DIAGNOSIS AND TREATMENT OF NEW-ONSET MYASTHENIA GRAVIS IN CRITICALLY ILL PATIENTS

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ABSTRACT

Myasthenia gravis is an autoimmune disease leading to weakness and pathological fatigue. The basis of the pathogenesis of myasthenia gravis is a disturbance of neurotransmission due to the influence of polyclonal autoantibodies on various structures of the neuromuscular junction. The recurrent or progressive course is common for the disease.

It is extremely difficult to suspect and diagnose this pathology for an anesthesiologist-resuscitator who doesn't treat patients with myasthenia gravis in everyday practice, since the patients often arrive to mainstream hospitals in critical condition with incorrect diagnosis. Only specialized units of neurology have electromyographs and equipment for particular immunological probes.

We report a case of myasthenia gravis in a patient admitted to a hospital emergency room with the other disease suspected.

Keywords: Paresis of the respiratory muscles, bulbar syndrome, neostigmine test, electromyography.

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CLINICAL OBSERVATION

A 42-year-old female patient T. fell acutely ill 11.11.13, when choked over solid food being overall healthy. With a diagnosis of "Foreign body aspiration," the patient was admitted by ambulance to the resuscitation unit of N.V. Sklifosovsky Research Institute for Emergency Medicine. On admission, the patient's condition was serious. Due to severe respiratory failure (dyspnea — 25 breaths per minute, and tachycardia up to 164 beats per minute) the patient had a endotracheal intubation and respiratory support immediately after admission. The level of wakefulness was deep stupor (a Glasgow Coma Scale score of 11), the patient had expressed agitation. The blood test of the acid-base composition revealed decompensated respiratory acidosis: pH — 7.073, $PaCO_2$ — 81.7 mmHg, PaO_2 — 96.6 mmHg. The chest X-ray revealed nongomogenous darkening and reduced transparency of the left lung field that evidenced atelectasis of the lower lobe of the left lung. The diagnostic fibrobronchoscopy was performed, after which hemorrhagic tracheobronchitis with a dominant lesion of the left bronchus was diagnosed. No foreign body was found. Sanitation of the tracheobronchial tree was performed.

From medical history we learned that breathing disorders had not been previously observed in the patient. However, in 2008, she suffered an acute ischemic stroke with swallowing disorders.

Twelve hours after admission, hemodynamic stabilization and normalization of arterial blood gas analysis, the patient was allowed to breathe independently. Within 30 min, breathing was rhythmic, saturation of hemoglobin with oxygen — 100%, dyspnea was absent. The patient was extubated. However, 10 minutes after extubation breathing became shallow, inefficient, involving muscles of the shoulder girdle. Chest excursion was almost absent, the intercostal muscles were not involved in therespiratory act. We urgently performed re-intubation and started respiratory support using synchronized intermittent mandatory ventilation (SIMV) with pressure support (PS), with the fraction of inspired oxygen (FiO_2) — 50%. The sanitation of the tracheobronchial tree revealed a small amount of mucopurulent sputum.

One hour after re-intubation during the neurological examination revealed right-sided partial ptosis, weakness of the front muscles of the neck, proximal extremities tetraparesis grade 1 in the flexors of the shoulder and grade 2 in the hip flexors according to *Medical Research Weakness Scale* (*MRC*). Tendon and periosteal reflexes were depressed, without lateralization. Muscle tone was moderately low, while pathological feet signs and meningeal reflexes were absent. There was no cough reflex during tracheal sanitation. Collection of medical history was not successful due to the agitation in the patient.

After re-fibrobronchoscopy and x-ray examination the diagnosis of "Aspiration" was abandoned, and respiratory disorder was associated with paresis of the respiratory muscles. For the differential diagnosis of myasthenia, prozerin test was made. The patient had the following medications administered: 0.05% prozerin solution — 2 ml subcutaneously and 0.1% Atropine solution — 0.5 ml subcutaneously. Fifteen minutes after administering of the drug, the level of physical

activity increased. The volume of active movements of the limbs fully recovered, there was a movement of the respiratory muscles, while at the same time, there was no cough reflex and the weakness of anterior neck muscles continued to persist. The patient was allowed to breathe independently and breathed with no signs of respiratory failure. However, 30 minutes later, the patient had a feeling of lack of air, and therefore the respiratory support was continued.

The result of the prozerin test was regarded as weakly positive. To confirm the diagnosis of myasthenia gravis it was necessary to carry out the electromyographic study, but in the absence of the myograph of the Institute, the diagnosis of "Myasthenia Gravis" was set and we started anticholinesterase therapy (0.05% solution of prozerin — 1 ml subcutaneously every 4 hours). However, the dose was sufficient only for 2.5 hours of spontaneous breathing, for which reason it was decided to start prednisolone therapy at a single dose of 250 mg by drop intravenous infusion.

In connection with the ischemic stroke with swallowing disorders in history, magnetic resonance imaging of the brain was performed. Data evidencing vascular pathology of the brain had not been received.

Taking into the account the clinical picture and multiple healed scars from cuts on both forearms, evidencing suicide attempts, hysterical genesis of respiratory disorders couldn't be excluded.

On the third day after admission, the patient showed positive dynamics, resulting in an improved work of the respiratory muscles, restored muscle strength in the limbs and jugulated ptosis. Periods of spontaneous breathing were already 3.5 hours.

One day after administering 250 mg of prednisolone and the beginning of anticholinesterase therapy, the patient was able to breathe independently for no more than 3.5 hours. Given the continued paresis of the respiratory muscles, lack of efficacy of 2-day-long anticholinesterase therapy, it was decided to start prednisolone pulse therapy.

On the 4th day of hospitalization the patient had 1,000 mg of prednisolone administered intravenously. After 3 h after infusion of prednisolone and 2 ml subcutaneous injection of 0.05% prozerin the duration of spontaneous breathing was 4.5 hours. After 4.5 hours, the patient was administered 2 ml of 0.05% prozerin subcutaneously, without the respiratory support. Thus, the desired therapeutic effect appeared after administration of prozerin: the patient could breathe spontaneously over 4 hours.

In order to identify a thymoma, the computed tomography of the chest was conducted. There were no signs of a thymoma found.

The psychological state of the patient improved, she became more cooperative. We found out that five years ago, the patient had experienced swallowing difficulties after a severe stress during the third pregnancy. She applied to the district hospital, where she was diagnosed with the stroke and offered admission, but the patient refused. The determined therapy (details are not remembered) done at home was ineffective. Difficulties in swallowing food continued, the nasal voice and general weakness appeared. Periodically she had double vision and partially drooping right eyelid, which cleared up on its own. The patient had not consulted a doctor or received any therapy. She ate very small portions, chewing food long and thoroughly. Thus, we were getting more and more evidence to support the diagnosis of "Myasthenia Gravis".

On the 5th day of stay in the resuscitation unit, the patient was visited by the specialist of Moscow Myasthenia Center. Examination was performed 8 hours after the last administration of prozerin. The patient was on assisted ventilation. The neurological status included right-sided semiptosis, bulbar syndrome with difficulties in swallowing and chewing, loss of strength in the facial muscles grade 3 and in the proximal extremities — grade 2-3. The weakness of the front group of muscles of the neck — grade 3 of the MRC scale. Cough impulse and chest excursion were decreased. The severity of bulbar syndrome decreased 40 min after 2 ml subcutaneous injection of 0.05% prozerin and muscle strength increased by 2 grades. Prozerin test was regarded as positive.

The patient was diagnosed with: "Myasthenia gravis, a generalized form with bulbar impairment, severe course, the lack of compensation on anticholinesterases therapy (4B-5 according to the Myasthenia Gravis Foundation of America (MGFA))".

On the 6th day after admission the patient underwent electromyographic study of neuromuscular transmission — decrement test, which revealed disorders of neuromuscular transmission of myasthenic type. Prozerin had been canceled for 8 hours before the study. The patient was put on the ventilator. Prior to the administration of prozerin, amplitude of the M response in m. Digastricus was 0.84 mV (decreased), the amplitude of the M response decrement was 37.2% (normal result is up to 10%). Functional tests were positive. The tetanization revealed the 50% amplitude decrement. Phenomena of post activation facilitation and post activation exhaustion were positive. Forty minutes after subcutaneous injection of 2 ml of prozerin solution (0.05%), the increase of the M response amplitude to normal levels and the amplitude decrement of up to 7% (normal) was indicated.

On the 8th day after admission to the Institute, the patient was clearly conscious, neurological deficit persisted in the form of front neck muscles weakness grade 4. Respiration was independent, $SatO_2$ 100%. Tracheal extubation was performed. After extubation respiratory rate was 14 breaths per min, coughing and swallowing remained preserved. The patient was breathing on her own during 24 hours with no signs of respiratory failure.

On the 9th day after admission, the patient was transferred to a specialized neurological department.

DISCUSSION

Myasthenia gravis is a rare neurological disorder with a frequency of only 5 cases per 100 000 population. Women suffer from myasthenia 2—4 times more often, and the peak incidence occurs between the ages of 20 to 40 years. According to the international classification of clinical myasthenia gravis, there is form A, without bulbar disturbances, and

form B with bulbar impairment [2, 3]. Depending on the involvement of skeletal muscle, there are 5 severity degrees of myasthenia gravis. The class I is isolated ocular muscle weakness, class II — mild weakness of the muscles of the trunk, proximal extremities, oropharyngeal muscles. In the class III myasthenia gravis, the pathological process involves the respiratory muscles, and the class IV is characterized by severe weakness of the muscles of the trunk, proximal extremities and oropharyngeal or respiratory muscles. The class V respiratory muscle weakness requires the patient to be put on the ventilator.

The diagnosis is considered unquestionable upon confirmation by four criteria: clinical, pharmacological, immunological, and electromyographic. When having three criteria, the diagnosis is firm, two — probable, and one — doubtful. [3]

Clinical criterion is the presence of a specific muscle weakness. This symptom is characterized by lability during the day, the week, the discordance of paresis localization with innervation zones, combination of lesions of the proximal arm and the front muscles of the neck. Depending on the immunoclinical form, it can be lesion of the eye muscles, weakness of facial muscles, bulbar disturbances, and weakness in the legs or paresis of the respiratory muscles. The differential diagnosis is carried out with such diseases as progressive ptosis, endocrine ophthalmopathy, blepharospasm, amyotrophic lateral sclerosis, multiple sclerosis, vascular and neoplastic lesions of the brain, acute inflammatory demyelinating neuropathy type (Guillain-Barré syndrome**),** Lambert-Eaton myasthenic syndrome, congenital and acquired myopathies [1, 4].

Pharmacological criterion — the positive prozerin test. The test is considered positive if after 2 ml subcutaneous injection of 0.05% prozerin solution muscle weakness significantly reduces. Compensation of muscle weakness after injection of prozerin may be complete, incomplete or partial.

Electromyographic criterion is a positive decrement test — study of neuromuscular transmission using stimulating electromyography overlaying surface electrodes.

Immunological test is identification of antibodies to acetylcholine receptors, tinin protein, muscle-specific tyrosine kinase and ryanodine receptors of the sarcoplasmic reticulum.

In our case, the first 6 days after admission, the assessment of only the clinical and pharmacological criteria was available. Therefore, the diagnosis of myasthenia we considered as probable. Only after the decrement test, we were able to consider the diagnosis as firm.

Treatment of myasthenia gravis is characterized by staging. The first stage is compensating, using anticholinesterase drugs. When the first stage is not effective enough, the second stage is began, which includes corticosteroid or immunosuppressive therapy, administration of immunoglobulins, thymectomy or radiation therapy at the area of the anterior mediastinum [3, 4]. In our practice, we have concluded about the lack of prozerin efficacy during the first day after the beginning of anticholinesterase therapy. Therefore, hormone therapy with prednisolone was started immediately, which allowed to achieve the desired therapeutic effect in a short time and put the patient on spontaneous respiration.

In conclusion, it should be noted that in addition to the undoubted clinical interest of the diagnostic search, this clinical observation confirms the importance of routine neurological examination of critically ill patients.

REFERENCES

1. Gekht B.M., Ilyina N.A. *Nervno-myshechnye bolezni* [Neuromuscular diseases]. Moscow: Meditsina Publ.,1982. 350 p. (In Russian)
2. Barohn R.J., McIntire D., Herbelin L., et al. Reliability testing of the quantitative myasthenia gravis score. *Ann NY Acad Sci*. 1998; 841: 769–772.
3. Dedayev S.I., Sanadze A.G., Sidnev D.V. Ispol'zovanie shkaly QMGS dlya kolichestvennoy otsenki tyazhesti dvigatel'nykh rasstroystv u bol'nykh miasteniey [Using QMGS scale to evaluate the severity of movement disorders in patients with myasthenia gravis]. *Zhurnal nevrologii i psikhiatrii im. S.S. Korsakova*. 2012; 7: 32–35. (In Russian)
4. Gekht B.M., Sanadze A.G., Kasatkina L.F., et al. Diagnostika i lecheniye miastenii: informatsionnoye pis'mo MZ RF [Diagnosis and treatment of myasthenia gravis: an information letter of Health Ministry]. Moscow, 2003. 24 p. (In Russian)
5. Sharov M.N., Stepanchenko A.O., Suslina Z.A. Sovremennyj opyt primeneniya antikholinesteraznykh preparatov v nevrologii [Modern experience in the use of anticholinesterase drugs in neurology]. *Lechashchiy vrach*. 2008; 5: 91–94. (In Russian)

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