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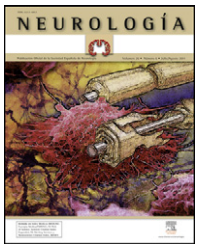

REVIEW ARTICLE

Monoclonal antibodies in inflammatory disease of the muscle and peripheral nervous system☆

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KEYWORDS
Autoimmune neuropathies;
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Chronic demyelinating polyneuropathy;
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Myasthenia;
Lambert-Eaton;
Polymyositis;
Dermatomyositis;
Inclusion body myositis;
Monoclonal antibodies;
Rituximab;
Alemtuzumab

Abstract
Introduction: A significant group of neuromuscular diseases are of autoimmune origin, but the classic immunomodulatory drugs are not often effective. For this reason, there is a need to find new more effective treatments that will lead to better control of these conditions, particularly those that are usually more resistant. In the last few years, the use of monoclonal antibodies against specific antigens of lymphocyte populations or against pro-inflammatory molecules has seen a great expansion, and has been demonstrated to be a useful alternative in autoimmune diseases.

An intensive search was made in Medline using the key words: neuromuscular, myopathy, neuropathy, myasthenia, Lambert-Eaton, monoclonal antibody, rituximab, alemtuzumab, and anti-TNF-α.

Development: Clinical trials performed to evaluate the efficacy of monoclonal antibodies in neuromuscular disease are very limited and of reduced size. Thus, the experience in this field is basically limited to anecdotal cases or short series of patients on open-label treatment. The published data are encouraging, with favourable responses having been observed in patients resistant to classic treatments and in diseases that do not normally respond to the usual immunosuppressant drugs. On the other hand, it has been observed that anti-TNF-α antibodies may trigger the appearance of autoimmune neuromuscular diseases.

Conclusions: Monoclonal antibodies could be an effective alternative treatment in autoimmune neuromuscular diseases, but the favourable responses observed need to be confirmed by means of controlled clinical trials with a sufficient number of patients.

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PALABRAS CLAVE
Neuropatías autoinmunitaria;
Guillain-Barré;
Polineuropatía desmielinizante crónica;
Multineuritis multifocal motora;
Neuropatía anti-MAG;
Miastenia;
Lambert-Eaton;
Polimiositis;
Dermatomiositis;
Miositis de cuerpos de inclusión;
Anticuerpos monoclonales;
Rituximab;
Alemtuzumab

Anticuerpos monoclonales en patología inflamatoria del sistema nervioso periférico y músculo

Resumen
Introducción: Un importante grupo de enfermedades neuromusculares son de origen autoinmune, pero con relativa frecuencia los fármacos inmunomoduladores clásicos no son eficaces. Por este motivo, se hace necesario encontrar nuevos tratamientos más eficaces, que permitan mejorar el control de estas entidades, especialmente aquellas que habitualmente son más resistentes. En los últimos años, el uso de anticuerpos monoclonales contra antígenos específicos de poblaciones linfocitarias o contra moléculas proinflamatorias ha conocido una gran expansión, y se han revelado como una alternativa útil en las enfermedades autoinmunitarias.

Se ha realizado una búsqueda intensiva en Medline usando como palabras clave: neuromuscular, miopatía, neuropatía, miastenia, Lambert-Eaton, anticuerpo monoclonal, rituximab, alemtuzumab, anti-TNF-α.
Desarrollo: Los ensayos clínicos realizados para valorar la eficacia de los anticuerpos monoclonales en patología neuromuscular son muy escasos y de tamaño muy reducido, de modo que la experiencia en este ámbito se limita fundamentalmente a casos anecdóticos o series cortas de pacientes tratados de forma abierta. Los datos publicados son esperanzadores, habiéndose observado respuestas favorables en pacientes resistentes a tratamientos clásicos y en patologías que habitualmente no responden a los fármacos inmunosupresores habituales. Por otro lado, se ha observado que los anticuerpos anti-TNF-α pueden provocar la aparición de enfermedades neuromusculares autoinmunitarias.
Conclusiones: Los anticuerpos monoclonales pueden ser una alternativa terapéutica eficaz en la patología neuromuscular autoinmune, pero es preciso confirmar las respuestas favorables observadas mediante ensayos clínicos controlados con un número suficiente de pacientes.

Introduction

A considerable group of neuromuscular diseases, including neuropathies and myopathies, or diseases of the neuromuscular junction, have an autoimmune pathogenesis. Among neuropathies these include Guillain-Barre syndrome, chronic demyelinating neuropathies, demyelinating multiple neuritis or Lewis-Sumner syndrome, multifocal motor neuropathy (MMN) with conduction blocks, neuropathies associated with gammopathies and paraneoplastic neuropathies. Among myopathies, there are polymyositis, dermatomyositis and, to some extent, inclusion body myositis. Finally, the two most common motor endplate diseases, myasthenia and Lambert-Eaton syndrome, also have an autoimmune pathogenesis. The current treatment of these entities is immunomodulating drugs such as corticosteroids, various immunosuppressants (particularly azathioprine), high-dose intravenous immunoglobulin and plasmapheresis. However, these drugs are not always effective, especially in some of these entities, and their side effects are sometimes severe. For this reason, it is necessary to find new, more effective treatments to improve the control of these entities, especially those that are generally more resistant.

In recent years, the use of monoclonal antibodies against specific antigens of lymphocyte populations or against proinflammatory molecules has undergone a great expansion, especially in rheumatic inflammatory diseases. The field of neuroscience has begun to use these drugs primarily in inflammatory diseases of the central nervous system, especially in multiple sclerosis. However, experience from other fields, such as inflammatory pathology of the peripheral and muscular nervous system, has also accumulated gradually. In the latter field, B lymphocytes have been established as the primary therapeutic target and rituximab as the most commonly used drug.[1]

In this work we will review the published experience with monoclonal antibodies in various neuromuscular diseases with an inflammatory basis.

Autoimmune neuropathies

Chronic autoimmune neuropathies are a continuous spectrum ranging from the most polyneuropathic and predominantly sensitive forms, which would be those neuropathies with anti-myelin associated glycoprotein (MAG) antibodies, to the purely motor forms with a multineuritic pattern, which would be multifocal motor neuropathy, including intermediate, more polyneuropathic forms (chronic inflammatory demyelinating polyneuropathy or CIDP) or more multineuritic forms (Lewis-Sumner syndrome).

Anti-MAG neuropathy

Neuropathy with anti-MAG antibodies is a well-characterised clinical entity that appears with progressive sensory ataxia. The pathogenic relationship between anti-MAG antibodies and polyneuropathy has been clearly demonstrated, since deposits of antibodies capable of fixing complement in