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CASE REPORT | PATHOLOGY

Graft-Versus-Host Disease of the Upper Gastrointestinal Tract After an Autologous Stem Cell Transplant

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Abstract

Graft-versus-host disease (GVHD) in recipients of autologous stem cell transplantation (SCT) is less common compared to recipients of allogeneic SCT, but its existence has been well documented. Similarly, the diarrheal component of the disease is highlighted when discussing its gastrointestinal (GI) manifestations, with less emphasis given to upper GI symptoms like nausea and vomiting. We present a case illustrating the upper GI tract signs and symptoms of GVHD after autologous SCT, and emphasize that prompt treatment can rapidly improve morbidity and prevent disease progression.

Introduction

Acute graft-versus-host disease (GVHD) is a common complication following allogeneic stem cell transplantation (SCT). Dermatitis, bilirubin elevation, and diarrhea are common disease presentations. Gastrointestinal (GI) manifestations of acute GVHD are typically associated with secretory diarrhea that can progress to bloody diarrhea and ileus.[1] Nausea, vomiting, anorexia, abdominal pain, and weight loss can occur when the disease involves the upper GI tract. Chronic GVHD includes more fibrotic changes of organs, but can also present with overlapping symptoms of acute GVHD.[1] Clinical features are mainly used to distinguish acute and chronic disease.[2] Although GVHD is often considered to be primarily a complication of allogeneic SCT, there have been many reports of GVHD after autologous and syngeneic SCT.[3–9] It is important to recognize upper GI GVHD even in non-allogeneic transplant recipients, because proper treatment often provides rapid symptomatic relief.

Diagnosis of GI GVHD is confirmed through tissue histology. Rectal tissue is commonly sampled in diarrhea-predominant disease, whereas gastric and intestinal tissue sampling confirms disease in the upper GI tract. Acute GI GVHD can mimic and co-exist with enteric infections like *Cytomegalovirus*, which should be ruled in or out if there is suspicion for GVHD.[3]

Case Report

A 54-year-old man with multiple myeloma diagnosed 21 months prior presented with 2 months of persistent nausea, vomiting, and inability to tolerate oral intake. His treatment included radiation therapy to the right maxilla combined with dexamethasone, followed by chemotherapy (bortezomib and lenalidomide, then bortezomib, cyclophosphamide, and dexamethasone; last administration received 4 months prior to admission) and autologous SCT 2 months prior to admission. His GI symptoms began a few days after the autologous SCT. He was able to tolerate oral hydration but not solid food. Within minutes to hours of oral intake, he would vomit bilious, non-bloody digested contents. He vomited 1–6 times daily, leading to anorexia and weight loss, but denied any diarrhea. His vital signs were normal and physical exam revealed a benign abdomen. Admission labs were unre-

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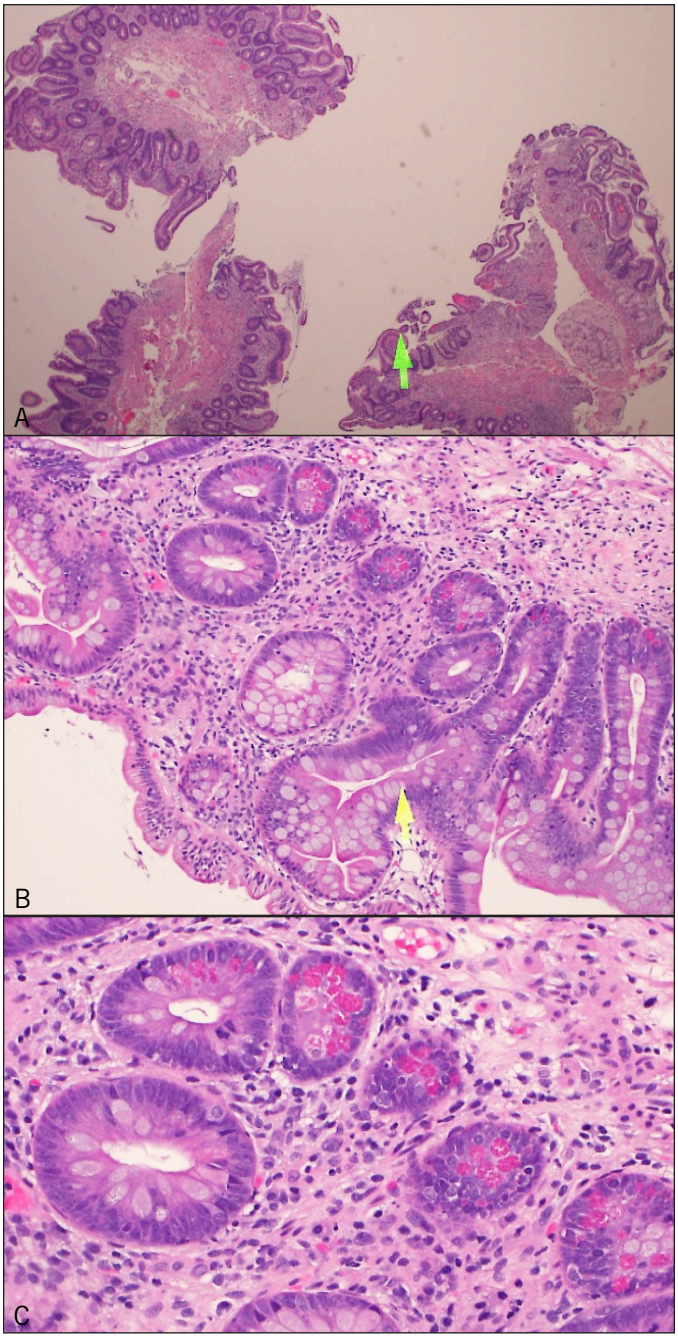

Figure 1. Duodenal biopsy at (A) 4x, (B) 20x, and (C) 40x magnification showing mucosa with mild reactive change and increased apoptotic activity (up to 6 per 10 consecutive glands/crypts), suggestive of mild or early GVHD.

markable and abdominal films showed no bowel dilation or obstruction. An upper GI series revealed decreased gastric peristalsis with delayed progression of oral contrast.

Esophagogastroduodenoscopy revealed LA Grade D esophagitis, mild diffuse gastritis, normal duodenum, and no gastric outlet obstruction. Duodenal biopsy revealed mucosa with mild reactive change and increased apoptotic activity (up to 6 per 10 consecutive glands/crypts), suggestive of mild or early GVHD (Figure 1). Immunostaining was negative for *Cytomegalovirus*, and esophageal brushings were negative for malignancy or fungus. The patient then developed hyperpigmented skin lesions. Punch biopsy of the skin lesion revealed perivascular lymphocytic infiltrate consistent with early-grade GVHD. Prednisone 60 mg daily by mouth was started with marked improvement in nausea, vomiting, and oral intake within 2 days. The patient was discharged on a prednisone taper with resolution of presenting symptoms.

Discussion

Acute GVHD from allogeneic SCT is mediated by damage from donor T lymphocytes and cytokines.[1] Genetic disparity should not theoretically exist in autologous SCT. Theories on the pathophysiology of GVHD after autologous SCT focus on diminished self-tolerance secondary to an altered immune system. Newer drugs used for multiple myeloma treatment, like lenalidomide and bortezomib, both of which our patient received, have been postulated to alter regulatory T cell function that could potentially lead to GVHD in these patients.[6]

GI GVHD after autologous SCT has become increasingly recognized in recent years. Cogbill et al diagnosed lower GI GVHD in 17 recipients of autologous SCT.[6] Holmberg et al identified that 90 of 681 (13%) recipients of autologous SCT developed acute GVHD, 90% of whom presented with upper GI symptoms of nausea and vomiting.[7] Numerous other cases of GVHD in such patients have been described, many of which focus on GI disease.[4,5,8,9]

Our case highlights GVHD after autologous SCT and stresses the non-diarrheal manifestations of GI GVHD. The Glucksberg grade and the International Bone Marrow Transplant Registry are the current grading systems for assessing severity and prognosticating acute GVHD. Both systems focus on the extent of involvement in the skin, liver, and gut, and assess gut involvement based exclusively on diarrheal symptoms. However, Appleton et al postulated that upper GI GVHD represents an earlier stage of disease that can progress to lower GI involvement.[2] If this is true, perhaps the grading system of GVHD should better emphasize upper GI symptoms to help physicians recognize and treat earlier disease. Steroids have been shown to be highly efficacious in patients with upper GI GVHD.[4,7] Greater emphasis on upper GI symptoms of GVHD may help guide earlier recognition, diagnosis, and effective treatment, ultimately leading to symptom resolution and avoidance of more severe downstream complications.[10]

Disclosures

Author contributions: B. Barbash wrote the manuscript and is the article guarantor. S. Kramer, D. Tzimas, and P. Saitta revised and edited the manuscript.

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