An international survey of developing classification criteria for juvenile dermatomyositis-scleroderma overlap

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Rheumatology key message: Definition of juvenile dermatomyositis-scleroderma overlap phenotype is important to tailor patient's management.

Sir,

Juvenile dermatomyositis (JDM) is a heterogeneous autoimmune-mediated disease, which may overlap with other connective tissue disorders, including systemic sclerosis (SSc), systemic lupus erythematosus (SLE) and mixed connective tissue disease (MCTD)[1, 2]. However, there is no internationally agreed definition of 'JDM-Scleroderma overlap' syndromes in children and a paucity of published data on the clinical characteristics, laboratory features and outcome in this specific group. In adults with dermatomyositis, scleroderma overlap commonly presents with sclerodactyly, facial skin changes, and interstitial lung disease (ILD) and gastrointestinal involvement; and may progress to include many SSc features[3]. Some authors suggest that myositis with features of scleroderma should be considered a separate entity known as 'scleromyositis'[4] but, in JDM, 'overlap' features may develop after an initial classical JDM presentation[5]. The goal of this survey was to define the clinical characteristics of JDM-Scleroderma overlap and identify whether experienced clinicians believe overlap features may affect outcome and management to support the development of clusters based on clinical features and biomarkers to help tailor patient's management.

An initial Delphi survey compiled by two clinicians (PK and SCL) and approved by the UK JDCBS Steering committee, it was circulated to 152 members of the Juvenile Dermatomyositis Research Group (JDRG) and the Paediatric Rheumatology European Society (PRES) JDM working group. The survey listed clinical criteria expected to be helpful and clinically relevant in making the diagnosis of JDM-Scleroderma overlap. Each individual was asked to identify the most characteristic clinical manifestations, to rank them in terms of frequency, and to give an expert opinion with regards to outcome and management. The survey attempted to capture the clinical and serologic features, which played a role in the diagnosis of overlap and whether autoantibodies influence the outcome and management. Survey respondents were also asked if they had treated JDM-Scleroderma overlap patients. The survey was circulated to members by e-mail.

The survey had a response rate of 26.9% (41 individuals) from both JDRG and PRES JDM working party. 89% of participants who responded reported that they had seen patients with JDM-Scleroderma overlap. Results of this survey are shown in Figure 1. The most common features reported to occur in JDM patients with scleroderma overlap were sclerodactyly, sclerodermatous

skin change proximal to MCP joints, Raynaud's phenomenon and ulceration at the tip of fingers, respectively. 95.1% of responders thought the scleroderma overlap presentation influenced the outcome of JDM, while 86.4% agreed that these features influence the choice of treatment.

Myositis associated autoantibodies occurring in systemic sclerosis overlap (anti PM-Scl, anti U1-RNP and anti Ku) were thought to be the most commonly associated autoantibodies with JDM-Scleroderma overlap (78%), followed by systemic sclerosis specific autoantibodies (anti Scl70, anti RNA polymerase III) (44%), anti-synthetase autoantibodies (antiJO1, antiPL7, antiPL12) (16.41%) and other antibodies, such as anti-Ro (8.21%). Interestingly, all responders (100%) thought that negative myositis autoantibodies did not exclude the diagnosis JDM-Scleroderma overlap, but almost 11% of participants felt that myositis antibodies were needed to diagnose this subgroup of JDM. Although 83% felt that autoantibody profile influences the outcome, only 49% thought that autoantibody profile would influence the choice of medication.

To the best of our knowledge, this is the first attempt to develop criteria for JDM-Scleroderma overlap syndrome in the paediatric population. In this survey, the majority of clinicians believed that defining overlap phenotypes (clinical and serological) influences their treatment, suggesting that further research is warranted to more fully understand this group. A limitation of our study is that less than half of the surveyed physicians responded to our initial survey, so our findings may not represent a true consensus. This subtype of JDM is rare: the number of children seen by each contributor varied from 1-20 cases. However, our survey targeted the international community and almost 90% of participants had experience in managing this specific group.

Over the last decade, autoantibodies such as myositis specific autoantibodies (MSA) and myositis associated autoantibodies (MAA) have become important biomarkers in the diagnosis of idiopathic inflammatory myopathies, the identification of overlap features and the monitoring of patients[2, 6]. In our previous report[7], we defined JDM-Scleroderma overlap by the presence of two or more of Raynaud's, sclerodactyly, or sclerodermatous skin changes. MAA, in particular, anti PM-Scl and anti U1-RNP, were frequently detected in this group. Notably, these three features were ranked by clinicians as the top 3 in this survey.

This process is the first step in developing meaningful criteria for the diagnosis of JDM-Scleroderma overlap. The next step would be to validate the criteria in a second cohort, and then to ask experts to submit patient cases that include the features we have identified as well as patients with other connective tissue disorders. The derivation of a proposed definition of scleroderma overlap would then require a consensus based meeting of international experts to generate a proposal.

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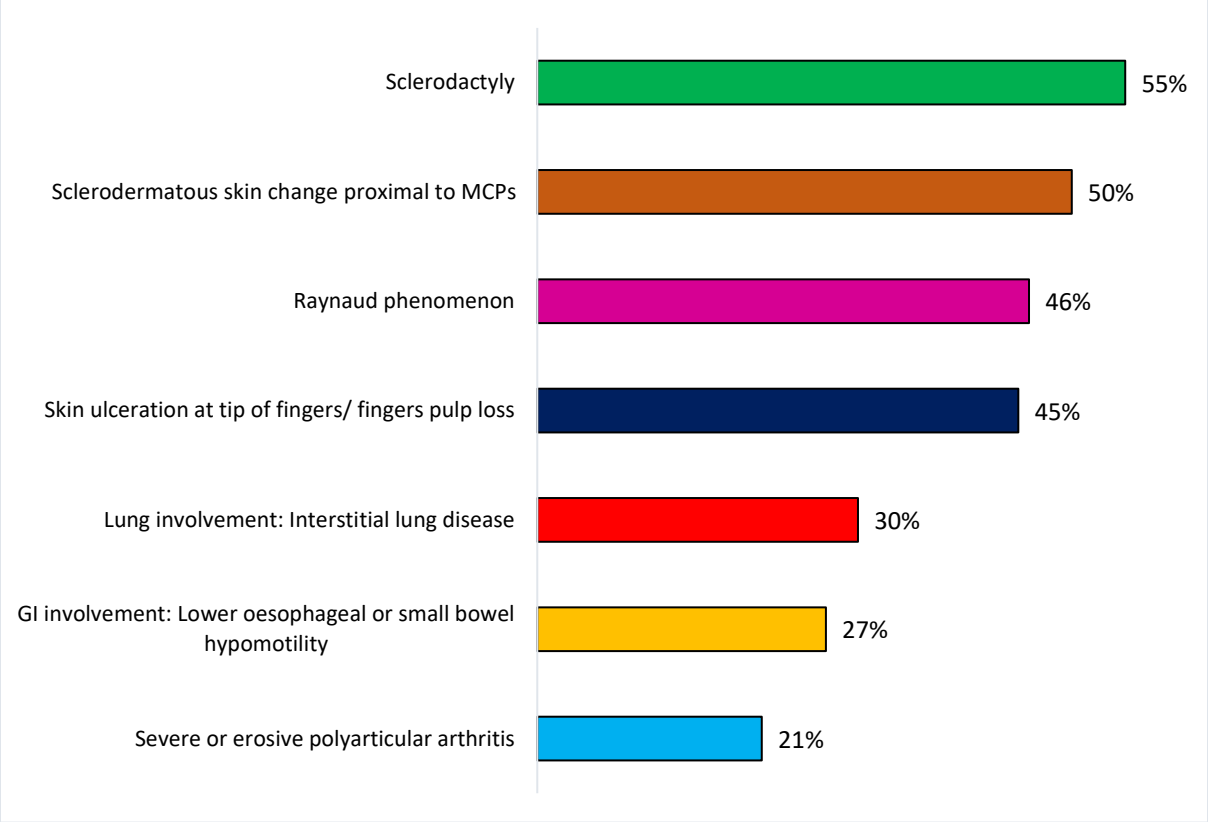

Figure 1: Clinical features reported to occur in JDM/Scleroderma overlap patients. The top four characteristics ranked in term of frequency are sclerodactyly, sclerodermatous skin change proximal to MCP joints, Raynaud's phenomenon and ulceration at the tip of fingers, respectively