FATAL OUTCOME IN A CASE OF DERMATOMYOSITIS AND HAMMAN-RICH SYNDROME

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ABSTRACT

We present the fatal outcome in a 31-year-old woman of Latin-American origin diagnosed with dermatomyositis. There were three months between death and the onset of symptoms. The initial presentation was normal dermatological symptoms to which were shortly added clinical signs of effects on the lungs, as was shown radiologically and through pulmonary function tests which were subsequently identified histologically as Hamman-Rich syndrome. The patient was treated with high doses of corticosteroids, intravenous (IV) immunoglobulin, cyclophosphamide and cyclosporin. We carried out a review of the literature on pulmonary compromise in dermatomyositis, clinical and anatomopathological forms and treatment alternatives.

Keywords: Interstitial lung disease; Dermatomyositis; Hamman Rich Syndrome

CASE DESCRIPTION

A 31-year-old woman of Latin-American origin with no history of drug abuse and a normal pregnancy 6 years earlier was sent to our department from the emergency unit due to dyspnoea.

Seven weeks earlier she had presented with erythematous, desquamative lesions distributed in the form of plaques with ill-defined edges on both eyelids, the forehead, breasts, periumbilical region, buttocks, metacarpophalangeal joints of the fingers and the dorsal cervical region. A skin biopsy showed a chronic perivascular and periadnexal infiltration with accumulation of histiocytes in the papillary dermis and mucin deposits in the reticular dermis. From these findings she was diagnosed with amyotrophic dermatomyositis at anoth
tracorporeal membrane oxygenation (ECMO) was initiated.

There was consultation regarding the possibility of a lung transplantation, but this was ruled out due to the patient’s acute condition.

After six days with ECMO, the patient suffered cardiac arrest and died. The necropsy showed diffuse alveolar damage with type II pneumocyte hyperplasia, foci of alveolar haemorrhage and complete absence of signs of infection.

**DISCUSSION**

**CLINICAL-PATHOLOGICAL CLASSIFICATION**

In accordance with exclusively clinical criteria and based on the initial presentation and its severity, pulmonary interstitial disease in patients with dermatomyositis may be classified in three groups: acute, progressive and asymptomatic disease\(^1\).

The acute form, known as acute interstitial pneumonia (AIP) is synonymous for Hamman-Rich syndrome\(^1,2\). Hamman-Rich syndrome progresses with a histological form known as diffuse alveolar damage (DAD) and is practically indistinguishable from that which appears with adult respiratory distress syndrome. There are two presentations of DAD: exudative or acute and subacute. The exudative presentation is the earliest. It appears in the first week and is characterised by intra-alveolar oedema, the presence of hyaline membranes and type II pneumocyte hyperplasia, intra-alveolar haemorrhage and interstitial infiltration of mononuclear inflammatory cells. Subsequently, two weeks after the lesion, a second phase appears, known as the proliferative phase, characterised by a massive fibroblastic proliferation in the interstitial tissues and the alveolar space. Hyperplasia of the type II pneumocytes is also observed, with a discrete degree of nuclear atypicality, thrombosis of the small arteries and squamous metaplasia in the bronchial epithelium\(^2\).

Subacute DAD, known also as the progressive DAD, corresponds to subacute interstitial pneumonia (SAIP). The difference between AIP and SAIP is in the onset of symptoms. While AIP appears in the first month, SAIP may appear between the first and third months\(^3\).

SAIP also has three different histological forms: bronchiolitis obliterans organising pneumonia (BOOP), usual interstitial pneumonia (UIP) and non-specific interstitial pneumonia (NSIP). The NSIP form is histologically very similar to the acute form of DAD.
except for the presence of large amounts of collagen in the fibrotic areas. BOOP also has similar histological characteristics to acute DAD except it is mainly patchy and affecting the peribronchiolar area in particular. UIP is characterised by a fibrotic and homogenous pattern that does not vary with time. This pattern may be observed in patients who have received mechanical ventilation with high concentrations of oxygen. Special mention should be made of the fact that cryptogenic organising pneumonia (COP) is normally an interchangeable term for BOOP. COP certainly refers to histological patterns of BOOP in which a known underlying pathology has not been identified.

The third group of patients, estimated as 22 to 25% of all cases of PM/DM, is made up of asymptomatic patients with respect to respiratory function who have typical radiological findings: parenchymatous micromodules, linear opacities, irregularities in the pleura-lung interface, ground-glass opacity, honeycomb patterns, bronchiectasis and bronchiolocystasis.

TREATMENT ALTERNATIVES

Interstitial lung disease in patients the dermatomyositis (DM/ILD) has a poor prognosis in itself. Furthermore, DAD worsens the prognosis. It is normal to observe lower CK levels in patients with DM/ILD compared to patients with PM/ILD and levels may even be normal in patients with DM/ILD. According to some authors, low CK levels are factors for poor prognosis and bad response to corticosteroids in ILD. According to Nawata et al., the use of prednisolone pulses is still the first line of treatment in ILD and is the most frequently observed recommendation. Although most patients in their series responded well to pulses, only one of them was diagnosed with DM. Currently, therapy with corticosteroids alone, in pulses or not, appears to have more chance of success in patients with PM/ILD in histological forms compatible with BOOP or NSIP, and in clinical forms of ILD corresponding to AIP.

Also, two studies support the use of cyclosporine A (CYP-A) in patients diagnosed with DM/ILD and AIP. Kameda et al. published a series of over 500 patients diagnosed with DM, 27 of whom developed ILD and were treated with 0.5 mg/kg/day of prednisolone, 10-30 mg/kg of CYC IV every 3-4 weeks and 2-4 mg/kg/d of CYP-A. According to their findings, survival increased to 50%. The most recent work supporting the use of CYP-A was published by Kotani et al. in 2011. With a dose of 4 mg/kg/d of CYP-A and 1 mg/kg/d of prednisolone, they reported an improvement in pulmonary function tests and radiological findings and one case of mortality in 14 patients who were followed.

Therapy with rituximab (RTX) has been considered in patients with DM/ILD having previously failed with corticosteroids and other conventional therapies. Despite the lack of case reports, the results appear to be optimistic in the medium term; however, there are no positive results in situations of rapid progression. The use of anti-CD20 therapy has been reported in patients with ILD and antisynthetase syndrome. The longest series was published by Sem et al. They reported 11 cases of antisynthetase syndrome and ILD. Three of them showed rapid deterioration of respiratory function and were treated with RTX before cyclophosphamide, obtaining improvement in DLCO of at least 15%. In 65% of all patients, a minimum of 10% gain in pulmonary vital capacity was observed that was only demonstrable in the first month of treatment.

The case we present is a rapidly developing DM/ILD, with low CK levels, compatible with an AIP and histologically corresponding to Hamman-Rich syndrome. Given the rapid deterioration in lung function, an infectious process was suspected, hence empirical antibiotic treatment was administered together with immunosuppressant therapy. Particularly striking was the lack of response to all treatment strategies: use of corticosteroids at high doses and in IV pulses, immunoglobulins, cyclophosphamide and cyclosporin A. The use of RTX was not considered in this patient due to the lack of a short-term favourable response. One day before death, the possibility of lung transplantation was considered, but this was ruled out due to the patient’s acute condition.

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