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RAPID COMMUNICATION

Depression and anxiety levels in therapy-naïve patients with inflammatory bowel disease and cancer of the colon

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Abstract

AIM: To assess whether depression and anxiety are more expressed in patients with the first episode of inflammatory bowel disease (IBD) than in individuals with newly discovered cancer of the colon (CCa).

METHODS: A total of 32 patients with IBD including 13 males and 19 females, aged 27 to 74, and 30 patients with CCa including 20 males and 10 females, aged 39-78, underwent a structured interview, which comprised Hamilton's Depression Rating Inventory, Hamilton's Anxiety Rating Inventory and Paykel's Stressful Events Rating Scale.

RESULTS: Patients of the IBD group expressed both depression and anxiety. Depressive mood, sense of guilt, psychomotor retardation and somatic anxiety were also more pronounced in IBD patients. The discriminant function analysis revealed the total depressive score was of high importance for the classification of a newly diagnosed patient into one of the groups.

CONCLUSION: Newly diagnosed patients with IBD have higher levels of depression and anxiety. Moreover, a psychiatrist in the treatment team is advisable from the beginning.

Key words: Crohn's disease; Ulcerative colitis; Colon cancer; Mood disorder

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INTRODUCTION

Patients with inflammatory bowel disease (IBD-the common term which comprises Crohn's disease and ulcerative colitis) and cancer of the colon often report serious psychological and emotional morbidities[1,2]. Though specific pathophysiological links between psychiatric disorders such as depression or anxiety and inflammatory bowel disease have largely been discredited[3,4], little is known about the influences of depression and anxiety on the ongoing adaptation that these patients make to the aversive symptoms of their chronic disease[5]. It is almost impossible to tell whether the psychiatric discomfort influences the severity of the gastrointestinal symptoms or, conversely, could gastrointestinal symptoms aggravate the psychiatric status. Stressful life events and psychological distress have been shown in patients without IBD to be associated with common bowel symptoms such as irregularity, gas and bloating, and abdominal pain, often labeled as irritable bowel syndrome or functional bowel diseases[6,7].

This study presents pilot data in which we sought to investigate the effects of common psychiatric illnesses (i.e., anxiety and depression episodes) on the appearance and functional disability in 32 first episode, therapy-naïve patients with IBD, and 30 patients with newly diagnosed cancer of the colon. We hypothesized that the presence and intensiveness of one or both current psychiatric disorders (depression and anxiety) have a higher impact on the appearance of one of the diseases of interest. Also, we attempted to estimate the eventual difference of the initial levels of the psychological suffers, and which one, if not both, of the two groups of patients requires the routine preliminary psychiatric evaluation prior to the beginning of gastroenterological treatment.

MATERIALS AND METHODS

Setting

This study is a subset of a larger investigation of 71 patients with the first episode of IBD and 40 patients with newly diagnosed cancer of the colon (CCa), out of which

32 patients with IBD (21 with ulcerative colitis [UC] and 11 with Crohn's disease [CD]), 13 (8 with UC and 5 with CD) males and 19 females (13 with UC and 6 with CD), aged 27 to 74 years (49.16 ± 16.58) and 30 patients with CCa, 20 males and 10 females, aged 39-78 years (63.47 ± 9.14) met with the recruiting criteria and were included in the study. The study was conducted at the Department of Gastrointestinal Surgery, Clinical Center of Serbia, and Department of Gastroenterohepatology, Clinical and Hospital Center "Bezhanijska Kosa". All patients of 18 years old or over attending the Gastroenterology Clinics and Gastrointestinal Surgery Department from March to October 2003 who presented symptoms common for IBD and CCa: blunt abdominal pain, rectorrhagia and diarrhea syndrome on the first visit, were eligible for the study. The participating gastroenterologist or gastrointestinal surgeon (M.K. T.R., and B.F.F.) screened the clinic appointment schedule each morning and directly communicated with the other staff gastroenterologists or surgeons on a daily basis to recruit their patients into the study. Patients were interviewed at the end of their medical appointments or at a more convenient time, no later than 2 d from their medical visits or admission to hospitals. Only patients who satisfied all the recruiting criteria were selected for the study. The results of the interviews were matched with the final diagnosis, but no matched pair procedure between groups was used. The entire testing was designed and supervised by the psychiatrist (BRF). The study was approved by the Ethical Committee of the School of Medicine, Belgrade.

Recruiting criteria

The patients included in the study met the following criteria: No previous treatment for one of the diseases of interest; a negative family history of IBD and CCa; no previous treatment for any psychiatric illness or disorder; no self-medications for any kind of gastrointestinal or psychiatric illnesses; weight loss not surpassing 5 kg in the last month and they were not under weight loss regimes; radiographs of the lungs and ultrasonographic examination (N.M. M.K. and B.F.F.) of the abdominal and pelvic cavities free of metastasis and anatomical abnormalities; no surgical intervention in past three years; no abdominal or any kind of mutilating surgical intervention; not treated for any kind of malignancy; not suffering from an immunodeficiency disease, especially human immunodeficiency virus infection or systemic lupus; a negative history of bowel inflammation caused by infectious agents in last one year; and hepatitis B (HBs) or hepatitis C negativity. The definitive diagnosis was confirmed after immediate endoscopy-guided biopsy and subsequent histopathological examination. During the interview, 39 IBD patients were found to be unsuitable while 10 patients with colorectal cancer were omitted from further investigation. The difference was caused by more pronounced sincerity in answers during the admittance and higher motivation to be part of the study among patients with CCa.

Structured interview

All the patients, after being informed in detail about the study and signing a written consent, underwent the structured psychiatric interview, which involved Hamilton's depression inventory consisting of 21 items[8] and Hamilton's anxiety inventory consisting of 14 items[9]. Results were interpreted using Hamilton's depression and anxiety rating scales. All the items were rated in 5 grades: 0, absent; 1, mild; 2, moderate; 3, severe; 4, incapacitating (some items, like insomnia, hypochondriasis, diurnal mood variations, insight into the illness and obsessive-compulsive symptomatology are only graded in three levels: 0, absent; 1, doubtful or trivial; 2, present). Usually, Hamilton depression and anxiety inventories contain items related to gastrointestinal symptoms and weight loss. This time they were omitted because the mentioned symptomatology is part of the illness. Interpretation of the total score of Hamilton's depression rating scale is: less than 8, without depression; 9-17, mild depression; 18-24, moderate depression; higher than 24, severe depression requiring hospitalization. According to the Hamilton's anxiety rating scale, persons with generalized anxiety disorder and panic disorder tended to have a total anxiety score of above 20. The 61 item-Paykel's scale for stressful events[10] was used to evaluate the possible influence of different life events in the past one-year period on the appearance of the diseases of interest. The interview was performed by three previously trained interns in psychiatry as part of their professional educations in liaison psychiatry. All the testing was conducted in Serbian language, and priory to the final diagnosis was reported to the patient. To the moment, the definitive diagnosis was available only to the relevant intern and surgery specialists (B.F.F., M.K., N.M. T.R.).

Clinical evaluation

Index of the activity for patients of the IBD group was computed according to the standard procedures for patients with newly diagnosed CD and UC. For patients with CD, a routine Crohn's disease activity index (CDAI)[11] comprising eight items was categorized as follows: (1) Number of liquid or very soft stools in one week × 2; (2) Sum of seven daily abdominal pain ratings (0: none; 1: mild; 2: moderate; 3: severe) × 5; (3) Sum of seven daily ratings of general well-being (0: well; 1: slightly below par; 2: poor; 3: very poor; 4: terrible) × 7; (3) Symptoms or findings probably related to CA (arthritis or arthralgia, iritis or uveitis, erythema nodosum, pyoderma gangrenosum, aphthous stomatitis, anal fissure, fistula or perirectal abscess, other bowel-related fistula, febrile episodes over 37.8℃ during the past week) × 20; (4) Taking Lomotil® or opiates for diarrhea (yes or no) × 30; (5) Abnormal mass (0: none; 0.4: questionable; 1: present) × 10; (6) Hematocrit (normal average: male, 47, female, 42), obtained values should be subtracted from the average. Score is multiplied with 6; (7) Body weight: 100 × [1 - actual body weight/ standard weight], where standard weight is computed from the tables using the body height and age of the patients; (8) Active phase of CD takes values between 220 and 450. Average index in our group was 289.84 ± 45.37 (221-375). For UD activity index, a modified Ulcerative Disease Scoring System[12] was used: (1) Stool frequency (0: normal number; 1: 1-2 stools more than normal; 2: 3-4 stools

Table 1 Expression of the depression symptoms according to the results from Hamilton's Depression Inventory (IBD/CCa)

Symptom	0	1	2	3	4	Statistical analysis
Depressive mood	2/9	3/8	7/8	6/3	14/2	$\chi^2 = 16.75$, DF = 4, $P = 0.002$
Guilty feelings	15/23	0/4	5/3	6/0	6/0	$\chi^2 = 18.14$, DF = 4, $P = 0.001$
Suicide	28/29	-	2/0	-	2/1	$\chi^2 = 2.28$, DF = 2, $P > 0.05$
Early insomnia	17/10	2/10	13/10			$\chi^2 = 4.48$, DF = 2, $P = 0.024$
Transitory insomnia	15/11	3/11	14/8			$\chi^2 = 6.77$, DF = 2, $P = 0.034$
Late insomnia	18/12	3/7	11/11			$\chi^2 = 2.74$, DF = 2, $P > 0.05$
Work and life activities	13/17	5/7	5/3	7/3	2/0	$\chi^2 = 4.91$, DF = 4, $P > 0.05$
Retardation psychomotor	17/21	4/9	7/0	2/0	2/0	$\chi^2 = 13.29$, DF = 4, $P = 0.01$
Agitation	6/13	4/9	4/6	9/2	9/0	$\chi^2 = 18.31$, DF = 4, $P = 0.01$
Anxiety-psychological	5/14	5/8	1/4	12/4	9/0	$\chi^2 = 19.71$, DF = 4, $P = 0.01$
Anxiety-somatic	14/10	7/8	2/10	6/2	3/0	$\chi^2 = 11.04$, DF = 4, $P < 0.05$
Hypochondriasis	28/28	4/1	0/1			$\chi^2 = 2.738$, DF = 2, $P > 0.05$
Insight into the presence of the illness	13/8	17/6	2/16			$\chi^2 = 17.29$, DF = 4, $P < 0.001$
Diurnal variations of the mood	13/15	9/13	10/2			$\chi^2 = 2.738$, DF = 2, $P > 0.05$
Depersonalization and derealization, presence of the nihilistic ideas	24/29	5/1	1/0	2/0	-	$\chi^2 = 6.08$, DF = 3, $P > 0.05$
Paranoid ideas	30/29	0/1	2/0	-	-	$\chi^2 = 2.96$, DF = 2, $P > 0.05$
Obsessive-compulsive symptomatology	29/29	1/1	2/0			$\chi^2 = 1.94$, DF = 2, $P > 0.05$
Mean score ± SD				18.56 ± 877/10.83 ± 5.26; $t = 4.17$, DF = 60, $P < 0.001$		
Centroids: IBD = 0.513, CCa = - 0.547				Equation for the selection: -2.033 + 0.137 × total depressive score		
Section point (average of the centroids) = -0017						

more than normal; 3: 5 or more stools than normal). Each subject reported his/her degree of abnormality of the stool frequency. (2) Rectal bleeding (0: no blood; 1: streaks of blood with stools less than half the time; 2: obvious blood with stools most of the time; 3: blood alone passed). The daily bleeding score represents the most severe bleeding of the day. (3) Modified Baron Score for findings of endoscopy (0: normal or non-inflamed mucosa; 1: mild disease-erythema, decrease vascular pattern, mild friability; 2: moderate-marked erythema, absent vascular pattern, friability, erosions; 3: Severe-spontaneous bleeding, ulcerations). (4) Physician's global assessment: 0: normal; 1: mild disease; 2: moderate; 3: severe. The physicians' global assessment acknowledges three other criteria, the subject's daily record of abdominal discomfort and general sense of well-being, and other observations, such as physical findings and subject's performance status. Rating of the severity: 1-5, mild; 6-10, moderate; 11, severe. Average UC activity index in our study group was 8 ± 2 (range, 5-12). Clinical evaluation of cancers was performed by TNM classification as follows: Stage Ⅰ (T2 N0 M0), 18 cases; Stage Ⅱ (T3 N0 M0), 10 cases; Stage Ⅲ (T3 N1 M0), 1 case and T3 N2 M0, 1 case. Indices were compared to the total scores of depression and anxiety rating scales in order to investigate the eventual correlation between them.

Statistical analysis

After coding, all the answers were systematized in the common database, and the following statistical analyses were performed: The Kolmogorov-Smirnoff *Z* test was used to evaluate distribution of the data. The results were satisfactory: all the values belonged to normal distribution, which made them adequate for the subsequent statistical testing. Besides usual parameters of central tendency (descriptive statistics: mean, standard deviation [SD], extreme values); Pearson's Chi-square test and Fisher's exact probability test were used to reveal the differences in attributive values. Student's *t* test for independent samples was applied to evaluate possible differences in parametric data. The Pearson's bivariate correlation was used to investigate the interconnection between the depression and anxiety scores and in-group's life span. This test was enforced by the difference in average life span between groups, mostly dependent on the nature of the very illness: 49.16 ± 16.58 for persons in IBD groups and 63.47 ± 9.14 for persons with CCa (*t*-test = -5.094, degrees of freedom [DF] = 30, $P < 0.01$). No correlation was obtained whatsoever $r = -0.225$, N = 62, $P > 0.05$, for the depression score, and $r = -0.149$, N = 62, $P > 0.05$, for the anxiety score. The same test was used to correlate the IBD activity indices with total scores of depression and anxiety questionnaires. Discriminant function analysis (DFA) was used to determine which variable(s) discriminate between two groups: IBD and CCa. Centroids are mathematically derived grouping values whereas the section point between groups used the average of the centroids. The entire testing was performed at 95% level of confidence.

RESULTS

Depression levels

Differences in the levels of the depression symptoms are shown in Table 1. The main difference was found in the intense of the depressive mood and in the sense of guilt, which were significantly higher in the group with IBD. Also, IBD patients expressed problems with early and transitory insomnia and had a poorer ability to focus their attention on various activities and manual or intellectual work, which resulted in slow down in everyday activities. Agitation, anxiousness, early and transitory insomnia and somatic symptoms were more pronounced in the IBD group, likewise. On the other hand, awareness that something is going wrong with them was expressed in CCa patients. Twenty-two out of 32 patients with IBD and

Table 2 Expression of the anxiousness symptoms according to the Hamilton's Anxiety Rating Inventory (IBD/CCa)

Symptom	0	1	2	3	4	Statistical analysis
Anxious mood-greed, hopelessness	4/9	1/8	6/5	10/5	11/3	$\chi^2 = 13.55$, DF = 4, $P = 0.009$
Tension	4/7	1/8	6/5	10/9	11/1	$\chi^2 = 14.69$, DF = 4, $P = 0.005$
Fears: dark, loneliness, animals	19/26	2/1	4/2	7/0	0/1	$\chi^2 = 10.03$, DF = 4, $P = 0.04$
Intellectual impairments-memory problems, difficulties in communication	18/22	6/4	5/4	3/0	-	$\chi^2 = 3.85$, DF = 3, $P > 0.05$
Depressive aspect	5/15	3/4	4/8	6/1	2/14	$\chi^2 = 19.003$, DF = 4, $P = 0.002$
Somatic symptoms: muscular symptoms, sensory symptoms-tinnitus, blurred vision, attacks of heath, itching, etc., cardiovascular symptoms-tachycardia, palpitations, sense of pulsing, irregularities in heart actions, respiratory symptoms, urogenital symptoms	16/9	3/3	7/10	2/7	4/1	$\chi^2 = 7.01$, DF = 4, $P > 0.05$
Neurovegetative symptoms-face blushing, mouth dryness, vertigo, sweating	20/18	1/6	7/6	4/0	-	$\chi^2 = 7.7$, DF = 4, $P > 0.05$
Behavior during the interview-restlessness, agitation, walking around, frowned face, tense, sobbing, accelerated breathing, pallor, gulping and belching, vivid muscular reflexes, jerks, dilated pupillae, exophthalmus	4/10	0/5	8/13	10/0	10/0	$\chi^2 = 24.06$, DF = 4, $P < 0.001$
Mean score ± SD	16.22 ± 7.42/9.73 ± 6.03; $t = 3.76$, DF = 60, $P < 0.01$					

5 CCa patients could be considered seriously depressive because their total score surpassed the accepted limit of 16 points (*F*-test: $P = 4.02 \times 10\text{-}5$). A correlation between IBD activity indices and the depression total score was not revealed: For CD, $r = 0.39$, df = 17, $P > 0.05$; for UC, $r = 0.004$, df = 10, $P > 0.05$. The TNM system for cancer staging was not adequate for any kind of correlation testing.

Anxiousness levels

The trend disclosed in the depression evaluation remained when the anxiousness level was analyzed (Table 2): Patients with IBD expressed higher levels of anxiousness, nervous tension and susceptibilities to different kinds of fears. Despite the absence of significant differences in neurovegetative symptom intensity, the behavior of IBD patients exhibited more pronounced neurotic components: vivid facial mimics and gesticulation, gulping and belching during the conversation, with occasional staring into the examiner, associated with intermittent jerks of facial muscles and musculature of the extremities (not the ticks). The total anxiousness score did not correlate with IBD activity indices: for CD, $F = 0.06$, df = 17, $P > 0.05$; for UC, $F = 0.013$, df = 10, $P > 0.05$.

Paykel's scale for stressful events

Evaluation of the impacts of events, mostly stressful ones, on the appearance of either IBD or CCa showed no significant differences between the groups (Table 3). Financial difficulties, major or minor, dominated among stressors. The necessities for hospitalization of one of the family members seemed to bother more people who had cancer than those with IBD, while separation from a close person seemed to influence more IBD patients. On the other hand, only three patients of the IBD group and six from CCa group had no stress events at all in the past one year.

Discriminant function analysis (DFA)

This analysis was used to investigate whether one of the obtained parametric values (total scores of depression and/or anxiety) possessed a predictive potential, i.e. could it be used for classification of a newly discovered case into one of the groups of interest. This analysis delineated total depressive score as such a parameter that an equation for an a priori selection was computed (Table 1). Application of this equation to our samples showed 79.04% of accuracy (13 out of 62 cases were inadequately classified). The main problem was represented by the patients with IBD and low depressive scores and, *vice versa*, CCa patients with high depressive scores. Nonetheless, almost 80% of correctly classified patients were quite satisfactory for the accuracy of the DFA equation.

Finally, no gender-based and in-group differences between patients with UC and CD were obtained.

Table 3 Major stressful events (revealed in five or more persons in at least one of the groups) in IBD and CCa suffering patients according to the Paykel's scale

Event	IBD group (*n*)	CCa group (*n*)
Death of family members	8	7
Major financial difficulties	12	10
Business failure	5	2
Hospitalization of the family member due to serious illnesses	4	8
Frequent argues with parents	5	0
Separation from close person	7	2
Death of close friend	3	5
Minor financial difficulties	9	8
Mild organic illness	4	7
No stressful events at all	3	6

$\chi^2 = 12.83$, DF = 9, $P > 0.05$.

DISCUSSION

In this interview-based case-control study we intended to investigate how great the impact of anxiety and depression was on patients with IBD and cancer of the colon. The results suggested that psychological conditions influenced the pathogenesis of IBD. The uncontrolled trial, relatively

restrictive criteria and not very large sample limited the interpretation of the results. Nevertheless, proclaimed criteria were necessary to eliminate the influence of the genetic factors, major surgery consequences and other impacts on the appearance of IBD or CCa. The difference in life span and gender between our groups could be interpreted by the nature of the illnesses: IBD has already been reported as an illness with slight female predominance[13], while, according to epidemiological studies, males have higher mortality rate of cancer of the colon (8.4: 6.0/100 000 inhabitants)[14]. Surprisingly, women smokers have milder forms of IBD and less need for hemicolectomy[15]. Moreover, ethnic-based differences in the prevalence of IBD exist as well, and it is higher in Caucasians than in the Hispanic population of North America[16].

Still, there are some dilemmas about emotional status in IBD and CCa: one of the most frequent is: Could the depression be of the reactive type and could the symptoms of the gastrointestinal disease influence the presence of emotional instability? Moreover, patients are required to observe his/her own blood in the stool, in addition to suffering the abdominal pain and tenderness. Results of several studies have suggested that IBD patients more frequently suffer from psychiatric illnesses, particularly depression and anxiety at a triple higher rate than either the general population or patients with other kinds of chronic illnesses[17-19]. Individuals with IBD and similar bowel disorders experience a frequency of depression that is triple those of the general population. It is important for clinicians to assess depression and suicidal ideation among their patients with active IBD symptoms, particularly among those reporting moderate to severe pain[20]. The results of some studies suggested that psychoimmunological components might be involved in the etiology of IBD[21,22], but such a possibility is relatively uncertain due to the small relative risk for persons with depression affected by IBD[21]. Some authors tried to link the IBD occurrence with some personality traits[19,23], such as neuroticism or introversion, but we did not examine personality traits or disorders, thus we remained limited to depression and anxiety as ICD-10 recognized diagnoses. Nonetheless, emotional abuse, depression, self-accusing and the sense of guilt, have already been reported to be more common in women with irritable bowel syndrome[24], and, according to our results, sense of guilt, which involves self-blame as well, were emphasized in persons with IBD[21]. On the other hand, judging from the data obtained in this study, CCa patients had better insight into the illness and this could be the reason why patients with IBD, to our highly empiric observation, more frequently abandon the therapy as soon as they get better, without the permit of their gastroenterologists.

Recent studies showed that depression occurring with the recurrence of IBD in chronic patients and with anxiety and poor quality of health condition may exert a negative influence on the course of IBD[25]. Furthermore, some investigators reported simultaneous rise of CDAI and depression rate, estimated by Beck's depression self rating scale during disease progression, an evaluation independently confirms the lack of correlation between the clinical activity of the illness and the level of anxiety and depression revealed by Hamilton's rating scale, considering the high correlation between two mentioned scales in sensitivity for mood changes[26]. Also, antidepressants in the therapy of IBD is suggested for two reasons: first, the reduction of the depression and anxiety and, second, but not less important, the pain relief[20,27]. Recent studies, however, warn that the treatment with Selective seritonin reuptake inhibitors (SSRIs) could increase the bleeding risk in patients with IBD[28].

No difference in the impact of stressful events was found in our study. According to the investigation using Paykel's scale published elsewhere, stressful events are correlated with the major depression and generalized anxiety disorder, but no specificities in life events could be delineated[29]. We can speculate that stressful events could indirectly influence the IBD occurrence, worsening the depressive and anxiety symptoms that are undeniably related to the presence of IBD. For CCa, genetic, nutritional or environmental factors seem to be decisive, while circumstances play an ambiguous and, probably, less relevant role in its pathogenesis[30-32].

In conclusion, patients with newly obtained inflammatory bowel disease have higher levels of depression and anxiety, compared with individuals with newly diagnosed colon cancer. The discriminant function analysis reveals the total depression score as a parameter of importance for the classification of a newly diagnosed patient into one of the groups of interest. Our analysis indicates that the psychiatrist should take part in the treatment of IBD, although, according to our results, the initial IBD activity indices show no correlation with the depression or anxiety scores. On the other hand, events in the past one year do not have a particular influence on the occurrence of either inflammatory bowel disease or colon cancer.

COMMENTS

Background

It has already been reported that the level of depression and anxiety is augmented in patients with inflammatory bowel disease (IBD) and cancer of the colon (CCa). The present study compares the level of anxiety and depression in therapy-naïve, first episode IBD patients to those suffering from newly discovered CCa, using Hamilton's Depression Scale and Hamilton's Anxiety Scale.

Research frontiers

Both IBD and CCa should be recognized as complex illnesses, especially IBD and it is advisable that psychiatrists should be included in the team for the treatment.

Innovations and breakthroughs

No comparison has been made between emotional states in IBD and CCa suffering patients so far. The current study emphasizes the impact of depression and anxiety on the appearance of IBD, rather than the formation of CCa.

Applications

Continual psychiatric evaluation is recommended in IBD suffering patients and psychiatric treatment is necessary, parallel to the IBD medication in order to restrict the depression and to improve the pain in IBD suffering individuals.

Peer review

This study compares anxiety and depression levels in patients with IBD and patients with CCa. It is understandably written and discriminates certain reasons of

depression and anxiety in patients with IBD. The study is well designed and results are convincing. The presentation and readability of the manuscript is satisfactory.

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