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Anti-TNF Treatment for Extraintestinal Manifestations of Inflammatory Bowel Disease in the Swiss IBD Cohort Study

For ReachMD, this is Audio Abstracts. I'm Dr. Kunjal Gandhi, gastroenterologist at the Nemours Al Dupont Hospital for Children and a member of Crohn's & Colitis Foundation's Rising Educators, Academics, and Clinicians Helping IBD group, or REACH-IBD.

Extra-intestinal manifestations, or EIMs, in inflammatory bowel disease are very common, with reported prevalence rates as high as 47%.

Most frequently we see involvement of the joints, skin, eyes and hepatobiliary tree. Specifically, this includes peripheral arthritis, axial arthropathy, erythema nodosum, pyoderma gangrenosum, uveitis, and primary sclerosing cholangitis. Some of these parallel intestinal disease activity but not all of them.

Although little is known about the underlying pathogenesis of EIMs, it's believed that the mechanism involves a similar TNF-dependent pathway as seen in the intestines of IBD patients. We hypothesize this because of clustering patterns of EIMs and also because of the clinical responses of EIMs to anti-TNF α therapy.

However, there are only a few small studies that support evidence for the efficacy of anti-TNF agents in EIM and these studies vary widely in their design and measurement outcomes. Therefore the authors of one study by Vavricka and colleagues from Switzerland aimed to investigate the role of three different anti-TNF agents on the evolution of various EIMs.

The authors analyzed data from the Swiss IBD Cohort Study which is a comprehensive nation-wide cohort from all regions of Switzerland enrolling IBD patients since 2006. The evolution of EIM under anti-TNF treatment was judged by the relevant specialists taking into account patient history, clinical findings and laboratory parameters. Evolution was classified into 3 categories: clinical improvement, stable disease, and clinical worsening.

The cohort included a total of 1249 patients between January 2006 and March 2010. 366 or 29.3% patients suffered from at least 1 EIM at some point in their lifetime. Of these 366 patients, 213, or 58.2%, were treated with at least one anti-TNF agent and analyzed further in this study. The profile of the treated patients is that 36.2% were men, 18.8% had Ulcerative Colitis, 77.5% had Crohn's Disease, and 2.8% had IBD unclassified. Mean age at IBD diagnosis was 25.2 years and median age at enrollment into the cohort was 39.2 years.

The most common EIMs were peripheral arthritis in 75.6%, aphthous stomatitis in 23.5% and axial arthropathy in 21.6%. A little over half the patients suffered from 1 EIM, about one third suffered from 2 EIMs, and the rest had 3 or more. Duration from IBD diagnosis to EIM ranged from -17.7 to 34.2 years with a median of 4.4 years. 69% of patients were treated with only 1 anti-TNF. Infliximab was most commonly used, in 63.2% of patients, followed by adalimumab in 22.4% and then certolizumab in 14.4%.

In approximately half the patients, anti-TNF therapy was initiated for intestinal activity, whereas in 43.2% it was initiated for EIM treatment. With pyoderma gangrenosum and axial arthropathy, the anti-TNF therapy was more commonly initiated for the treatment of the EIM. By contrast, for erythema nodosum and stomatitis, the anti-therapy was rarely initiated for the treatment of EIM. No anti-TNF therapy was initiated for primary sclerosing cholangitis.

In 11 patients, a total of 14 different EIMs developed under anti-TNF treatment. These included peripheral arthritis, axial arthropathy, stomatitis, psoriasis and uveitis. 11 of the 14 EIMs were observed under infliximab, 2 under adalimumab, and 1 under certolizumab. Most of these EIMs improved with continuation of the anti-TNF agent and may have been side effects of the drug rather than true new EIMs.

Overall, there was good response to EIMs under anti-TNF therapy. 71.8% of patients had clinical improvement of the underlying EIM, 26.4% had no response, and only 1.8% had worsening. Looking closely at the specific drugs, the rate of improvement was best for

infliximab at 74%, followed by adalimumab at 70% and then certolizumab at 56%. The EIMs that responded the best were psoriasis, erythema nodosum, stomatitis, peripheral arthritis and uveitis - all with response rate >72%. The response rate for primary sclerosing cholangitis and axial arthropathy were modest at approximately 62%. The response rate for pyoderma gangrenosum was lowest at 50%. Prior reports have not shown anti-TNF therapy to be beneficial in primary sclerosing cholangitis, so it's surprising to see an effect here. It would be of interest to review this study's criteria for determining improvement.

Although a significant number of patients were on concomitant therapy with steroids and immunomodulators, there was no difference in response rates comparing patients on anti-TNF therapy alone vs. those on concomitant immunosuppressive therapy. This would suggest the effect is mainly due to anti-TNF therapy.

This study is one of the largest analyses of EIM management but is limited in its retrospective design. Nonetheless, the findings verify that anti-TNF agents are a valuable treatment option – especially for psoriasis, erythema nodosum, stomatitis, peripheral arthritis and uveitis. To clearly establish their role, a randomized controlled trial is needed.

This has been a presentation of AudioAbstracts. For more information, and for reference links to this article in the *Inflammatory Bowel Diseases Journal*, visit [ReachMD.com\[JM1\]](https://ReachMD.com/JM1).

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