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CASE REPORT

Triple immune mediated neuromuscular syndrome-coexistence of polymyositis, polyneuropathy and myasthenia gravis

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Abstract
The inflammatory myopathies are a group of acquired skeletal muscle diseases that includes polymyositis (PM), dermatomyositis (DM), and inclusion body myositis (IBM). Myositis patients can also develop additional autoimmune diseases, as seen in the "overlap syndromes". We recorded a case presenting the simultaneous occurrence of inflammatory myositis, neuropathy, and myasthenia gravis (with positive acetylcholine receptor antibodies).
Key words: dermatomyositis, myasthenia gravis, polymyositis

Introduction

The inflammatory myopathies are a group of acquired skeletal muscle diseases that includes polymyositis (PM), dermatomyositis (DM), and inclusion body myositis (IBM).[1] Myositis patients can also develop additional autoimmune diseases, as seen in the "overlap syndromes". Immune-mediated neuromuscular disorders include pathologies of the peripheral nervous system, neuromuscular junction (NMJ), and muscles.[2] Current research suggests that the condition may occur when immune system cells infiltrate and attack peripheral nerve, NMJ and muscle tissue (an autoimmune process). The term of "neuromyositis" was given to this entity including acute or subacute occurrence of neuropathic signs and muscular signs, with pathological signs of inflammation in nerves and muscles.[3]

The predominant symptom of PM is muscle weakness. Weakness is symmetric, affecting the proximal muscles of the extremities as well as the neck flexors.[4] The onset of weakness is usually gradual, occurring over 3 to 6 months with difficulty getting up from chairs, climbing stairs, or lifting objects. Patient can also have muscle ache, fatigue, drop head, and swallowing, breathing, and speech troubles.[5]

PM is treated with high doses of corticosteroids as a first course of treatment. Other immunosuppressive medications are considered which includes Methotrexate, Azathioprine, Cyclophosphamide, Chlorambucil, Cyclosporine, Mycophenolate, Rituximab. In severe cases of PM, the intravenous infusion of immunoglobulins (IVIG) has been an effective treatment. Physical therapy is also important in the treatment of polymyositis.[6] We are presenting the simultaneous occurrence of inflammatory myositis, neuropathy and myasthenia gravis (with positive acetylcholine receptor antibodies).

Case report

A 35 years old male presented to GGSMC&H Faridkot with chief complaints of insidious onset, gradually progressive bilateral upper and lower limb weakness, proximal more than the distal, for 5 months. It was associated with numbness of bilateral hands and feet, and bilateral ptosis.

On clinical examination, we found drop head, ptosis, difficulty in swallowing and dysphonia. Patient had a generalized reduced muscular power; and deep tendon reflexes were weak in both the upper and lower limbs. No muscle fasciculations were found. Rest of the systemic examination was normal.

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Laboratory investigations revealed hemoglobin (Hb) - 13.9 g/dL, total leucocyte count (TLC) -10500/mm^3, platelet count - 413000. Renal function tests revealed blood urea - 14 mg/dL, serum creatinine - 0.5 mg/dL, serum sodium - 136 meq/l, serum potassium - 4.5 mEq/L. Serum calcium was 9.2 mg/dL, and vitamin D was 34 ng/mL. Total serum protein and serum albumin were 7.2 g/dL and 4.0 g/dL, respectively. Total creatine phosphokinase (CPK) was 2646 IU/L, and CPK MB was 355.8 IU/L. ESR was 15 mm/1st hour and CRP was 2.2 mg/L. Liver function tests revealed total bilirubin - 0.8 mg/dL, aspartate transaminase (AST) - 214 IU/L, alanine transaminase (ALT) - 145 IU/L and alkaline phosphatase (ALP) - 59 IU/L. ANA and Anti-PM/Scl antibodies were positive, Anti- acetylcholine receptor (AChR) antibodies were absent and carcinoembryonic antigen (CEA), alpha fetoprotein (AFP), and cancer antigen 19-9 (CA 19-9) were negative.

Contrast enhanced MRI BRAIN with screening spine was done which revealed T2/STIR hyperintensity in all visualised muscles, focal T1 hyperintensity involving body of corpus callosum. No diffusion restriction was seen on DWI, no blooming on SWI with no enhancement seen on post GAD images. On CECT thorax and lower neck, the cervical and distal thoracic oesophagus were found collapsed, and no wall thickening was seen. Ultrasound whole abdomen revealed no sonographic abnormality. Upper GI endoscopy and biopsy showed normal study. Ice pack test and neostigmine challenge test were positive. Repetitive nerve stimulation showed a marked decremental response at 3 Hz stimulation. In the lower limbs, needle electromyography (EMG) showed early recruitment with spiky motor units on the quadriceps muscles (myogenic pattern) but also a reduced recruitment of the motor units in tibialis anterior (neurogenic pattern); there was no spontaneous activity. Muscle biopsy showed pattern of inflammatory myopathy. Nerve conduction study (NCS) findings were suggestive of polyneuropathy.

Discussion

Autoimmune neuromuscular disorders affecting peripheral nerves, NMJ or muscle have a wide clinical spectrum with diverse pathogenetic mechanisms.[7] Peripheral nervous system may be targeted in the context of post-infectious immune reaction, paraneoplastic syndromes and often we do not find any triggering or preceding events.[8] Pathogenetic mechanisms involve complex interactions between antigen-presenting cells, B cells and different types of T cells.[9] Various immunomodulating and cytotoxic treatments block proliferation or activation of immune cells by different mechanisms attempting to control the response of the immune system. Most treatment protocols for autoimmune neuromuscular disorders are based on the use of IVIG, corticosteroids and plasmapheresis, with cytotoxic agents mostly used as steroid-sparing medications.[10] More recently, development of specific monoclonal antibodies targeting individual cell types allowed a different approach targeting specific immune pathways, but only time will tell whether these new treatments are as effective and safe as “classic” regimens.[11] We reported a 35 years old male patient presenting the simultaneous occurrence of inflammatory myositis, neuropathy and myasthenia gravis.

Mathis et al[12] reported a case of simultaneous combined myositis, inflammatory polyneuropathy, and overlap myasthenic syndrome in a 67-year-old woman who complained of severe asthenia, loss of weight, and overall muscular weakness for five months. Her medical history only showed osteoporosis (without any fracture). On clinical examination, they observed a generalized decrease of the muscular strength: the motor weakness was proximal and distal in the four limbs but predominantly in the upper limbs {Medical Research Council (MRC) grade 3 in the upper limbs and grade 4 in the lower limbs}. Amyotrophy was moderate and restricted to the hands. She also complained of paresthesia in her hands (for five months).

Neuropathies with immune-mediated etiologies may manifest acutely or chronically, resulting in primary demyelination or axon loss. Similarities between peripheral nerve glycolipids and myelin proteins with various infectious agent components may result in molecular mimicry and trigger an immune response cross-reacting with peripheral nerves. In animal model of experimental autoimmune neuritis (EAN), immunization with peripheral nerve components leads to autoimmune reaction and peripheral nerve inflammation resembling Guillain Barre syndrome and allowing the study of different autoimmune and inflammatory pathways.[13]

Acquired myasthenia gravis is one of the most studied human autoimmune diseases and animal model of experimental autoimmune myasthenia helped us to elucidate its autoimmune mechanisms. The autoantibodies in myasthenia gravis result in loss and dysfunction of the acetylcholine receptors on the post-synaptic muscle membrane, and eventually transmission failure which leads to the clinical symptoms. Antibodies against the AChR are detected in up to 85% of patient with generalized disease and 50% of patients with ocular myasthenia gravis. Autoimmune myasthenia is associated with frequent abnormalities of thymus, especially thymic hyperplasia, and 10-15% of patients may have a thymic tumor. More recently, elevated titers of antibodies targeting muscle-specific kinase (MuSK) have been described in almost half of the “seronegative” patients.[14]

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Conclusion

Authors reported a rare case of a 35 years old male who presented with insidious onset and gradually progressive bilateral upper and lower limb weakness and muscles ache, neck pain and inability to hold neck, difficulty in swallowing and bilateral ptosis. Patient was found to have elevated serum CPK levels and positive ANA and Anti-PM/Scl antibodies. EMG and muscle biopsy were suggestive of myositis and NCS was suggestive of polyneuropathy. Ice pack test and neostigmine challenge test came positive and repetitive nerve stimulation showed a marked decremental response at 3 Hz stimulation, confirming myasthenia gravis.

References

1. Gorson KC, Ropper AH. Positive salivary gland biopsy, Sjogren syndrome, and neuropathy: clinical implications. Muscle Nerve. 2003;28(5):553–60.
2. Gondim FA, Brannagan TH, 3rd, Sander HW, Chin RL, Latov N. Peripheral neuropathy in patients with inflammatory bowel disease. Brain. 2005;128:867–79.
3. Burns TM, Dyck PJ, Aksamit AJ. The natural history and long-term outcome of 57 limb sarcoidosis neuropathy cases. J. Neurol. Sci. 2006;244(1-2):77–87.
4. Stern BJ, Aksamit A, Clifford D, Scott TF. Neurologic presentations of sarcoidosis. Neurol. Clin. 2010;28(1):185–198.
5. Vernino S, Low PA, Fealey RD, Stewart JD, Farrugia G, Lennon VA. Autoantibodies to ganglionic acetylcholine receptors in autoimmune autonomic neuropathies. N Engl J Med. 2000;343(12):847–55.
6. Greenberg SA, Sanoudou D, Haslett JN, Kohane IS, Kunkel LM, Beggs AH, Amato AA. Molecular profiles of inflammatory myopathies. Neurology. 2002;59(8):1170–82.
7. Hill CL, Zhang Y, Sigurgeirsson B, Pukkala E, Mellemkjaer L, Airio A, Evans SR, Felton DT. Frequency of specific cancer types in dermatomyositis and polymyositis: a population-based study. Lancet. 2001;357(9250):96–100.
8. Miller T, Al-Lozi MT, Lopate G, Pestronk A. Myopathy with antibodies to the signal recognition particle: clinical and pathological features. J Neurol Neurosurg Psychiatry. 2002;73(4):420–8.
9. Seton M., Wu C. C., Louissaint A., Jr. Case records of the Massachusetts General Hospital. Case 26-2013—a 46-year-old woman with muscle pain and swelling. N Engl J Med. 2013;369(8):764–73.
10. Reimann J., Kornblum C., Tolksdorf K., Brück W., Van Landeghem F. K. H. Myopathy and neuropathy with pipestem capillaries and vascular activated complement deposition. Neurology. 2011;77(4):401–3.
11. Kung SL, Su JM, Tsai SJ, Lu TM, Chen CM. Concurrent Guillain-Barré syndrome and myasthenia gravis: the first case in Taiwan. Acta Neurologica Taiwanica. 2009;18(3):193–7.
12. Mathis S, Magy L, Corcia P, Ghorab K, Richard L, and Vallat JM. Simultaneous combined myositis, inflammatory polyneuropathy and myasthenic syndrome. Journal of the Peripheral Nervous System. 2014; 19:274.
13. Chitnis T, Khoury SJ. Immunologic neuromuscular disorders. Journal of Allergy and Clinical Immunology 2003; 111: 659–68.
14. Hausmanowa- Petrusewicz I, Blaszczyk M, Jablońska S. Coexistence of scleromyositis associated with PM-SCL antibody and myasthenia. Neuromuscular Disorders 1995; 5: 145–7.