter of patients needed prolonged ventilation (> 15 days). Younger patients with PE tended to undergo successful early extubation, while older male patients with atelectasis tended to have poor outcomes [3].

As for recurrence of MC, because the patients who underwent thymectomy had significantly fewer MC episodes and a longer duration between MC attacks [3], we decided to perform thymectomy in our patient immediately after stabilization of his condition, 3 weeks after extubation. This decision turned out to be correct because the patient was stable after thymectomy. That our decision was not premature is confirmed by the experience of other authors, who performed thymectomy on their patient during MC, when the patient was still on artificial respiration [11].

That myasthenia crisis is not exclusively associated with thymoma is proven by the fact that thymoma is seen only in a quarter of patients in crisis [3]. The histopathological findings in our patient pointed to thymic hyperplasia.

Progress in the recognition and treatment of MC over the past few decades has dramatically improved the prognosis of MC, and decreased the mortality rate from 75% to the current rate of less than 5% [2, 9].

Conclusion

Patients in MC require accommodation in the intensive care unit, intubation, recognition and treatment of triggers, and correction of previous therapy. Since thymectomy is useful in prevention of MG recurrence, it was performed immediately after extubation in our patient. After thymectomy the patient was stable.

There is a need for individual approach to each patient with MC.

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