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Review

Impact of treatment on survival in polymyositis and dermatomyositis. A single-centre long-term follow-up study

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ABSTRACT

Objective: To assess the long-term outcome in polymyositis (PM) and dermatomyositis (DM), with a particular emphasis on mortality and influence of treatment.
Methods: Diagnosis was based according to the Bohan and Peter's criteria. Patients have been followed up by a standardised protocol. Deaths were registered and causes of death were ascertained. Survival probability at 5 and 10 years was estimated according to the Kaplan–Meier method, in the overall series and by a diagnostic group and an initial treatment. Mortality hazard ratios (95% CI) for major clinical and demographic features were estimated through univariate and multivariate Cox proportional hazard models.
Results: 91 patients (43 PM and 48 DM) were available for the study. Baseline characteristics were not different from those previously reported. Twenty-two patients (24%) died after a median follow-up of 8.7 years. As for idiopathic myositis, the survival probabilities at 5 and 10 years from the diagnosis were 96.2% and 88.8% for PM respectively; and 93.9% for DM, whereas a higher mortality was documented for cancer-associated myositis and overlap myositis. Male sex [HR = 2.4, 95% CI 1.0 to 5.6], heart involvement (HR = 1.8), interstitial lung disease (HR = 2.3) and arthritis (HR = 1.8) increased the risk of mortality, these risk excesses were confirmed in the multivariate analysis. Independent of these features, a higher mortality was documented for patients treated with glucocorticoids (HR = 2.3) or immunosuppressants (HR = 2.1) when compared to patients treated with immunoglobulins.
Conclusion: Our study, with longitudinal and statistical analyses, suggests that survival has considerably increased in patients with PM/DM. Prognostic factors for mortality are male sex, and heart and lung involvement. Immunoglobulin treatment, intravenously or subcutaneously, is associated with a better survival.

Contents

Abbreviations: CTD, connective tissue disease; DM, dermatomyositis; IBM, inclusion body myositis; IVIg, intravenous immunoglobulin; NM, necrotizing myositis; PM, polymyositis; SCIg, subcutaneous immunoglobulin.

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1. Introduction

Idiopathic inflammatory myopathies include dermatomyositis (DM), polymyositis (PM), necrotizing myopathy (NM) and inclusion body myositis (IBM) [1]. Different DM subsets have been identified until now. These include classic DM, with muscular and skin involvement; amyopathic DM, when the disease affect only the skin; hypomyopathic DM, when cutaneous manifestations are associated with subclinical evidence of myositis; post-myopathic DM, when patients with a previous classic DM present a recovery of myositis but skin rashes remain active; and DM sine dermatitis, when no rash is detected but a histology feature of the muscular biopsy sample is indicative of DM [2]. PM is best defined as a subacute myopathy that evolves over weeks to months, affects adult but rarely children and that mimics many other myopathies and remains a diagnosis of exclusion [3]. Clinically, NM is indistinguishable from PM. This disorder includes autoimmune inflammatory mechanism, paraneoplastic conditions, exposure to toxins or drugs as well as combinations of these mechanisms [1]. IBM is considered to be the most frequently acquired myopathy after the 50th year of life. It develops slowly, leading to a mainly asymmetric paresis. The flexion of hand and fingers and knee extension are typically affected [1]. Whilst DM, PM and NM mainly respond well to treatment with immunosuppressants, IBM is usually resistant to these drugs, and only in few patients immunoglobulins may display a temporary beneficial effect [1].

All these disorders have in common the presence of moderate to severe weakness and inflammation in the muscle [3] and they are clinically important because they are potentially treatable. Given their rarity, it is difficult to evaluate their outcome and the real impact of the treatment on the disease.

We here describe our experience with patients suffering from PM and DM, with a particular emphasis on mortality and the impact of treatment.

2. Patients and methods

2.1. Patient population

The patient population consisted of 91 consecutive in- and outpatients with new-onset PM or DM who were diagnosed, treated and followed up by the Clinical Medicine Section of the Department of Clinical and Molecular Sciences from the Marche Polytechnic University, Ancona, a single referral university hospital in the centre of Italy. The first assessment occurred in 1985 and since then patients were prospectively followed-up. The diagnosis of definite myositis was made according to the Bohan and Peter's criteria [4]. Patients with inclusion body, necrotizing autoimmune and juvenile myositis were excluded from this study. Patients had idiopathic PM (Group I, 28 cases), idiopathic DM (Group II, 38 cases), cancer-associated myositis (Group III, 13 cases) or overlap myositis (Group V, 12 cases). In this last case, myositis occur together with other connective tissue diseases (CTDs) such as systemic sclerosis (SSc), systemic lupus erythematosus (SLE), Sjogren's syndrome (SS), mixed connective tissue disease (MCTD) or rheumatoid arthritis (RA); all diagnosed according to the international criteria. Demographic, clinical and serological data (see below) were collected at diagnosis and during subsequent follow-up with a standardised protocol. The minimum follow-up to enter this study was 24 months, although patients who died before this period were included in the study. Deaths were registered and causes of death were ascertained by a death certificate.

2.2. Clinical evaluation

For each patient a careful medical history and a physical examination were performed at the initial presentation and every 6 months during the follow-up period or when clinically indicated.

2.2.1. Muscle evaluation

Changes in the skeletal muscle strength were evaluated using the Medical Research Council (MRC) scale, in which 0 is the lowest and 5 is the highest score, performed by trained physicians (LP and SG). Nerve conduction and concentric needle electromyographic (EMG) studies were performed according to standard techniques by one of us (FL) [5,6]. Muscle biopsy specimens taken from patients were examined at the initial presentation by means of a light and electron microscopy.

2.2.2. Skin and organ evaluation

The type and extent of skin lesions were assessed. In all cases the specific investigations comprised pulmonary function, the diffusion capacity of the lung for carbon monoxide expressed as a percentage of the predicted value (DLCO) and chest radiography. High-resolution computed tomography (HRCT) was achieved in subjects with reduced DLCO. Other examinations were performed when clinically indicated. Raynaud's phenomenon (RP) was evaluated using a nail fold capillary microscopy. Lung involvement was defined in the presence of respiratory muscle involvement, interstitial lung disease or pulmonary hypertension. Gastrointestinal involvement was characterised as dysphagia or dismotility of the oesophagus. The heart involvement was defined in the presence of cardiomyopathy, myocarditis or rhythm disturbance. All of the patients were studied for *underlying malignancy*.

Among the *biochemical analyses* we collected data related to creatine-kinase (CK) (normal values <170 U/L).

The *immunologic parameters* were documented as follows: antinuclear antibodies (ANA) with indirect immunofluorescence test (IF-ANA); anti-double stranded (ds)-DNA antibodies by the RIA-Farr technique; anti-extractable nuclear antigen (ENA) antibodies with immunoblotting analysis to detect the different patterns. ANA titres $\geq 1:80$ were considered positive. The research of myositis-specific antibodies was not available in our hospital (except for anti-Scl70 and anti-Jo1, detected by ELISA and anti-PM-Scl performed by immunodiffusion in patients with a speckled/nucleolar pattern in immunofluorescence). In all of the patients, all the tests were performed at the inclusion and then when clinically indicated.