WEDNESDAY, 14 JUNE 2017

The differential diagnosis of diffuse skin sclerosis and of Raynaud's phenomenon and a practical approach to assessment

SP0013 WIDESPREAD CUTANEOUS THICKENING – COULD THIS BE EARLY DIFFUSE CUTANEOUS SYSTEMIC SCLEROSIS?

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A case of diffuse sclerosing skin disease shall be presented. The features that initially led the treating team to consider a diagnosis of systemic sclerosis shall be discussed, alongside subsequent features that emerged that cast doubt over this diagnosis and led the team to undertake additional investigative studies. The presentation shall provide a chronological description of the clinical features, laboratory studies, microvascular imaging and histological studies that helped the team to reach a definitive diagnosis and plan management accordingly.
Disclosure of Interest: None declared
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SP0014 THE DIFFERENTIAL DIAGNOSIS OF DIFFUSE SCLEROSING SKIN DISEASE AND A PRACTICAL APPROACH TO ASSESSMENT

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The differential diagnosis for sclerosing skin disease is broad but there are clinical and laboratory features that can help guide clinicians to the correct diagnosis. This presentation shall provide a comprehensive review of the spectrum of sclerosing skin disease. A practical approach to interpreting the clinical, serological, microvascular imaging and histological features that can help differentiate disease states shall be presented to provide rheumatologists with a practical approach to the assessment of patients with sclerosing skin disease. Case histories shall be used to illustrate the pertinent clinical features and investigative approaches that can help distinguish systemic sclerosis from other sclerosing skin conditions such as scleroedema, pan-sclerotic morphoea, lipodermatosclerosis and chronic graft versus host disease. A specific focus shall be placed on the role of autoantibodies in the diagnosis of systemic sclerosis, including recent work reporting the presence of novel systemic sclerosis-specific autoantibodies in patients with antinuclear antibody-negative diffuse cutaneous systemic sclerosis.
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SP0015 NEW ONSET RAYNAUD'S PHENOMENON – COULD THIS BE EARLY LIMITED CUTANEOUS SYSTEMIC SCLEROSIS?

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A case shall be presented of a patient with Raynaud's phenomenon and whether this could be early limited cutaenous systemic sclerosis. The presentation shall describe the clinical features and investigative approaches that helped us reach a diagnosis, with a particular focus on the role for microvascular imaging and the detection of SSc-associated autoantibodies.
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SP0016 THE DIFFERENTIAL DIAGNOSIS OF RAYNAUD'S PHENOMENON AND PRACTICAL APPROACH TO ASSESSMENT WITH A FOCUS ON IMAGING

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Raynaud's phenomenon is the term used to describes episodic vasospasm of the digital vasculature in response to cold exposure and/or emotional distress. The majority of people with Raynaud's phenomenon have primary (idiopathic) Raynaud's phenomenon which is 'benign' in that it does not progress to irreversible digital ischaemia, and is not associated with any underlying disease. Conversely, when Raynaud's phenomenon is secondary to an underlying disease/condition (for example to a systemic sclerosis-spectrum disorder), it can be severe, sometimes progressing to digital ulceration and/or gangrene. Raynaud's phenomenon is often the presenting feature of connective tissue disease and therefore provides a window of opportunity for early diagnosis.
The first step in management of Raynaud's phenemenon is establishing the diagnosis. Is this primary or secondary Raynaud's, and if secondary, then to what? While a careful history and examination are always the first steps, different laboratory tests and vascular imaging studies can be used to reach the correct diagnosis. This presentation will provide practicing rheumatologists with a practical approach to the diagnosis and assessment of Raynaud's phenomenon, focussing on the diagnostic and prognostic role of vascular imaging (including nailfold capillaroscopy and thermography).
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Controling the balance between cancer and autoimmunity

SP0017 SHARED MECHANISMS IN CANCER AND AUTOIMMUNITY

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Some rheumatic disease autoantibodies are powerful markers of subgroups of patients who have distinct disease phenotypes and trajectories. Of particular interest are markers of several disease subgroups in whom cancer and rheumatic disease onset are clustered together in time. For example, a subgroup of scleroderma patients have coincident onset of cancer and scleroderma. This is observed in scleroderma patients with autoantibodies against the RNA polymerase-3 (POLR3), and more recently with autoantibodies recognizing the minor spliceosome. In autoimmune myopathies, temporal clustering of diagnosis of cancer and myositis is associated with autoantibodies to NXP2 and components of the TIF1 complex. Interestingly, although the incidence of cancer is higher in patients with these autoantibodies, most patients with these autoantibodies manifest cancer, even with extended periods of follow-up. These observations provide an important opportunity to investigate the potential mechanisms which operate at the cancer-immune interface during development of rheumatic diseases.
We have investigated such mechanisms in scleroderma patients with autoantibodies to POLR3 who also had a cancer diagnosed an average of -2.6 years from scleroderma onset. In cancers from these patients, we found genetic alterations of the POLR3A locus in six of eight patients with antibodies to POLR3 but not in eight patients without these antibodies. 3 antibody-positive patients had somatic mutations in POLR3A; 5 patients had loss of heterozygosity at the POLR3A locus. Analyses of peripheral blood lymphocytes and serum suggested that POLR3A mutations sparked cellular immunity and cross-reactive humoral immune responses. These results offer insight into the pathogenesis of scleroderma, and potentially other autoimmune syndromes. They suggest that somatic mutations in autoantigens in different cancers might initiate an immune response to the mutated autoantigen, which spreads to include the wild type version. Tissues (e.g. blood vessels, regenerating muscle) in which specific autoantigens are expressed at high levels, or potentially play critical functional roles, may be particularly susceptible to immune-mediated dysfunction. The results also provide support for the idea that acquired immunity helps to control naturally occurring cancers in patients with autoimmune rheumatic diseases; it is possible that this immune response may sometimes be fully effective, preventing the emergence of cancer.
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SP0018 CONTROLING THE BALANCE BETWEEN CANCER AND AUTOIMMUNITY

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Immunotherapy is revolutionizing cancer therapy with a paradigm shift: antibodies are now designed to target immune cells rather than cancer cells with the aim of stimulating the anti-tumor immune response. Monoclonal antibodies targeted against CTLA-4, PD-1 or PD-L1 and anti-CTLA-4 + anti-PD-1 combinations have shown potent activity with significant improvements in the overall survival of patients. Multiple other immunomodulatory drugs are currently in development. These novel therapies generate immune related adverse events that mimick auto-immune diseases. These side effects represent a major challenge for the implementation of immunotherapy in oncology. The aim of this talk will be to provide an update on the clinical results of combination therapies and discuss the current challenges and perspectives for the future of immuno-oncology.
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