Churg-Strauss syndrome and Wells' syndrome: coincidence or pathogenetic association? A new case report

Sirs,

Churg-Strauss syndrome (CSS) and Wells' syndrome (WS) are two rare conditions both characterized by peripheral eosinophilia and tissue eosinophilic infiltrates (1, 2), suggesting a possible common pathogenetic background. However, their association is very unusual. To date, only two cases have been published (3, 4). Here we report a new case of this association.

In February 2005, a 43 year-old man was admitted to our Unit with fever, symmetric arthritis of the hands and a recent history of skin erythematous-violaceous plaques and vesicular-bullous lesions in hands and feet. His past medical history revealed chronic rhinitis, recent onset of asthma, Raynaud's phenomenon and peripheral eosinophilia (22.1%, 1863 cells/mmc). A few weeks before admission, the patient received high dose prednisone for a symptomatic pericarditis. There was no history of other drugs assumption.

On admission, some violaceous skin papules in the second interdigital space of the left hand were still evident (Fig. 1A) along with rhinolalia, small joints synovitis of the hands and asymmetrical distal hypoanesthesia involving the right foot and the left hand. Electrophysiological tests demonstrated a mononeuritis multiplex. CT scan revealed hypertrophic polyposis of medium sinus. Chest radiography and heart sonography were normal. Apart from peripheral leukocytosis (13,200 cells/ml) with true eosinophilia (absolute number 4,356 cells/ml), abnormal C reactive protein (1.50 mg/dl) and positive rheumatoid factor, other laboratory tests including ESR, total serum IgE, cryoglobulins, ANA, ANCA, test for Borreliae, Chlamydiae and common parasites, were all negative. A punch biopsy of the skin lesion revealed moderate achantosis and hyperkeratosis of epidermis with heavily infiltration by eosinophils with "flame figures" in the perivascular and interstitial derma and subcutaneous tissue, highly suggestive for Wells' syndrome (Fig. 1B). According with ACR criteria (5) a diagnosis of CSS was made and high dose prednisone (1 mg/kg/day) was started. Systemic features quickly recovered, eosinophilia rapidly normalized and skin lesions healed completely in two weeks. At the follow-up, steroid dosage was gradually reduced and, 12 months later, the patient still feels good assuming low-dose steroids.

Wells' syndrome or eosinophilic cellulities, is a rare inflammatory dermatitis characterized by indurated erythematous plaques, whose most typical findings, although not pathognomonic, are tissue eosinophilia, aggregates of histiocytes and giant cells surrounding collagen bundles coated with eosinophilic granules, the so-called "flame figures". Interestingly, vasculitis aspects are not observed. Peripheral eosinophilia occurs in approximately 50% of the cases (2, 6, 7). Skin involvement is not rare in CSS, occurring in about 40-70% of cases but bullous lesions are very uncommon and 'flame figures' have never been observed (8). Conversely these aspects are common findings in WS.

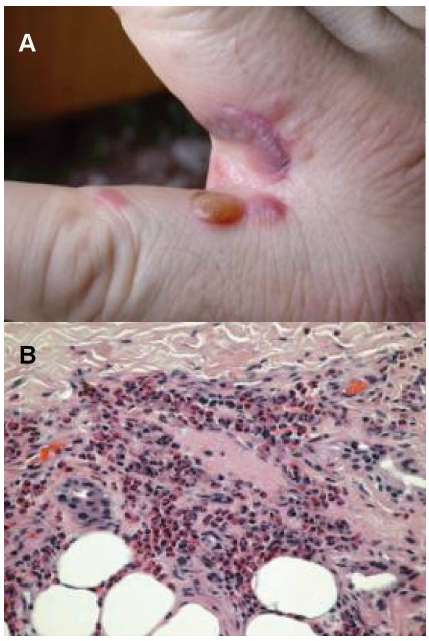

Fig. 1. A: Vesicoulo-bullous lesion and violaceus erythematous skin plaque in the 2nd interdigital space of the hand.
B: Skin biopsy : eosinophilic infiltrations of deep derma and subcutis with characteristic "flame figure".

Although the association between these two disease may be coincidental, it can also be hypothesized that a common pathogenetic background exists since these two conditions share common features (i.e. peripheral eosinophilia and widespread eosinophilic tissue infiltrates). These findings represent a clinical challenge in differentiating these conditions from Hyper-eosinophilic Syndrome (HES) (9). Although this condition has not formally ruled out in our patient, because he refused bone marrow biopsy, the clinical picture and course argued against this hypothesis.

Pathogenesis of both CSS (recently reviewed by Hellmich *et al*. (10) and WS remains obscure. The latter has been considered a non-specific hypersensitivity reaction and may be associated with HES, many exogenous and endogenous triggers and myeloproliferative disorders (6).

Since 'flame figures' have never been described in CSS, it can be assumed that its formation could be ascribed to an additional, unknown, factor acting on the abnormal hyper-reactive eosinophilic background of CSS. It is worth noting that so far, CSS has always antedated the occurrence of WS suggesting that CSS should be included in the group of systemic diseases which, in presence of a further co-stimulating factor, may induce WS.

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XIII International Vasculitis and ANCA Workshop

Cancun, Mexico, 26-29 April 2007

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Foreword

This year's Clinical and Experimental Rheumatology Vasculitis supplement sees the light in coincidence with the 13th International Vasculitis and ANCA Workshop, held in Cancun, Mexico, from April 26th to 29th, 2007. It hosts seven mini-reviews, two of them divided in several sections. These manuscripts, written by the top experts, summarise recent issues on the current state, not only of the ANCA -associated vasculitis (AASV), but also on three other primary systemic vasculitides (PSV). The review section begins with Dr. Savage´s excellent manuscript on the interactions of endothelium and white blood cells, which will certainly represent a key aspect to the overall understanding of the pathogenesis of vasculitis. Lamprecht *et al*. focus on the process of granuloma formation in Wegener's granulomatosis (WG). Unveiling those complex mechanisms will allow halting the autoimmune response that gives rise to the fearful granulomas of WG, which sometimes seem more relapsing and difficult to treat than the vasculitic lesions, as judged from many of the abstracts presented in the Workshop. The need for diagnostic criteria has clear-cut implications as described by Luqmani. The conjunction of histolopathologic, clinical, serological, imagenologic and genomics and proteomics research elements would lead to more proper classifications, while we await on disclosing the causes of these diseases. Drs. Dasgupta, Dillon and Yeung pinpoint which areas are critical in the respective conditions they have written on: giant cell arteritis, Schönlein-Henoch purpura and Kawasaki disease, and how to translate the observations from laboratory to clinical settings. Finally, the last mini-review sums up the results and future directions in treatment, and the golden opportunity the clinical observations provide to open new paths in research, such as those fueled from what has come out from B-cells targeted therapies.

The Cancun Workshop received an unprecedented amount of collaboration. They range from interesting studies in genomics, with key works on the complementary peptide autoantibody generation hypothesis, to advances in the knowledge of target antigens expression, the interplay of regulatory elements and their clinical correlations. Many groups work on B and T, dendritic and endothelial cells, and their products. Interesting observations were received, for example, on the potential role of complement in AASV or the expression of chemokine receptors. These advances will lead to developing newer therapies or better indications for the existing ones, which can be tested in experimental models, many of which are exploring external agent influences or genetic regulation of key actors in the pathogenesis. The characterisation of clinical subgroups and identification of prognostic markers needs to be brought under the scope of the increasing data from populations other than Caucasian, either in Europe or USA. In this Workshop, we have seen the contrasting epidemiology of AASV in the UK and Japan, or the peculiar behaviour of WG and microscopic polyangiitis in the same region (Latin America) as observed from the reports of Peru and Mexico.

It is worthwhile to mention that the 2007 Workshop provided the chance for other countries' interested colleagues in the field to attend, being more international than ever, and featured four additional working sittings: a precongress course, the EUVAS/VCRC meeting, a seminar on diagnostic serological issues coordinated by Allan Wiik, and a GCA/PMR group session, led by Bhaskar Dasgupta and Eric Matteson. Cancun's natural charm also imprinted to the conference its own, different seal.

We thank the meeting's sponsors and their executives: Bio-Rad Laboratories, Euroimmun AG, Euro Nippon Kayaku GmbH/Nippon Kayaku Co. Ltd., Abbott Laboratories de México, Biosimex/Biosystems, the Vasculitis Foundation, Genzyme Corp., AESKU-Kipp Institute, AMGEN Latin America, Eurodiagnostica and INOVA Diagnostics Inc.

Also, to those collaborating with the meeting project, especially to Clinical and Experimental Rheumatology (Prof. Stefano Bombardieri, Luisa Marconcini and Wendy Doherty),Vision Entertainment (Roberto González and Liliana Alvarado) and the American College of Physicians, Chapter Mexico (Dr. José Halabe Cherem – Governor).

We express our acknowledgement to the Instituto Nacional de Ciencias Médicas y Nutrición, Mexico, from the vision of the late Dr. Donato Alarcón-Segovia, to the invaluable support of its present General Director, Fernando Gabilondo Navarro, and to its Department for Health Education (Dr. Mariano García Viveros and Jorge Velázquez) for providing the support needed for this enterprise, foreseeing its expansion to other areas of the globe.

Our gratitude to the reviewers and members of the Advisory and Scientific Committee. Dr. Flores-Suárez especially thanks Dr. Graciela Ibáñez-Landín for her constant and key work.

We hope you find this Vasculitis 2007 issue an enjoyable learning experience as much as we did in putting it together.

Finally, many of the accomplishments in such a complex field as the vasculitides cannot be understood without the scientific contributions of the late Prof. Dr. Fokko J. van der Woude. His leadership and objective criticism will certainly be missed by all those who met him in the areas in which he enthusiastically participated, from patients to fellow colleagues.

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