DEFINITION

1. A chronic disorder of the neuromuscular junction marked by abnormal fatigability and weakness of selected muscles.

CLINICAL MANIFESTATIONS

2. Myasthenia gravis has a prevalence of at least 1 in 7500. It affects all age groups, but peaks of incidence occur in women aged 20-30 and men aged 50-60. Women are affected more frequently than men.

3. The hallmark of myasthenia gravis is weakness of skeletal muscle that increases with exercise. The most common presenting symptoms are ptosis and double vision, and in some patients symptoms remain confined to the eye muscles. There may be difficulty in chewing and swallowing, and in holding the head up. Weakness in the limbs particularly affects the arms and the proximal muscles in the legs. Muscle wasting is rare.

4. Diagnosis is confirmed by the presence of a raised serum titre of anti-acetylcholine receptor antibody, which is specific for myasthenia gravis. The natural course of the disease is variable; exacerbations and remissions may occur, but remissions are rarely complete or permanent.

AETIOLOGY

5. The underlying defect in myasthenia gravis is a decrease in the number of available acetylcholine receptors at neuromuscular junctions due to an antibody-mediated autoimmune attack. The **thymus gland**, which generates T lymphocytes, appears to play a role in this process.

6. Apart from a rare congenital variety, **myasthenia gravis is an acquired autoimmune disorder**.

7. The body's immune system provides an essential barrier to a large range of pathogenic organisms. **Autoimmune disease** occurs if the immune network response becomes directed at the body itself rather than at foreign antigens, and thereby causes damage to the body's tissues.

8. Most work on autoimmune disease and its mechanisms have been done in animals. Despite recent advances in the molecular biology of the immune response, the precise aetiology of autoimmune disease remains unknown. In humans genetic factors are thought to play a part. This is supported by studies of familial aggregation of the conditions, and high concordance in monozygotic twins. However concordance is not complete and therefore genetic factors alone are insufficient for disease to develop.

9. Environmental factors which have been postulated as producing disease in predisposed individuals include infection (viral and bacterial), drugs and toxins. However positive identification of specific factors in the individual conditions and cases is very rare.

10. Individuals with one autoimmune disease appear to be at increased risk of other autoimmune conditions. These further conditions do not arise as a consequence of the first, rather the common factor is the genetic predisposition.

11. The initiating event leading to antibody production in myasthenia gravis is unknown, and nothing is know about factors which trigger the disease itself. There is a concordance of 50% in monozygotic twins.

12. Most patients with myasthenia gravis have an **abnormality of the thymus gland**. The commonest abnormality is lymphoid hyperplasia, which is present in 60% of patients with early onset disease. 10-15% are found to have an epithelial cell tumour of the thymus (**thymoma**). The aetiology of thymoma is not known.

13. **Penicillamine** treatment (for example in rheumatoid arthritis) can cause true myasthenia gravis, but the patient eventually recovers within a few months of stopping the drug.

14. Infection, emotional stress, and the use of muscle relaxants during anaesthesia can **precipitate** the onset of clinical features of the disease.

15. Malignant disease, most commonly small cell carcinoma of the lung, may trigger an autoimmune response in predisposed individuals. This gives rise to a myasthenia-like syndrome, rather than true myasthenia gravis.

CONCLUSION

16. Myasthenia gravis is a chronic disease manifest as weakness of various skeletal muscles. It is recognised as an **autoimmune disease**, but the triggering factors have not been identified. Abnormalities of the thymus gland are commonly found in patients with the disease.

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