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ORIGINAL ARTICLE

Retrospective Study

Frequency and associated factors of hair loss among patients with inflammatory bowel disease

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Abstract

AIM: To identify the frequency of hair loss among patients with inflammatory bowel disease (IBD) and associated clinical and disease related factors.

METHODS: We performed a cross sectional study in a tertiary referral adult IBD clinic. Self-reported history and characteristics of hair loss as well as clinical and demographic information were collected. Data were analyzed using univariate and multivariate analyses.

RESULTS: Two hundred and ten consecutive IBD patients were recruited; one hundred and fifty patients met predefined inclusion and exclusion criteria. Thirty-three percent of patients reported a history of hair loss. Age, gender, IBD type and disease duration were not associated with hair loss. Hair loss was reported less frequently among patients with use of mesalamine (54% *vs* 73%, $P = 0.03$) and anti-tumor necrosis factor medications (anti-TNF) (14% *vs* 40%, $P = 0.001$). In multivariate analyses adjusting for gender, IBD type and duration of disease, these associations with mesalamine and anti-TNF remained significant [(adjusted values for mesalamine (OR = 0.43, 95%CI: 0.19-0.86) and anti-TNFs (OR = 0.28, 95%CI: 0.08-0.98)].

CONCLUSION: Hair loss is common among patients with IBD. Mesalamine and anti-TNF medications were associated with lower odds of hair loss. Further studies are required to assess the mechanism of hair loss among patients with IBD.

Key words: Inflammatory bowel disease; Ulcerative colitis; Crohn's disease; Alopecia

Core tip: Inflammatory bowel disease (IBD) is associated with several extra-intestinal manifestations, which can significantly impact a patient's life. Anecdotally, patients have reported hair loss with medications to treat IBD, but no prior study has examined this association in depth. We report the results of a retrospective study

showing hair loss to be common in patients with IBD and associated with mesalamine and infliximab use. These results suggest physicians should consider hair loss an EIM associated with IBD and specific medications might reduce the risk of hair loss.

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INTRODUCTION

Inflammatory bowel disease (IBD) is a chronic, relapsing, and remitting disease of the gastrointestinal tract[1]. Anecdotally hair loss is commonly reported by patients with IBD; however the exact cause, prevalence, and relationship to IBD medications and disease activity are poorly defined. Previously, a retrospective case series in patients with ulcerative colitis (UC) described an overall low prevalence of hair loss. This study was limited, however, by its retrospective design, which could introduce measurement bias and confounding from medications independently associated with hair loss.

Through case reports and series, hair loss has been associated with concomitant autoimmune diseases (alopecia areata, telogen effluvium), and medications commonly used in IBD, specifically azathioprine and infliximab[2-5]. Also, IBD can lead to several nutritional deficiencies, including vitamin B12 and iron, which have been associated with hair loss[6-9]. No large study exists to evaluate the associations between medications and alopecia among patients with IBD.

The aim of our study was to prospectively identify the frequency of hair loss among patients with IBD and associated clinical and disease related factors.

MATERIALS AND METHODS

Subjects and study design

We performed a cross sectional study at the Baylor College of Medicine IBD Center, a tertiary referral center. The institutional review board of Baylor College of Medicine approved the protocol and all patients provided written informed consent.

We consecutively enrolled patients between January 2010 and December 2011. Eligible patients were 18 years or older with endoscopically or histologically confirmed IBD. Patients were excluded if they had another diagnosed autoimmune disease independently associated with hair loss (diabetes mellitus type 1, rheumatoid arthritis, thyroid disease, sarcoidosis or systemic lupus erythematous) or previously were exposed to medications independently associated with hair loss (warfarin, heparin, propylthiouracil, isotretinoin, lithium, metoprolol, propranolol or colchicine)[10].

Table 1 Demographic and inflammatory bowel disease disease characteristics *n* %

Characteristic	Hair loss *n* = 50	No hair loss *n* = 100	*P* value
mean, yr	34.7	32	0.27
Gender			
Male	15 (30)	46 (46)	0.08
IBD type			
Ulcerative colitis	21 (42)	35 (35)	0.47
Crohn's disease	29 (58)	65 (65)	
Duration of disease			
< 1 yr	7 (14)	12 (12)	0.80
1-10 yr	22 (44)	59 (59)	0.09
> 10 yr	21 (42)	29 (29)	0.14

At recruitment patients completed a self-administered survey, including questions about demographic information (age, gender), type of IBD [UC or Crohn's(CD)], self-reported disease activity at the time of encounter (remission, mild, moderate or severe), duration of IBD (< 1 year, 1-10 years and > 10 years), history of prior nutritional deficiencies (iron, vitamin B12 and vitamin D), prior medication use (sulfasalazine, mesalamine, olsalazine, 6-mercaptopurine, azathioprine, methotrexate, cyclosporine, infliximab, adalimumab, certolizumab pegol, natalizumab, ciprofloxacin, metronidazole, prednisone and budesonide) and hair loss characteristics [timing of hair loss, location (scalp or non-scalp or both), extent (focal or diffuse), and association with self-reported IBD flare]. Disease characteristics were confirmed by medical chart review. Subjects with discrepancies between survey results and chart review were excluded.

Iron deficiency anemia was defined as a ferritin < 45 ng/mL. Vitamin B12 deficiency was defined as < 100 pg/mL. Vitamin D deficiency (25-hydroxy vitamin D) was defined as < 20 ng/mL.

Statistical analysis

Categorical variables were compared using the Fisher's exact or χ^2 tests and continuous variables were compared with the student's *t*-test. Univariate analyses and multivariate analyses were performed. Variables with *P*-values < 0.2 were included in multivariate analyses. Statistical analysis was performed using STATA version 11 software.

RESULTS

Demographic and IBD related characteristics

Two hundred and ten consecutive patients were recruited. Sixty patients were excluded from the analysis based on incomplete data or discrepancies in the survey results and chart review. A total of 150 patients were included for analyses. The mean age for patients with hair loss was 34.7 years and for the no hair loss group was 32 years. In the hair loss group, there were 15 male patients (30%), 21 UC patients (42%) and 29 CD patients (58%). In the hair loss group, 7 had their disease for less than 1 year (14%),

Table 2 Proportions with prior medication exposures divided by group *n* (%)

Class	Medication	Hair loss *n* = 50	No hair loss *n* = 100	*P* value
Aminosalicylate				
	Mesalamine	27 (54)	73 (73)	0.03
Immunomodulators				
	6-mercaptopurine/Azathioprine	8 (16)	16 (16)	1.0
	Methotrexate	5 (10)	11 (11)	1.0
Anti-TNF's				
	Anti-TNF	8 (16)	56 (56)	0.001
	Infliximab	3 (6)	25 (25)	0.01
	Adalimumab	4 (8)	17 (17)	0.21
	Certolizumab	2 (4)	14 (14)	0.09
Steroids				
	Prednisone	24 (48)	48 (48)	1.0
	Budesonide	5 (10)	13 (13)	0.81

Table 3 Proportions with nutritional deficiencies by group *n* (%)

Characteristic	Hair loss *n* = 50	No hair loss *n* = 100	*P* value
Iron deficiency	16 (32)	40 (40)	0.44
Vitamin B12 deficiency	8 (16)	10 (10)	0.42
Vitamin D deficiency	8 (16)	29 (29)	0.12

22 had their disease between 1 and 10 years (44%) and 21 had their disease more than 10 years (42%).

Among included patients, 50 (33%) reported a history of hair loss. Both groups were similar with respect to IBD type, gender, current age, or duration of disease with a reported history of hair loss (Table 1). A numerical trend was seen with a higher proportion of men in the no hair loss group, but this did not reach statistical significance (P = 0.09). At the time of recruitment, 13 patients in the hair loss group and 22 in the no hair loss group reported lack of IBD symptoms.

Hair loss characteristics

All patients with hair loss reported loss of hair from the scalp and four patients also reported hair loss on their torso or extremities. Among the patients who reported hair loss, 66% reported diffuse scalp hair loss compared to only 34% with patchy hair loss. Sixty-two percent of patients with hair loss experienced their hair loss around the time of an IBD flare.

Medication associations

History of mesalamine and anti-TNF use was associated with lower odds of hair loss (OR = 0.43, 95%CI: 0.21-0.88 and OR = 0.24, 95%CI: 0.10-0.60, respectively) (Table 2). There were consistent trends of lower odds of hair loss with all anti-TNF agents independently, however this was statistically significant only for infliximab (P = 0.004, OR = 0.19 95%CI: 0.05-0.67). The proportion of patients with prior use of immunomodulators and steroids were similar among patients with and without hair loss (Table 2). On multivariate analyses including gender, duration of disease, mesalamine and infliximab, the protective effects of mesalamine (OR = 0.43, 95%CI: 0.19-0.86), anti-TNFs (OR = 0.28, 95%CI: 0.08-0.98) and infliximab (OR = 0.60, 95%CI: 0.11-3.27) remained significant.

Nutritional deficiencies

The proportion of patients with iron and vitamin B12 deficiency were similar between patients with and without hair loss. Numerically, vitamin D deficiency was more common among patients without hair loss, but this did not reach statistical significance (P = 0.12) (Table 3).

DISCUSSION

We observed that hair loss was common among IBD patients (33%). Prior exposure to mesalamine and anti-TNF agents was associated with lower odds of having hair loss.

Two prior studies have documented the potential association of hair loss and IBD, but they did not evaluate for associated risk factors. Katsinelos *et al*[11] describe a retrospective chart review of patients with UC, CD and celiac disease with a prevalence of alopecia of 0.8%. Similarly, Muller *et al*[12] performed a retrospective chart review of patients diagnosed with alopecia and found a 2% prevalence of UC. In our study, 33% of patients reported a history of hair loss. The wide discrepancy between our study and prior studies could be explained by several factors. The prior studies assessed alopecia by chart review, which may reflect recall bias or lack of documentation. Our study is the first to use a prospective survey design specifically asking about hair loss and therefore may reflect a more accurate rate of hair loss among IBD patients.

Prior studies have reported an association between mesalamine and immunomodulators with alopecia[5]. Interestingly, we observed a protective effect of mesalamine for hair loss, and no effect of immunomodulators on hair loss. No prior literature exists to associate mesalamine with hair loss, but one case report of a patient with CD demonstrated an association of azathioprine and hair loss. In that report, a 20 year old male had improvement of hair loss after starting azathioprine on 2 separate occasions[2].

This is the first study to show use of infliximab was more common in patients without hair loss compared to patients with hair loss. Prior studies, mostly case reports,

have implicated infliximab in hair loss[3-5]. The differences between these prior case reports and our study potentially arise from the difference in number of patients seen, since these were case studies and our study had a much larger sample size. Interestingly, the other biologic agents showed a trend towards less hair loss with their use, but this did not reach statistical significance.

Various vitamin and mineral deficiencies have been described in IBD patients; however our study did not find any difference in prevalence of these deficiencies between the groups. Despite evidence describing the presence of anemia, vitamin B12 and vitamin D deficiency in patients with IBD and small, retrospective case series associating these deficiencies with hair loss, we did not detect an association[6-9,13]. Possibly explanations for this discrepancy include the retrospective and small nature of prior studies or the small numbers in our study, which possibly caused a type 2 error. Larger, adequately powered studies may be needed to confirm these associations.

The limitations of our study include small sample size, potential recall bias and lack of etiology for the hair loss. The size of our study and consequently a lack of power to examine some associations could have led to a type 2 error. Due to the design of our study, the potential for recall bias exists regarding clear temporal relationships between medication use and hair loss. However, our study has several strengths; we collected data regarding self-reported hair loss directly from the patient compared to prior studies based only on chart review. In addition we were able to assess possible associations of hair loss with nutritional status.

In conclusion, our study demonstrates that hair loss is common among patients with IBD. Use of mesalamine and anti-TNF agents were associated with lower odds of hair loss after adjusting for age, gender, IBD type and duration of disease. Further studies will be needed to better define the factors associated with hair loss and develop effective management strategies.

COMMENTS

Background

Inflammatory bowel disease is characterized by extraintestinal manifestations (EIM), which can significantly impact a patient's quality of life. Retrospective studies have noted hair loss as an EIM, but no studies have explored the risk factors for hair loss.

Research frontiers

Inflammatory bowel disease (IBD) is associated with several EIM's of disease, but specific EIM's may be improperly attributed to IBD or medications, which could prompt unneeded changes in care. Studies exploring these EIM's and potential determinants may allow for further optimizing of care for patients with IBD.

Innovations and breakthroughs

This is the largest study to specifically characterize hair loss in IBD patients and explore its association with medications and vitamin deficiencies. The most striking results from this study were the self-reported events of hair loss and the associations noted between no hair loss and mesalamine or infliximab use.

Applications

These results suggest physicians treating patients with IBD should counsel them regarding possible hair loss. Further studies are needed to confirm these findings and further explore potential associations with vitamin deficiencies.

Peer review

The submitted manuscript tries to figure out the role of medication on hair loss in IBD. In a retrospective manner the charts from 150 cases were reviewed and patients were questioned whether they had experienced hair loss or not. Mesalamine and TNF antagonists were identified to be more often used in the group without hair loss. The authors suggest that these medications might have a protective role.

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