

EMERGENCE OF SEVERE SPONDYLOARTHROPATHY RELATED ENTHESEAL PATHOLOGY FOLLOWING SUCCESSFUL VEDOLIZUMAB THERAPY FOR INFLAMMATORY BOWEL DISEASE

S. Dubash*^{1,2}, T. Marianayagam⁴, I. Tinazzi⁵, T. Al-Araimi⁶, C. Pagnoux⁶, A. V. Weizman⁷, P. Richette⁸, M.-L. Tran Minh⁹, M. Allez⁹, A. Singh¹⁰, F. Ciccia¹¹, J Hamlin³, A. L. Tan^{1,2}, H. Marzo-Ortega^{1,2}, D. McGonagle^{1,2}.

¹Department of Rheumatology, NIHR Leeds Biomedical Research Centre, Leeds Teaching Hospitals NHS Trust, ²Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, United Kingdom, ³Department of Gastroenterology, Leeds Teaching Hospitals NHS Trust, ⁴East and North Hertfordshire NHS Trust, Stevenage, United Kingdom, ⁵Rheumatology Unit, Division of General Medicine, Sacro Cuore-Don Calabria Hospital, Negrar, Italy, ⁶Division of Rheumatology, Mount Sinai Hospital, University of Toronto, Canada, ⁷Division of Gastroenterology, Mount Sinai Hospital, Department of Medicine, University of Toronto, Canada, ⁸Department of Rheumatology, Hôpital Lariboisiere, Assistance Publique Hopitaux de Paris, University Hospital of Ile-de-France, Paris, France, ⁹APHP, Hôpital Saint Louis, Department of Gastroenterology, Paris Diderot, Sorbonne Paris-Cité University, Paris, France, ¹⁰Department of Rheumatology, Royal Free Hospital, London, United Kingdom, ¹¹University of Palermo, Piazza delle Cliniche 2, 90127 Palermo, Italy.

Introduction/ Aim: Vedolizumab (VDZ) therapy for inflammatory bowel disease (IBD) has been associated with mild spondyloarthritis (SpA) related features including sacroiliitis and synovitis. Following presentation of an index case, we collaborated with other centres to determine if severe SpA had occurred after IBD therapy with VDZ. Herein, we report a series of cases demonstrating the emergence of severe SpA associated enthesitis/osteitis following successful IBD treatment with VDZ.

Materials and Methods: We evaluated 11 VDZ treated patients with IBD across 7 centres that developed severe SpA and/or enthesopathy with the aim of characterising the VDZ associated SpA or enthesal flares. Imaging features demonstrating particularly severe disease were recorded.

Results: De novo SpA developed in 9 of 11 patients in total and flare of established SpA in 2 patients. Four patients required hospitalisation due to disease severity. Available data showed that 1/7 were HLA-B27 positive. The median time from VDZ initiation to flare was 12 weeks with IBD activity ameliorated in 7/10 (no data 1 case) at flare. Severe SpA enthesitis/osteitis was evident on magnetic resonance imaging (MRI) or ultrasound (figure 1) including acute sacroiliitis (n=5), extensive vertebral osteitis (n=1), peri-facetal oedema (n=1), and isolated peripheral enthesitis (n=3). Due to SpA/enthesitis severity, VDZ was discontinued in 9/11 cases and changes in therapy were initiated including alternative anti-TNF.

Discussion: As we anticipate increasing use of $\alpha 4\beta 7$ inhibition, awareness of this paradoxical reaction and specific phenotype amongst rheumatologists and gastroenterologists alike, can facilitate combined management decisions for effective treatment of IBD and SpA or enthesitis. These cases also tell us about the disease process and why in the face of quiescent gut disease do patients develop a severe SpA/ enthesitis? We believe that $\alpha 4\beta 7$

bound to adhesion molecules MADCAM-1/ VCAM-1 for T-cell transportation into mucosal or vascular tissue, is not dependent for enthesal or joint tissue and therefore would not hinder adaptive T-cell responses at these locations. This proposed model of pathogenesis offers an explanation for these severe SpA/enthesitis flares.

Conclusion: Severe SpA, predominantly HLA-B27 negative, with osteitis/enthesitis, may occur under successful VDZ treatment for IBD.