Journal of Pediatric Surgery 52 (2017) 1718–1722

Contents lists available at ScienceDirect

Journal of Pediatric Surgery

journal homepage: www.elsevier.com/locate/jpedsurg

Review Articles/Meta-Analyses

Surgical treatment of intestinal complications of graft versus host disease in the pediatric population: Case series and review of literature

Camille A. Gutierrez [a], Mehul V. Raval [b], Hannah R. Vester [c], Sonali Chaudhury [d], Daniel von Allmen [c], David H. Rothstein [a,e,*]

[a] Jacobs School of Medicine and Biomedical Sciences, University at Buffalo, State University of New York, Buffalo, NY
[b] Division of Pediatric Surgery, Department of Surgery, Children's Healthcare of Atlanta, Emory University School of Medicine, Atlanta, GA
[c] Division of General and Thoracic Surgery, Cincinnati Children's Hospital Medical Center, Cincinnati, OH
[d] Division of Hematology, Oncology and Stem Cell Transplantation, Ann and Robert H. Lurie Children's Hospital of Chicago, Chicago
[e] Department of Pediatric Surgery, Women and Children's Hospital of Buffalo, Buffalo, NY

ARTICLE INFO

Article history:
Received 26 December 2016
Received in revised form 22 May 2017
Accepted 23 June 2017

Key words:
GVHD
Intestinal complications
Pediatric surgery
Perforation
Obstruction
Hemorrhage

ABSTRACT

Background/purpose: Intestinal complications of acute graft-versus-host disease (aGVHD) include hemorrhage and perforation in the short-term, and stricture with bowel obstruction in the long-term. As medical management of severe aGVHD has improved, more patients are surviving even advanced stages of intestinal aGVHD. This review summarizes the available pediatric literature on surgical treatment of complications of intestinal GVHD.
Methods: A systematic review was performed using PubMed, Cochrane, Embase, and Scopus databases. Any publication that addressed surgical treatment of acute and chronic intestinal GVHD in the pediatric population was reviewed in detail. Furthermore, we included information on 5 additional patients from the institutions of this review's authors, which had not been previously published.
Results: We identified 8 studies, comprising 13 patients. Surgical interventions were undertaken for a variety of intestinal GVHD complications, including small bowel obstruction owing to stricture (n = 8), enterocutaneous fistulae (n = 2), gastrointestinal hemorrhage/perforation (n = 1 each), and esophageal stricture (n = 1). Among eight patients with bowel obstruction as an indication, pathology revealed ulceration with fibrosis in all but one; 3 had signs of persistent GVHD. Surgical mortality was reported in 4 patients (31%) at an average of 6 weeks postoperatively. The median overall follow-up time was 20 months (IQR, 2–21).
Conclusions: Although intestinal aGVHD management is almost exclusively medical, a small subset of patients develops complications of intestinal GVHD that require surgical intervention. With expanding indications for stem cell transplantation as well as improved survival after previously fatal bouts of intestinal aGVHD, it is likely that surgical intervention will become more common in these complicated patients.
Systematic review: Level of Evidence: Level IV.

Contents

* Corresponding author at: Women & Children's Hospital of Buffalo, University at Buffalo, State University of New York, 219 Bryant St, Buffalo, NY 14222, USA. Tel.: +1 716 878 7301 (o); fax: +1 716 888 3850.
E-mail address: drothstein@kaleidahealth.org (D.H. Rothstein).

http://dx.doi.org/10.1016/j.jpedsurg.2017.06.022
0022-3468/

Acute graft-versus-host disease (aGVHD) complicates hematopoietic stem cell transplantation (HSCT) in approximately 30%–60% of pediatric cases [1,2]. Such complications include skin rash, cutaneous blisters, anorexia, abdominal pain, diarrhea, persistent nausea and vomiting, gastrointestinal bleeding, and hepatitis with elevation of bilirubin and/or liver enzymes [3,4]. While intestinal complications of aGVHD have typically been considered amenable only to medical therapy [5–7], recent case reports have suggested that surgical intervention, particularly in cases of chronic intestinal obstruction, may have a role in the treatment of select patients [5,6,8,9].

The purpose of this study is to review available literature regarding intestinal complications of aGVHD in the pediatric population to help better characterize these complications and provide some guidance for surgical management thereof. As indications for HSCT increase [10,11] with improved supportive care leading to improved survival for patients with intestinal complications of transplantation, we postulate that the proportion of intestinal aGVHD complications amenable to surgical correction will increase. We focused specifically on intestinal complications, to the exclusion of hepatic and pancreatic complications, which more rarely lead to consideration for surgical intervention.

1. Methods

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were used to help select literature for review [12]. In addition, the records of five patients with intestinal complications of aGVHD who had undergone surgical treatment at one of the authors' institutions had been previously collected for review, but not published. These were added as a case series to the systematic review.

Each participating institution obtained individual Institutional Review Board (IRB) approval for data collection (Cincinnati, 2015-5419; University at Buffalo, 764585-1; Children's Healthcare of Atlanta, Exempted). The University of Buffalo served as the central data repository.

1.1. Search strategy and data extraction

Two authors (CAG and DHR) conducted independent systematic reviews using the PubMed, Embase, Cochrane, and Scopus databases with no date limits. Studies were limited to those in the English language. Keywords included GVHD/graft-versus-host disease, GI/gastrointestinal, obstruction, hemorrhage, perforation, stricture, pediatric, surgery/surgical, and stem cell transplantation. Pediatric was defined as patients 18 years of age and younger. The search results were combined and duplicate results eliminated. Initial results were culled by title/abstract review. Once we identified 4 articles [5,6,8,9] specifically pertaining to our research topic, we utilized the 'similar papers' function within the databases to identify 3 additional articles. Seven studies were selected for detailed review.

1.2. Authors' additional case series

Data on patients who had undergone surgical procedures to treat intestinal complications of aGVHD after hematopoietic stem cell or bone marrow transplantations were obtained from three collaborating institutions. Patient lists were generated by medical record review, cross-

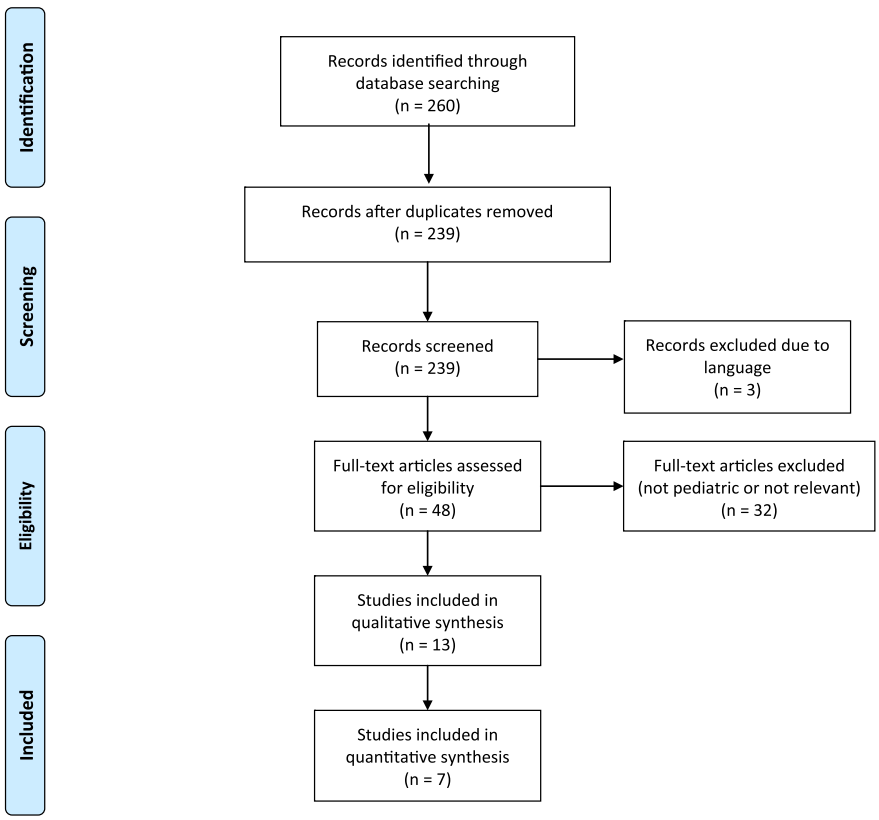

Fig. 1. PRISMA flowchart for study selection.