



Letter to editor: New onset/recurrence of inflammatory arthralgia/spondyloarthritis in patients treated with vedolizumab for intestinal bowel disease

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Vedolizumab (VDZ) is a gut-selective antibody to $\alpha 4\beta 7$ integrin for the treatment of inflammatory bowel disease (IBD). The role of VDZ in rheumatological manifestations is still not clear and conflicting data are reported in literature. New onset or exacerbation of arthritis and sacroiliitis in patients treated with VDZ has recently been reported in small case series [1, 2]. Furthermore, inflammatory arthralgia/arthritis was observed in 34 out of 247 patients (13.8%) receiving VDZ [3], yet the increased risk of developing arthralgia was reported as not significant in another study [4]. A selective increased risk of developing arthropathy has been reported in Crohn's disease (CD) but not in ulcerative colitis (UC) comparing anti-TNF with VDZ treated patients [5]. By contrast, other studies involving small cohorts [6] not only did not report new induction or flare of arthritis and/or sacroiliitis but noted improvement in patients with active spondyloarthritis (SpA) after VDZ. In addition, no increase of arthralgia was reported in patients exposed to VDZ compared to placebo in six clinical trials [7]. However, evaluating the issue of safety in a "real world experience" setting, Kopylov et al. [8] reported that 30% of adverse events were attributed to arthralgia that was the reason of treatment discontinuation in one third of cases. In addition, axial SpA has been reported during VDZ treatment in

patients without active SpA at baseline and no history of articular manifestations [9].

We report our observation of 7 patients with IBD who developed inflammatory arthralgia after treatment with VDZ (Table 1).

Four out of 7 patients were women; 6 patients had been diagnosed as CD, 1 as UC. The mean duration of IBD was of 14 years. The mean age was 49.8 years (range 24–63). None of the patients had previous diagnosis of arthritis/spondyloarthritis. One patient who was previously treated with infliximab and mesalazine presented a transient arthritis with spontaneous remission, 9 years before VDZ. Six out of 7 patients had previously been treated with biologic therapy, VDZ was the 2nd- and the 3rd-line therapy in 2 and in 4 patients respectively. Six patients fulfilled the ASAS criteria for spondyloarthritis [10]. The mean number of VDZ infusions received before the onset of symptoms was 3 (range 1–6) and the mean time of exposure to VDZ was 11 weeks (range 1–32). Five patients had high levels of CRP: mean 15.6 mg/L (range 0.6–42.2). Three patients with back pain performed a MRI that showed sacroiliitis. In 2 cases, HLA-B27 was investigated with negative result. Four patients discontinued VDZ, 3 restarted the previous biologic therapy with Adalimumab and 1 started Infliximab.

In our opinion, the short term after starting VDZ and onset of rheumatic manifestations could suggest a possible role of VDZ in unmasking latent spondyloarthritis. On the other hand, all our patients but one were previously treated with anti-TNF agents and arthritis or SpA might have been quiescent at baseline. Further studies are needed to investigate the role of VDZ in rheumatic diseases.

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Table 1 Demographic and clinical features of the seven cases developing arthritis during VDZ treatment. *F* female, *M* male, *SSZ* sulfasalazine, *MRI* magnetic resonance imaging, *US* ultrasound, *SI* sacroiliac, *BME* bone marrow edema

	Gender	Age	IBD	Concomitant therapy	ASAS criteria	Rheumatic features	Radiological findings
1	F	47	CD	None	Yes	Back pain, foot arthritis, family history of psoriasis	MRI: BME of the right SI joint, enthesopathy of great trochanter US left foot: II MTP joint synovitis, flexor digitorum longus and tibialis posterior tenosynovitis
2	F	50	CD	None	No	Shoulder pain	US: bursitis subacromial-subdeltoid
3	M	55	CD	None	Yes	Back pain, family history of psoriasis	MRI: active bilateral sacroiliitis and erosions, enthesopathy of great trochanter, trochanteric bursitis
4	F	63	CD	SSZ	Yes	Polyarthritis, psoriasis	MRI: enthesopathy of great trochanter
5	M	24	RCU	Mesalazine	Yes	Knee arthritis, family history of psoriasis	MRI: none
6	M	51	CD	Mesalazine	Yes	Back pain and wrist arthritis	MRI: BME of the SI joints and erosions US: right wrist synovitis
7	F	59	CD	SSZ	Yes	Knee enthesitis and arthritis, family history of psoriasis	MRI: left knee effusion US: enthesopathy of the biceps femoris

Compliance with ethical standards

Disclosures None.

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