28_CONCORSO PUBBLICO, PER TITOLI ED ESAMI, PER LA COPERTURA A TEMPO DETERMINATO, DELLA DURATA DI CINQUE ANNI PER N. 1 POSTO DI COLLABORATORE PROFESSIONALE DI RICERCA SANITARIA - CAT. D, DA ASSEGNARE ALLA SC NEUROLOGIA 4 – NEUROIMMUNOLOGIA E MALATTIE NEUROMUSCOLARI

PROVA I

1. La diagnostica di laboratorio delle Encefaliti Autoimmuni che test comprende?

2. A cosa serve il programma Microsoft Excel?
   a) realizzare fogli elettronici per analisi di dati
   b) realizzare presentazioni
   c) gestire spool di stampa

3. Leggere e tradurre il testo allegato

Allegato PROVA 1

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REVIEW ARTICLE

Blood biomarkers of peripheral neuropathy

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Traditionally, neurophysiology is the primary diagnostic and prognostic biomarker in peripheral neuropathy clinical practice; however, it may lack responsiveness in the context of slowly progressive neuropathies and where there is significant axonal damage. The development of ultrasensitive platforms for measuring serum proteins at the lower limit of detection of traditional ELISA techniques has transformed the field of blood biomarkers of peripheral neuropathy. A variety of blood biomarkers have been identified from inflammatory cytokines and apokines in diabetic neuropathy through to neuron-specific proteins such as neurofilament light chain, Schwann cell-specific proteins such as TMPRSS5 and microRNAs in other acquired and hereditary neuropathies. In this article, we review blood biomarkers of disease activity for the common subtypes of peripheral neuropathy including inflammatory demyelinating neuropathies, vasculitic neuropathy, diabetic neuropathy, chemotherapy-induced neuropathy and Charcot–Marie–Tooth disease and related disorders including TTR amyloidosis.

KEYWORDS
Biomarkers, Blood, Peripheral neuropathy

1 | INTRODUCTION

Historically, biomarkers of peripheral nerve disease have focused on neurophysiological parameters such as nerve conduction studies and electromyography. Although these remain the cornerstone of peripheral nerve diagnosis, due to the high skill levels required, inter-operator variability and lack of sensitivity and responsiveness over a desirable time frame (e.g. weeks in acute vasculitic neuropathy and 1–2 years in hereditary neuropathies), its use as a biomarker of peripheral nerve disease progression over time is limited. Whilst CSF and blood biomarkers have rapidly evolved in central nervous system disease, their use and development in peripheral nerve disease has lagged behind.[1]

Biomarkers of peripheral nerve disease have a role in diagnosis, clinical management and in research where much attention is focused on their use in natural history studies and clinical trials.[2,3] They have relevance for a broad range of peripheral nerve diseases including inflammatory neuropathies such as chronic inflammatory demyelinating polyneuropathy (CIDP) and vasculitic neuropathy, toxic neuropathies such as chemotherapy-induced painful neuropathy (CIPN), diabetic neuropathy and also genetic neuropathies such as Charcot-Marie-Tooth disease (CMT) and hereditary TTR amyloidosis (ATTR). This review will primarily focus on the use of blood biomarkers of peripheral neuropathy for clinical management and as outcome measures in clinical trials (See **Table 1**). The review will not focus on diagnostic blood biomarkers for peripheral neuropathy such as anti-ganglioside antibodies in CIDP that have been reviewed extensively elsewhere.[4]

2 | INFLAMMATORY NEUROPATHIES

Inflammatory peripheral neuropathies can be divided into those that are demyelinating (the most common of which are Guillain-Barre syndrome [GBS] and CIDP) and those that are axonal, for example peripheral neuropathy due to vasculitis. Treatment of these

PROVA NON ESTRATTA

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PROVA 2

1. La diagnostica della Miastenia gravis che test comprende?

2. Cos'è il pacchetto Office?
   a) un prodotto software di produttività aziendale composto da un insieme di programmi specifici
   b) un programma specifico di gestione contabilità
   c) un programma di grafica

3. Leggere e tradurre il testo allegato

Allegato PROVA 2

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NEUROLOGICAL UPDATE

Myasthenia gravis: a clinical-immunological update

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Abstract Myasthenia gravis (MG) is the archetypic disorder of both the neuromuscular junction and autoantibody-mediated disease. In most patients, IgG1-dominant antibodies to acetylcholine receptors cause fatigable weakness of skeletal muscles. In the rest, a variable proportion possesses antibodies to muscle-specific tyrosine kinase while the remainder of seronegative MG is being explained through cell-based assays using a receptor-clustering technique and, to a lesser extent, proposed new antigenic targets. The incidence and prevalence of MG are increasing, particularly in the elderly. New treatments are being developed, and results from the randomised controlled trial of thymectomy in non-thymomatous MG, due for release in early 2016, will be of particular clinical value. To help navigate an evidence base of varying quality, practising clinicians may consult new MG guidelines in the fields of pregnancy, ocular and generalised MG (GMG). This review focuses on updates in epidemiology, immunology, therapeutic and clinical aspects of GMG in adults.

Keywords Myasthenia gravis · MuSK · LRP4 · IgG4 · Cell-based assays · Neuromuscular junction · Thymectomy

Introduction

Myasthenia gravis (MG) represents the archetypic disorder of both the neuromuscular junction (NMJ) and autoantibody-mediated disease. In most patients, IgG1-dominant antibodies to acetylcholine receptors (AChRs) cause fatigable weakness of skeletal muscles with an ocular onset in up to 85 % [1]. A variable proportion of patients lacking AChR antibodies, termed seronegative MG (SNMG), possess antibodies to muscle-specific tyrosine kinase (MuSK) [2, 3] and intriguingly, these antibodies are principally IgG4 [3–5]. The remainder of SNMG is now rapidly being explained via cell-based assays (CBAs) using a receptor-clustering technique [6–8], and, to a lesser extent, proposed new antigenic targets [9].

The incidence and prevalence of MG are increasing, particularly in older individuals [10, 11]. However, MG remains a rare disease and there are well-documented impediments to clinical trials including low participant recruitment [12]. Indeed, the EPITOME trial [13] in ocular MG (OMG) had to close recently due to failure to recruit adequate numbers [14]. Nevertheless, rituximab appears to show promise in MuSK MG [15] and a much-anticipated randomised controlled trial (RCT) of thymectomy in non-thymomatous MG [16] is due to report in early 2016. These results will be of great value since thymectomy has been offered for many years in this setting, without incontrovertible evidence of benefit compared to purely medical management [17, 18].

Expert clinical guidelines have reviewed pregnancy in MG [19], and management guidelines have been published for OMG [20] and generalised MG (GMG) (with some comments on OMG) [21]. This review will focus on GMG, as recent updates on congenital myasthenia [22] and OMG [23] have already been published. However, in addition to the epidemiology, immunology, therapeutics and clinical management of GMG, ongoing efforts to define the risk of generalisation (ROG) from ocular to generalised MG will be described.

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PROVA 3

1. Quali sono i meccanismi d'azione degli anticorpi anti recettore dell'Acetilcolina sulla membrana della giunzione neuromuscolare?

2. Con il termine "Base di dati" si intende:
   a) una collezione di dati, inerenti una specifica attività, opportunamente strutturati e accessibili tramite un software di gestione
   b) un linguaggio di programmazione
   c) un insieme di dati distribuiti sulla rete e accessibili solo tramite un browser

3. Leggere e tradurre il testo allegato

Allegato PROVA 3

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Clinical experience and laboratory investigations in patients with anti-NMDAR encephalitis

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Abstract

Since its discovery in 2007, the encephalitis associated with antibodies against the *N*-methyl-D-aspartate receptor (NMDAR) has entered the mainstream of neurology and other disciplines. Most patients with anti-NMDAR encephalitis develop a multistage illness that progresses from psychosis, memory deficits, seizures, and language disintegration into a state of unresponsiveness with catatonic features often associated with abnormal movements, and autonomic and breathing instability. The disorder predominantly affects children and young adults, occurs with or without tumour association, and responds to treatment but can relapse. The presence of a tumour (usually an ovarian teratoma) is dependent on age, sex, and ethnicity, being more frequent in women older than 18 years, and slightly more predominant in black women than it is in white women. Patients treated with tumour resection and immunotherapy (corticosteroids, intravenous immunoglobulin, or plasma exchange) respond faster to treatment and less frequently need second-line immunotherapy (cyclophosphamide or rituximab, or both) than do patients without a tumour who receive similar initial immunotherapy. More than 75% of all patients have substantial recovery that occurs in inverse order of symptom development and is associated with a decline of antibody titres. Patients' antibodies cause a titre-dependent, reversible decrease of synaptic NMDAR by a mechanism of crosslinking and internalisation. On the basis of models of pharmacological or genetic disruption of NMDAR, these antibody effects reveal a probable pathogenic relation between the depletion of receptors and the clinical features of anti-NMDAR encephalitis.

Introduction

In 2005, a syndrome of memory deficits, psychiatric symptoms, decreased consciousness, and hypoventilation was reported in four young women with ovarian teratomas.[1] Specific autoantibodies to the N-methyl D-aspartate receptor (NMDAR) were soon detected in these and eight other patients with similar neurological symptoms, seven of whom also had ovarian teratomas.[2] During the following 3 years we identified 419 other patients with this syndrome, many of them children and young adults with or without an associated tumour.

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Contributors

JD examined patients, and interviewed physicians and families. JD and RB-G provided synaptic and cell-based experimental data. EM-H collected and analysed clinical data. EL and MRR did the literature search and examined the mechanisms related to genetic and pharmacological alterations of NMDAR. JD, EL, MRR, and RB-G wrote the paper.

Conflicts of interest

A patent application for the use of NMDAR antibody determination in patients' serum samples and CSF as a diagnostic test has been filed in USA and Europe by JD. EL has a training grant from Talecris, a company that sells human immunoglobulin. None of the other authors declare any conflicts of interest.

PROVA ESTRATTA

31/01/2024

Angelo Di Lino