

LETTER TO THE EDITOR

Melatonin usage in ulcerative colitis: a case report

To the Editor

Melatonin is an indoleamine with a range of biological and physiological properties, including those involved in immune defense [1]. Melatonin acts on the immune system by increasing natural killer cell activity [2–4] and Th2 cell-mediated immune responses [5, 6]. Additionally, melatonin regulates gene expression of several immunomodulatory cytokines including interleukin (IL)-2 and interferon (IFN)- γ by human CD4-T cells [7]. The effect of melatonin on the immune system is also supported by the existence of specific binding sites for melatonin on lymphoid cells [8, 9].

Ulcerative colitis (UC) is a chronic inflammatory disease resulting from different pathogenic mechanisms [10, 11]; the etiology is unknown, but the disease involves an excessive immune reactivity of the gut wall [12]. UC is associated with an atypical Th2 response mediated by a distinct subset of natural killer T cells that produce IL-13 and are cytotoxic for epithelial colon cells [4]. On the other hand, there is evidence that the lesion is related to antibody-mediated hypersensitivity (IgG1 type and complement activation) because it is associated with intermittent

inflammation in the mucosal wall, where the Th2 response might have some merit as it aids antibody responses [12, 13] (Fig. 1). The present case supports that there is a relationship between melatonin and the aggravation of UC symptoms.

We report a case of a 56-year-old man diagnosed in 1990 with UC affecting the distal part of the colon and rectum. The diagnosis of UC was based on symptoms including bloody diarrhea with mucus, abdominal cramps, lumbar pain, hematochezia, fever, fatigue, and loss of appetite with consequent weight loss. On questioning, he emphasized that there is no family history of inflammatory bowel disorders, that he is not a drug user, and that he does not drink alcoholic beverages, has taken no medications, has not been exposed to hepatoxins (as far as he knows), and has not traveled. Biochemical studies showed increases in sedimentary speed, C-reactive protein, acid α 1-glycoprotein and positive antineutrophil cytoplasmic antibody. Visual colonoscopy revealed a chronic inflammatory process with distal lesions of the colon and rectum. The intestinal biopsy revealed abscess of the crypts, a lymphoplasmacytic

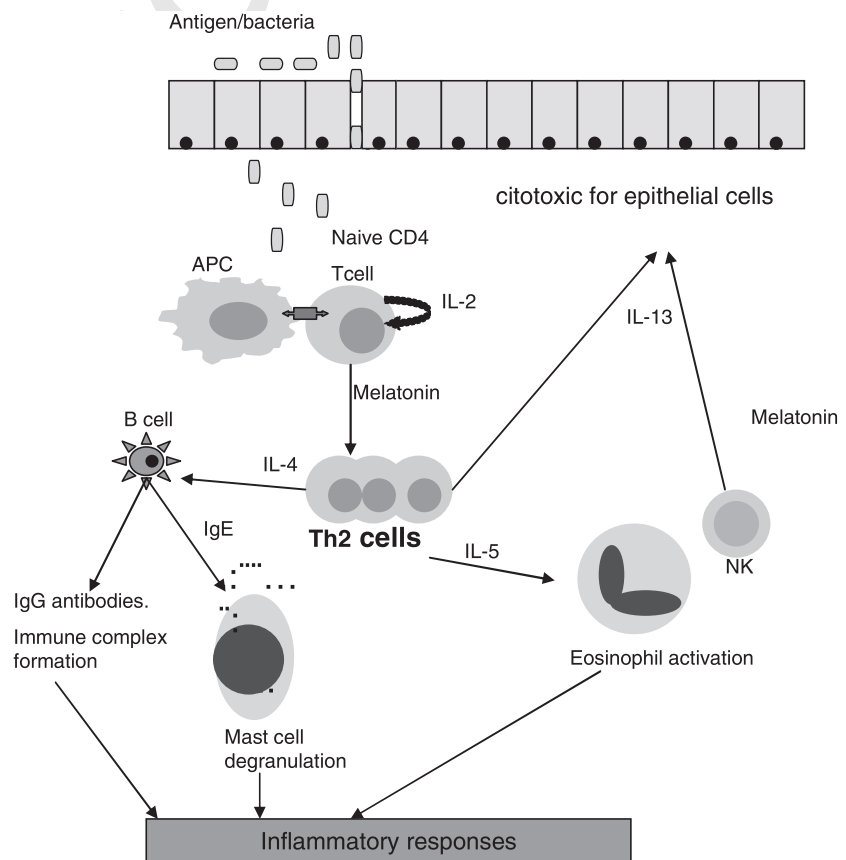


Fig. 1. Schematic model of how melatonin could act on pathogenesis of ulcerative colitis.

1 infiltration of the mucosal wall, and increased intraepithe-
2 lial lymphocytes, but without malignancy.

3 Illness control was more difficult during the first 5 yr of
4 evolution (1990–1995), the patient presented with re-acti-
5 vations of the UC associated normally with stress periods
6 and excessive work. In 1994, the patient modified his life
7 habits. Later (1995–2006), the evolution of the patient was
8 satisfactory following basic anti-inflammatory therapy
9 (corticoids and salicylazosulfapyridine) and diet (lactose-
10 free diet and increased fiber intake).

11 In September 2006, the patient decided by himself to
12 take melatonin capsules (3 mg) before going to sleep. Two
13 months later, the patient started to experience the symp-
14 toms of active UC, including bloody diarrhea with mucus.
15 He continued taking melatonin and the corticosteroids
16 began to be administered at higher dose and rectally
17 (enema). On this occasion, the disease did not remit and
18 the patient was hospitalized where gastroenterologist
19 recommended him to stop consuming melatonin; 24–
20 48 hr later there was a complete remission of the UC
21 symptoms.

22 Considering that melatonin is generally immunostimula-
23 tory, the question as to whether it should be taken by
24 individuals with an UC has been raised. Inflammatory
25 bowel disease (IBD) including Crohn's disease and UC is
26 habitually treated with salicylazosulfapyridine and corti-
27 costeroids whose curative effects promote the remission rate
28 and diminish the relapses. Curiously in both cases collected,
29 patients with UC or Crohn's disease [14] were receiving the
30 identical combination of drugs (salicylazosulfapyridine, **1**
31 corticosteroids, and melatonin). It is possible that individ-
32 ually these drugs have satisfactory effects to IBD, but this
33 unique conjunction of drugs, by mechanisms unknown,
34 could be harmful to IBD. To date, the information
35 regarding this issue is meager. In this case of UC and in
36 another report, Crohn's disease [14] was aggravated by
37 melatonin.

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