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BRIEF COMMUNICATION

Fecal calprotectin and serum albumin as markers of gastrointestinal graft versus host disease

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KEYWORDS
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Calprotectin;
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Abstract
Background: Acute graft versus host disease (aGVHD) affects approximately 30—60% of patients after allogeneic hematopoietic stem cell transplantation (HCT) and our ability to predict who develops this complication and their response to treatment is limited. Fecal calprotectin has recently gained popularity as an effective marker of GI inflammation in patients with Inflammatory Bowel Disease (IBD).
Methods: Fecal calprotectin and albumin were evaluated as prognostic and predictive markers of aGVHD in 60 adult and pediatric HCT patients. Stool samples were sent for calprotectin quantification prior to starting conditioning, at day 14 post-HCT, at day 28 post-HCT, and at onset of aGVHD ± 2 days.
Results: Fecal calprotectin did not differentiate patients with GI-GVHD and non-GI GVHD and did not vary based on severity. However, in patients with steroid-refractory GI aGVHD, significantly higher fecal calprotectin levels were noted. At onset of lower-GI symptoms, steroid refractory patients (n = 3) had a mean fecal calprotectin level of 449 ug/g (range 116—1111 ug/g) and a mean albumin of 1.93 g/dL (range 1.6—2.3 g/dL) compared with a mean fecal calprotectin of 24 ug/g (range 16—31 ug/g) and a mean albumin of 3.3 g/dL (range 2.3—3.9 g/dL) in steroid responsive patients (n = 9) (fecal calprotectin p = 0.032, albumin p = 0.027).

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Conclusion: Patients with steroid-refractory GI aGVHD had higher fecal calprotectin levels and lower albumin levels than patients with steroid-responsive disease. We recommend further studies to evaluate non-invasive tests with fecal calprotectin in combination with albumin in predicting steroid refractory disease at onset of symptoms to potentially identify patients that may benefit from upfront escalation in GVHD treatment.

Introduction

Acute graft versus host disease (aGVHD) is a common complication following allogeneic hematopoietic stem cell transplantation (HCT), affecting approximately 30–60% of patients [1]. About one-third of patients with aGVHD are refractory to initial treatment with steroids and have poor outcomes with an estimated 2-year overall survival of <20% [2,3]. Although serum levels of REG3α, ST2, and TNFR1 have been identified as prognostic markers of GI-aGVHD, testing is not universally available [4].

Fecal calprotectin has recently gained popularity as an effective marker of GI inflammation in patients with Inflammatory Bowel Disease (IBD). Calprotectin is a protein identified in the cytosol of inflammatory cells, is secreted from neutrophils during cell death, and serves as a surrogate marker of neutrophil migration across the GI mucosa during times of inflammation. It can be quantified in stool samples [5]. Fecal calprotectin is currently used to screen patients with gastrointestinal symptoms and effectively differentiates IBD from non-specific irritable bowel syndrome and infectious colitis using a cut-off of >50 μg/g [6]. Despite the widespread use of fecal calprotectin in the evaluation of IBD, few studies have evaluated calprotectin post-HCT, especially in pediatrics [5,6].

Albumin is an acute phase reactant synthesized by the liver and is inversely proportional to the degree of systemic inflammation. There have been reports that albumin can be a prognostic marker of aGVHD with a decrease in 0.5 g/dL from baseline associated with severe aGVHD and worse overall survival [7]. In addition, in GI-aGVHD, albumin <3.4 g/dL has been associated with worse overall survival [8].

Our study evaluated fecal calprotectin and albumin as predictive markers of aGVHD in HCT patients. We hypothesized that elevations in fecal calprotectin would precede the onset of clinical symptoms in those with aGVHD and would predict response to aGVHD treatment at the onset of symptoms; we also hypothesized that lower albumin would correlate with severity of aGVHD.

Methods

We prospectively enrolled 60 patients prior to allogeneic HCT at Ann and Robert H. Lurie Children's Hospital of

Table 1 Patient and transplant characteristics.

	No GVHD (n = 29)	Lower GI aGVHDGr 2–4 (n = 9)	Other aGVHD (n = 22)
Age (years)			
<18	16	3	10
18–60	7	4	7
>60	6	2	5
Gender			
Male	17	7	17
Female	12	2	5
Ethnicity			
Caucasian	16	6	16
Hispanic	9	2	1
African American	3	1	1
Other/not specified	1	0	4
Underlying diagnosis			
Thalassemia/hemoglobinopathy	1	0	1
Mucopolysaccaridosis	1	0	0
HLH	0	0	1
SCID	2	0	0
Aplastic anemia	2	1	3
Fanconi anemia	1	0	0
Hematologic malignancy	22	8	17

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