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Case Report

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A CASE REPORT OF INFLAMMATORY BOWEL DISEASE ASSOCIATED SERONEGATIVE SPONDYLOARTHROPATHY AND ITS OUTCOME WITH AN ALTERNATIVE THERAPY

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ABSTRACT

Inflammatory bowel disease (IBD) is an inflammatory disorder of the gastrointestinal (GI) tract that is both chronic and relapsing; it encompasses both Crohn's disease (CD) and ulcerative colitis (UC). In addition to affecting the GI tract, IBD has several extra-intestinal manifestations (EIM), including arthritis, ocular involvement, dermatologic manifestations, pulmonary manifestations, biliary tree complications, anemia, and thromboembolism. Arthritis is the most common extraintestinal manifestation of inflammatory bowel disease (IBD) and can have a significant impact on morbidity and quality of life. IBDassociated arthropathy is considered a subtype of seronegative spondyloarthropathy, with axial, peripheral, or a combination of both joint manifestations. While there have been advances in identifying predisposing genetic factors and in elucidating pathophysiology of inflammatory bowel disease, the mechanisms surrounding the development of arthritis in IBD remain unclear. Treatment of inflammatory bowel disease is not always sufficient for control of arthritis. While treatment with biologic agents is promising, there remains a great need for larger, randomized studies to address optimal therapy of IBD associated arthropathy.

KEYWORD: IBDassociated arthropathy, seronegative spondyloarthropathy.

INTRODUCTION

Inflammatory bowel disease (IBD) is an inflammatory disorder of the gastrointestinal (GI) tract that is both chronic and relapsing; it encompasses both Crohn's disease (CD) and ulcerative colitis (UC). In addition to affecting the GI tract, IBD has several extra-intestinal manifestations (EIM), including arthritis, ocular involvement, dermatologic manifestations, pulmonary manifestations, biliary tree complications, anemia, and thromboembolism.[1,2]

Arthropathy associated with IBD can involve both peripheral and axial joints. IBD associated arthropathy is considered a type of seronegative spondyloarthropathy (SpA). Spondyloarthropathies (which also include Ankylosing Spondylitis (AS), Psoriatic Arthritis, Reactive Arthritis, and Undifferentiated SpA), are characterized by axial and peripheral joint disease with inflammatory features and classically a negative rheumatoid factor.[3]

Orchard et al.[4] defined two categories of IBD patients with peripheral arthritis. Type 1 is a pauci/oligo-articular arthritis with swelling and pain of five or fewer joints, particularly affecting large joints in the lower extremities. Type 1 arthritis tends to be acute and self-limiting, and correlates with IBD activity. Joint symptoms can occur prior to the diagnosis of IBD. Type 2 peripheral arthritis has a more polyarticular (affecting greater than five joints), symmetrical distribution, affecting upper limbs predominantly (MCPs commonly affected). Type 2 peripheral arthritis may be chronic and is less likely to parallel the IBD activity. In both types, peripheral arthritis tends to be non-deforming and nonerosive. The possibility of an alternative diagnosis, such as Rheumatoid Arthritis or PsA should be considered in IBD patients who develop erosive arthritis.

CASE REPORT

This is a case report of 40 yrs old female suffering from Seronegative spondyloarthropathy.

Patient came to Dr. Appa Rao's clinic on Jan 2014 with complaints of joint swelling in elbow, knees and severe backache and swelling all over the body since 2 years i.e. from 2012.

Patient had complaint of pain abdomen with nausea, vomiting and loose motions since 3-4 years for which she was investigated and was diagnosed with intestinal tuberculosis(TB) and chrons disease in 2010. She was then started with category III ATT for 9 months in June

2010. Meanwhile she was also started with Pentasa (Mesalamine/5-aminosalicylic) 3g/day for treatment of inflammatory bowel disease. She was still continuing Pentasa for her IBD but with partial relief. She still complained loose motions and pain abdomen. Then she was started with Azoran 50mg (Azathioprine) in Dec 2010.

Her ATT stopped in July 2011. But at this point of illness she developed back pain which gradually progressed to joint swellings all over the body. Thus diagnosed with seronegative arthropathy in March 2012. She continued with pentasa and azoran 50mg but with no relief in IBD and joint pains. Then in Jan 2013 her pentasa was stopped and azoran 50 mg OD was continued. Then in Dec 2013 Azoran was increased to 100 mg OD.

At this point of her disease with not much relief inspite of 3 ½ years of treatment, exhausted with this long course and cost of the treatment, she came to know about Dr. Appa Rao's immunotherapy. Thus she visited Hyderabad and started his immunotherapy on 6 Jan 2014.

Injection Human normal immunoglobulin (12 mg) and histamine dihydrochloride (0.15 mcg). Two vials once in three days (3 doses) followed by two vials once in a week until 8 weeks. Aceclofenac 100mg twice a day for one month. Prednisolone tapered and maintained 5 mg per day. Ranitidine 150mg once a day in the morning. Tomato, Banana fruit, Prawns and milk were restricted in nutrition.

After two months of Dr. Appa Rao,s immunotherapy patient condition has improved and his there is a definite decrease in all her complaints. This is definitely a positive sign for the patient to be motivated. She is supposed to be on maintenance therapy as she is vulnerable to relapse for any immunological insults.

After 2 months, her Azoran dose was reduced from 100mg to 50 mg and then in Aug 2014 her Azoran was stopped completely. She responded so well that she is still continuing this treatment and this is evident from her ESR reports which shows remarkable drop in levels in just 8 months after starting treatment which is still maintained.

This shows her chronic inflammatory response is under check with this immunotherapy thus releaving her SNA complaints and helping her to lead a pain free life.

DISSCUSSION

Nearly 4 million individuals worldwide are affected with inflammatory bowel disease and approximately 1.4 million of these cases occur in the United States.[5] Two major theories to explain development of arthritis in the setting of IBD involve gut bacteria and migration of gut lymphocytes to the joint, but neither have been fully developed.[6] In the first, the HLA-B27/human β2 microglobulin transgenic rat model of SpA like disease, a germ free environment prevents the development of gut and joint disease, suggesting bacterial exposure is necessary for the development of SpA in the proper genetic background.[7]. This model does not explain the co-localization of inflammation to the synovium and gut or identify the specific bacterial antigens which may incite inflammation. In the second theory, lymphocyte trafficking to various tissues is dependent on various adhesion molecules and receptors.

Lymphocytes from the gut may migrate to the synovium, leading to inflammatory arthritis. Identical T cell clones have been indentified in synovium and gut mucosa from a patient with SpA.[8] In addition to lymphocytes, macrophages expressing the scavenger receptor CD163 have been found in gut mucosa from patients with CD and SpA[9] as well as in synovium.[10] It is possible that these cells could also migrate from the gut to the joint, as in vitro they can bind to synovial tissue vessels.[11] While these models exhibit the importance of lymphocyte and macrophage trafficking and explain how effector cells can co-localize to the gut and synovium, the inciting antigen or immune trigger remains unclear.

HLA-B27, as discussed above, may contribute to pathogenesis of arthritis in IBD, through presentation of arthritogenic peptides to T cells; alternatively, this genotype may predispose to protein misfolding leading to inflammation.[12] However HLAB27 appears to explain only a small portion of genetic susceptibility to arthritis in IBD. While the prevalence of HLA-B27 in idiopathic AS is greater than 90%[13] there is no overall increased frequency of HLA-B27 in IBD patients overall.

No laboratory test can make the diagnosis of IBD associated arthritis, or be used in isolation to determine disease activity. Diagnosis is largely clinical, based on the presence of peripheral or axial arthritis in the setting of IBD.

Polyarticular (as opposed to oligoarticular) and axial arthritis are more independent of IBD activity, and may require separate treatment from the underlying IBD. Conventional IBD therapies such as antibiotics or 5-ASA compounds are not effective for this type of arthritis as their activity occurs only within the gut. Treatment options for peripheral arthritis include NSAIDs, steroid injections and analgesics. NSAIDs may potentially exacerbate IBD. However COX-2 inhibitors such as Celecoxib, have not been shown to increase endoscopic relapse compared to placebo[14], and may be a therapeutic option, but this has not been studied in treatment of arthropathy in IBD. DMARDs may be considered for patients who are refractory to conservative measures. Sulfasalazine (SSZ) may be effective in treating peripheral arthritis and has activity for UC bowel

inflammation in UC, although it is not particularly effective for axial disease.[15]

For axial manifestations, older literature recommends that NSAIDs may be the first line therapy, though given the concern of NSAIDs in IBD, this recommendation must be taken cautiously. Physical therapy and exercise are important in preventing deformities and preserving range of motion.[16-18]

Glucocorticoids are often effective, but most patients, with taper, have recurrence of their joint pains and stiffness. Azathioprine (AZA) and 6-Mercaptopurine (6-MP) seldom induce remission of joint symptoms, especially if there is axial skeleton involvement.

Finally it is important to note that bone mineral density is decreased in patients with IBD due to use of steroids, inflammation, malabsorption, and nutritional factors. Osteoporosis is highly prevalent and bone density testing and osteoporosis treatments seem to be underutilized.[19]

CONCLUSION

The connection between gut and joint inflammation, and predisposing genetic factors, remain unclear. There are no laboratory tests which confirm the diagnosis. Oligoarticular arthritis may respond to treatment of IBD, but other forms of IBD associated arthritis may be less likely to respond to treatment of IBD. In general, there are few studies of treatment in IBD associated arthropathy and there is a need for larger and randomized controlled studies. This immunotherapy has promising results and hence can be used for treating such cases. Further large scale clinical trials are needed to confirm the efficacy of this immunotherapy in treating such cases.

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