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Case report

Multiple sclerosis and HLA-B27 negative sacroiliitis in a Crohn's disease patient

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SUMMARY

A relationship between inflammatory bowel disease and MS is supported by a higher than expected coexistence of these diseases among families and individuals.

A 32 year-old male with Crohn's disease of the terminal ileum diagnosed 4 years earlier and HLA-B27 bilateral sacroiliitis diagnosed two years earlier, was admitted to our hospital because of an acute episode of blurred vision. In addition the patient complained of urine incontinence. Before this admission the patient had been elsewhere administered three doses of Remicade and 16mg of methylprednisolone p.os. During admission the diagnosis of multiple sclerosis was made (MRI and IgG Index) and Remicade was discontinued.

The patient was started on therapy with interferon-beta for MS, oxybutynin hydrochloride (10mg/day) for urine incontinence, prednizolone (10mg/day), methotrexate (10mg/week) and azathioprine (100mg/day) for Crohn's disease and is now in excellent clinical status.

To the best of our knowledge this is one of the very rare cases of Crohn's disease with HLA-B27 negative sacroiliitis preceding multiple sclerosis diagnosis.

Key words: Crohn's disease, inflammatory bowel disease, ulcerative colitis, multiple sclerosis, Remicade

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INTRODUCTION

A relationship between inflammatory bowel disease and multiple sclerosis (MS) is supported by a higher than expected coexistence of these diseases among families and among individuals.[1] Furthermore, a possible relationship especially between Cronh's disease (CD) and MS has been widely documented, both in sporadic and in family cases[2].

Extraintestinal manifestations of Crohn's disease include muskuloskeletal abnormalities including ankylosing spondylitis and other kinds of various arthropathies regardless the HLA-B27 status of the patient[3].

Herein we report a Crohn's disease patient with HLA-B27 negative sacroiliitis who was diagnosed with multiple sclerosis (MS) four years after initial inflammatory bowel disease (IBD) diagnosis.

CASE REPORT

A 32 year-old Caucasian male of Northwest origin with Crohn's disease of the terminal ileum, diagnosed four years earlier and HLA-B27 negative bilateral sacroiliitis, diagnosed two years earlier, was admitted to our hospital because of an acute episode of blurred vision. In addition the patient complained of urine incontinence during the ten days.

Before this admission the patient had been elsewhere administered three doses of Remicade and 16mg of methylprednisolone p.os. The last dose of Remicade had been administered approximately four weeks prior to this admission. No neurological symptom or finding was recorded during Remicade administration. At the time of admission Crohn's disease activity index (CDAI) was 184 while peripheral blood and routine biochemical analysis did not show anything remarkable. Additionally,

routine radiological examinations, including abdominal ultrasonography, were within normal limits.

The patient is personal history included tonsillectomy twenty-two years previously, and a post-infectious arthritis twelve years previously. The patient had no evidence of any other extraintestinal manifestation related to Crohn's disease. Family history had been unremarkable and the patient had no brothers or sisters. The patient was a smoker (10 cigarettes/day) for the last decade and denied any alcohol intake.

Physical examination showed low back sensitivity and mild hypokinesia of both lower extremities. During admission the diagnosis of multiple sclerosis was made (based on brain magnetic resonance imaging and IgG Index) and Remicade was immediately discontinued.

The patient was started on therapy with interferon-beta for MS, oxybutynin hydrochloride (10mg/day) for urine incontinence, prednizolone (10mg/day), and azathioprine (100mg/day) for Crohn's disease. In addition, methotrexate (10mg/week) was added in order to control sacroiliitis symptoms. The patient is on follow-up, in excellent clinical status, and is on steroid tapering.

DISCUSSION

In cases of multiple sclerosis (MS) preceding Crohn's disease (CD) it has been speculated that MS may represent the result of a strongly HLA-associated genetic predisposition, while the additional occurrence of CD may have been either due to genetic factors or simply perhaps to chance[2]. This case, among a few others, outlines again the clinical phenomenon of diagnosing Crohn's disease preceding MS diagnosis.

Albeit in the absence of precise experimental data, it is legitimate to presume that those two diseases probably share common pathogenetic traits. Viewing this case in the context of epidemiological data so far reported (Table), we suggest that the development of CD and MS could be based on one or more common genetic factors apart from NOD2 gene variants[3], which act in conjunction with other presumably exogenous factors and trigger HLA antigens to express the phenotype of one or other disease. Furthermore, the existence of HLA-B27 negative sacroiliitis suggests that a more complicated phenotype with neurologic, musculoskeletal and gastrointestinal involvement can also occasionally be diagnosed in these patients. However, extensive information including HLA profile and NOD2 status was not available for this patient. In fact there is a single case report with a more or less similar triple association of Crohn's disease, MS and Charcot-Marie -Tooth syndrome[5].

Table. Reported cases of Crohn's disease and multiple sclerosis

Author	Country	No patients
Karper	UK	1
Gil H, et al	France	1
Buccino GP, et al	Italy	1
Purrmann J, et al	Germany	1
Kitchin LI, et al	USA	1
Constantinescu CS, et al	UK	2
Kimura K, et al	USA	1
Beaugerie L, et al	France	4
Yacyshyn B, et al	Canada	8

Results from clinical trials indicate that TNF alpha neutralizing therapy should not be given to patients with cardiac failure (class III or IV) or a history of demyelinating disease[6] and this was the reason for Remicade discontinuation in this patient. However, there is no convincing evidence available so far to support a causal role of anti-TNFa administration for the MS presentation in this particular patient. Additionally, avoiding Remicade infusions in the treatment of CD in patients already diagnosed with MS could be at the moment regarded as only a general precaution as long term prospective studies are lacking in this field[7].

Although during MS diagnosis, the patient was not on azathioprine therapy, we cannot safely speculate that lack of efficient immunosuppression had inevitably led to this MS outbreak. In fact, it has been reported that several CD patients were diagnosed with MS despite long-term azathioprine administration; two patients developed the first MS episode during a quiescent phase of their inflammatory bowel disease under long-term azathioprine therapy.[8] These cases show that long-term azathioprine administration, although maintaining inflammatory bowel symptoms under control, were been able to prevent the MS onset. In this case, the patient was on relatively active phase of his bowel disease; however according to current knowledge, bowel inflammatory activity does not seem to be an independent risk factor for MS, although increased intestinal permeability has been reported in a group of MS patients[9].

To the best of our knowledge this is one of the very rare cases[1-3,8-14] of Crohn's disease with HLA-B27 negative sacroiliitis preceding multiple sclerosis diagnosis.

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