Is Ustekinumab the best treatment option in patients with Crohn's disease and coexistent multiple sclerosis?

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To the Editor,

Crohn's Disease (CD) and Multiple Sclerosis (MS) are chronic diseases associated with an aberrant immune response upon an environmental trigger in genetically susceptible hosts. We present the case of a young patient with known MS diagnosed with new onset CD. Due to his young age, extended disease (Montreal A2L1,4B1) and smoking habits he was considered candidate for immunosuppression therapy but developed acute pancreatitis 2 weeks after azathioprine administration. Subsequently, ustekinumab was initiated. The patient showed clinical and biochemical response within the first 2 months of therapy and achieved mucosal healing (Simple Endoscopic Score for Crohn's Disease of 0 compared to 6 at baseline) at 12 months of therapy. No clinical episodes of MS or new lesions on MRI have developed 17 months after treatment commencement.

CD and MS patients have a 50% increased risk of being diagnosed with MS and CD respectively (1). Even though CD treatment armamentarium has largely expanded, options for patients with coexistent MS remain limited. Anti-TNF agents, the backbone of IBD treatment, are contraindicated in patients with demyelinating lesions. Vedolizumab has been shown to be effective in CD though there are no safety data in patients with coexistent MS and the risk of progressive multifocal leukoencephalopathy has yet to be abolished by long term studies. Ustekinumab has shown efficacy in CD while when studied in a phase II study in MS exhibited neither a benefit nor disease progression (2). Ustekinumab has also been used successfully in patients with coexistent psoriasis and MS (3).

IL-12 induces T-cell transformation into autoreactive Th-1 cells and facilitates their migration in CNS while IL-23 interferes in pathogenic Th-17 cells generation and activation. Both cell groups react with CNS antigens causing experimental autoimmune encephalomyelitis (EAE) in MS animal models (4).

Nonetheless, one case with demyelination in a CD patient treated with ustekinumab and previous exposure to anti-TNF agents has been reported (5). Albeit paradoxical for an IL-12/IL-23 inhibitor to induce demyelination, authors advised caution with ustekinumab use in IBD patients. We believe that data from animal studies showing EAE amelioration after IL-12/IL-23 inhibition as well as phase II study and psoriasis case series offer some evidence of safety of ustekinumab in MS patients. Ustekinumab may be carefully suggested in patients with coexistent CD and MS both in terms of efficacy and safety.

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Submission date : 21/12/2018
Acceptance date : 22/01/2019