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Application of Clinical Practice and Scientific Research in Undergraduate Teaching of Myasthenia Gravis

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Abstract: Objective: Under theoretical guidance, undergraduates learned the diagnosis, differential diagnosis and treatment of Myasthenia Gravis (MG)through clinical practice and scientific exploration. Methods: Theoretical basis was Chinese guidelines for the diagnosis and treatment of myasthenia gravis (2020 edition). Under the guidance of teachers, undergraduates cooperated with each other and learned step by step. Phase 1 was clinical trainee, determine the location and nature of the lesion through neurological examination and medical history. Phase 2 was classroom learning, simulate nerve conduction and repetitive nerve stimulation (RNS) to explore the differential diagnosis of diseases with similar clinical features. Phase 3 was classroom learning, watch the video of the neostigmine trial, explore the diagnosis and treatment of MG on the theoretical basis. Results: Phase 1, according to the localization signs and disease changes, the location and nature of the lesions were preliminarily determined. Phase 2, peripheral nerve disease, neuromuscular junction disease, and myopathy were differentiated by nerve conduction and RNS. Phase 3, according to the pathogenesis of MG, organize and understand the diagnostic criteria and target therapy provided in the guideline to guide the diagnosis and long-term treatment of MG. Conclusion: In undergraduate teaching, teachers provided appropriate teaching environment, theoretical support and teaching methods. Teachers guided undergraduates to participate in clinical practice and scientific exploration. During the learning process of MG, undergraduates train clinical thinking and establish scientific research awareness.

Keywords: Clinical Practice; Scientific Research; Undergraduate Teaching; Myasthenia Gravis.

1. Foreword

Myasthenia Gravis (MG) is an acquired autoimmune neuromuscular junction disease. The clinical classification is ocular MG (OMG) and generalized MG (GMG). Auxiliary examinations are needed to differentially diagnose diseases with similar clinical features. The pathogenesis of MG is complex, and there are many therapeutic targets. Individualized treatment affects prognosis. Learn the theoretical knowledge of MG through clinical practice and scientific exploration, reduce the difficulty of learning, and establish the connection between clinical and basic.

2. Methods

2.1. Theoretical Guidance

Guidelines for the diagnosis and treatment of MG in China (2020 edition) [1]

2.2. Teaching Form

Under the guidance of teachers, undergraduates cooperated with each other and learned step by step.

2.3. Teaching Process

2.3.1. Phase 1 was Clinical Trainee, Determine the Location and Nature of the Lesion through Neurological Examination and Medical History.[2]

Preparation for practice: Master neurological examination content and methods through video learning. Understand the relationship between movement and muscles, muscles and peripheral nerves, peripheral nerves and central nervous system by anatomy. Understand the characteristics of metabolic and nutritional disorders, inflammation, degeneration, tumors, infections, endocrine glands, genetics, poisoning or trauma, stroke, etc. by pathology.

Clinical trainee of the cases: Graves ophthalmopathy, Diabetes-related ophthalmopathy, GBS (miller-fisher snydrom, pharyngocervical brachial plexus type), MG (OMG, GMG), Polymyositis, etc.

Retrospective study of past cases: Intracranial tumor, NMOSD, Ischemic stroke, Infectious encephalitis, Orbital abscess, Orbital tumor, Unilateral cavernous sinus infection, Internal carotid cavernous fistula, Paraneoplastic syndrome, Wernicke encephalopathy, etc.

Clinical thinking training: Summarize localization signs and disease changes. According to the anatomical structure and pathological features, the localization and nature of the lesions were analyzed. Read the latest guidelines or consensus on related diseases to understand the basic outline of disease diagnosis and treatment. Clinical features were summarized on the basis of practice and theory.

2.3.2. Phase 2 was Classroom Learning, Simulate Nerve Conduction and Repetitive Nerve Stimulation (RNS) to Explore the Differential Diagnosis of Diseases with Similar Clinical Features. [3]

Preparation for practice: Watch a video on nerve conduction and RNS. Familiar with the anatomy and body surface landmarks of peripheral nerves and muscles, including limbs, face, neck, chest, abdomen, back, etc. Understand the basic points of nerve conduction operation, including electrodes, stimulator, stimulation site and stimulation intensity. Understand the basic concepts of nerve conduction outcomes, including action potential latency, amplitude, area, time course, and conduction velocity.

Simulation and summary: For similar diseases such as peripheral neuropathy, neuromuscular junction disease, myopathy, etc., select nerves and muscles for nerve conduction and RNS. Action potential maps were drawn with

reference to the results of different diseases. Explore the rationale for different outcomes in diseases with similar clinical features.

2.3.3. Phase 3 Was Classroom Learning, on the Theoretical Basis, Collate Data, Confirm Diagnosis, and Explore the Treatment of MG. [4]

Theoretical preparation: Read the guidelines for the diagnosis and treatment of MG in China (2020 edition). Summarize the diagnosis of MG and the treatment of different types of MG.

Practice and Summary: Watch a video of the Neostigmine trial. The case data of 2 MG patients (OMG, GMG) were sorted, including clinical features and auxiliary examinations. The diagnosis was made according to the MG diagnostic criteria. Develop a treatment and follow-up plan based on the patient's diagnostic classification.

3. Results

3.1. Phase 1, The Ocular Type is Mainly Manifested as III, IV, VI Palsy or External Ophthalmoplegia, and the Generalized Type is Mainly Manifested as Proximal Movement Disorders of the Limbs. A Preliminary Diagnosis is Made by Imaging, Nerve Conduction and RNS. See Table Below

Table 1. Phase 1, The Ocular Type

	Ocular type and Generalized type	
Location	Brain stem Spinal cord Eye	Peripheral neuropathy Neuromuscular junction disease Myopathy
Nature	Cerebrovascular, immune, infection, endocrine, tumor, trauma and other factors	
Examination	Image	Nerve conduction and RNS

3.2. Phase 2, Peripheral Neuropathy, Neuromuscular Junction Disease and Myopathy are Differentiated by Nerve Conduction and RNS. See Table Below

Table 2. Phase 2, Peripheral Neuropathy, Neuromuscular Junction Disease and Myopathy are Differentiated by Nerve Conduction and RNS

Action potential		Peripheral neuropathy	Neuromuscular junction disease		Myopathy
			MG	LEMS	
Terminal latency		Extend	Normal	Normal	Normal
Conduction velocity		Slow down	Normal	Normal	Normal
Amplitude	NS	Decrease	Normal	Decrease	Normal
	Low RNS	——	Decrease	Decrease	Normal
	High RNS	——	Decrease	Increase	Normal

3.3. Phase 3, According to the Pathogenesis of MG, on the Basis of Age [5], Sex, Physiological Status, Classification and Side Effect, the Therapy Provided in the Guideline is Organized and Understood. See Table Below

Table 3. Phase 3, According to the Pathogenesis of MG, on the Basis of Age [5], Sex, Physiological Status, Classification and Side Effect, the Therapy Provided in the Guideline is Organized and Understood

Treatment choice	Indications
Cholinesterase inhibitor	Pyridostigmine, first-line drug
Immunoglobulin	Late onset, severe disease, myasthenic crisis, severe bulbar symptoms Preoperative and perioperative treatment of thymectomy Contraindications to immunosuppressive therapy Refractory MG
Plasma exchange	
Glucocorticoids	Combine non-hormonal Immunosuppressant, reduce the side effects
Other Immunosuppressant	AZA: first-line drug, the onset is slow. MMF: safer and better tolerated than AZA. Tacrolimus: Intolerance or poor efficacy of other immunosuppressant.
Targeted biologics	Target B cells: Refractory GMG with poor response to immunosuppressant Especially MuSK-MG and some AChR-MG
	complement inhibitor: AChR-GMG with poor response to immunosuppressant
Thymectomy	MG with thymoma: early thymectomy Non-thymoma OMG: thymectomy after failure of other treatments Non-thymoma GMG: AChR-MG for early thymectomy Non-thymoma GMG: MuSK-MG for athymectomy
Autologous hematopoietic stem cell transplantation	Refractory and relapsed MG

4. Conclusion

4.1. Phase 1: Use Basic Skills and Basic Knowledge to Clarify Neurological Signs and Pathogenesis Characteristics, and Make Differential Diagnosis for Diseases with Similar Symptoms and Signs to MG

According to the pathogenesis, MG is a disease of the neuromuscular junction, mainly characterized by muscle weakness and muscle fatigue after exercise. Present medical history includes gender, age, muscle fatigue, localized pain, fever, etc. Past medical history includes thyroid disease, diabetes, hypertension, heart disease, connective tissue disease, smoking and drinking, etc.

The clinical classification of MG is ocular type with extraocular muscle dysfunction and generalized type with proximal limb movement disorders. In the neurological examination, the ocular type focuses on the size of the eye cleft, eyelid and eye movements, pupil size and reflexes, the movements of the facial muscles and throat muscles, and the function of other cranial nerves; The generalized type focuses on the proximal and distal limbs, including muscle strength, muscle tone, tendon reflexes, sensation, ataxia, pathological reflexes, and muscle strength of cervical and respiratory muscles.

Central nervous system disease and orbital disease are

diagnosed by imaging and laboratory tests [6][7]. The clinical features of nerve root and peripheral nerve disease, neuromuscular junction disease, and myopathy are similar, and further investigation is needed to identify the location of the lesion.

4.2. Phase 2: Understand the Process of Nerve Conduction, Understand the Application Value of Nerve Conduction and RNS, and Help to Identify Lesions between Peripheral Nerves and Muscles

In the result interpretation of nerve conduction, nerve conduction velocity is calculated by terminal latency. Since the conduction velocity of each nerve fiber in the nerve trunk is inconsistent, each muscle fiber cannot be excited at the same time. The conduction velocity is calculated as the distance between the proximal and distal stimulation points/ (proximal latent time minus distal latent time).

Terminal latency and nerve conduction velocities are usually altered in peripheral neuropathy but not significantly altered in neuromuscular junction disease and myopathy.

Myasthenia gravis is a disease of the postsynaptic membrane, in which acetylcholine is gradually depleted and the amplitude of action potentials decreases under low-frequency RNS [8]. Lambert -Eaton myasthenic syndrome (LEMS) is a presynaptic membrane lesion, in which the release of acetylcholine increases and the amplitude of action potential increases significantly under high RNS.[9]

4.3. Phase 3: Understand the Pathogenesis and Further Understand the Basis and Precautions of Individualized Treatment

With the in-depth development of research, researchers have a more comprehensive understanding of the pathogenesis of MG. In treatment, in addition to cholinesterase inhibitors, more therapeutic targets have been discovered, including immunosuppressant, targeted biologics, thymectomy, autologous hematopoietic stem cell transplantation, etc.

In MG patients, age and physiological status include children and adolescents, pregnancy, adults, and elderly; clinical types include OMG and GMG; subgroup classifications include AChR antibody positive, MuSK antibody positive, LRP4 antibody positive, antibody negative, Thymoma-related MG, etc.

MG patients are often complicated by certain diseases, including tumors, Graves disease, polymyositis, multiple sclerosis, Sjögren's syndrome, periodic paralysis, Hashimoto's disease, rheumatoid arthritis, systemic lupus erythematosus, aplastic anemia, etc. [10]. Treatment of these diseases requires simultaneous attention.

Individualized treatment of patients with MG requires a comprehensive analysis of treatment and patients. The pathogenesis of MG is still not fully understood, and many immunological and cellular biological processes remain to be elucidated. The treatment of patients also requires follow-up observation, summarizing experience and scientific research.

5. Closing Remarks

Teachers provide appropriate teaching environment, theoretical support and teaching methods. Undergraduates expand their thinking through clinical practice and scientific exploration. Clinical practice increases perceptual awareness and interest, and reduces the difficulty of learning. On the basis of students' self-study and cooperation, teachers give guidance. In MG, there are many types of diseases that need to be identified, the diagnosis needs to be classified, and the treatment needs to be individualized to improve the prognosis. In the process of diagnosis, differential diagnosis, treatment, and follow-up, sum up experience, find problems, train clinical thinking, and establish scientific research awareness.

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