



# Graft-Versus-Host Disease Associated Post-operative Complications After Pelvic Reconstructive Surgery: A Case Report

Christopher P Chung<sup>1</sup>, Auayporn P Nademane<sup>2</sup>, Grace Wakabayashi<sup>2</sup> and Maryam Sadeghi<sup>1,\*</sup>

<sup>1</sup>Department of Gynecologic Oncology Surgery, Department of Hematology and Hematopoietic Cell Transplantation, City of Hope National Medical Center, Duarte, California, United States

<sup>2</sup>Division of Gynecologic Oncology, City of Hope Medical Center, Duarte, California, United States

\*Corresponding author: Department of Gynecologic Oncology Surgery, Department of Hematology and Hematopoietic Cell Transplantation, City of Hope National Medical Center, Duarte, California, United States. Email: maryamsadeghi50@gmail.com

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## Abstract

**Introduction:** Graft-versus-host disease (GVHD) can occur after allogeneic bone marrow transplantation (BMT) and can affect the skin, gastrointestinal tract, lungs, liver, and vulvovaginal areas.

**Case Presentation:** This case report described a 65-year-old multiparous patient with myelodysplastic syndrome who underwent a matched unrelated donor transplant approximately 3 years before her surgery. After her BMT she developed GVHD. She underwent anterior and posterior repair and uterosacral ligament suspension for stage III post-hysterectomy vaginal vault prolapse. Her post-operative course was complicated by mental status changes, abnormal liver function tests, and increasing abdominal distention. All her post-operative symptoms were resolved with conservative management.

**Conclusions:** This case presentation highlights the potential atypical post-operative course of BMT patients with GVHD. The management of patients with GVHD relies heavily on the early involvement of hematologists.

**Keywords:** Graft-Versus-Host Disease, Bone Marrow Transplant, Pelvic Reconstructive Surgery

## 1. Introduction

Graft-versus-host disease (GVHD) can occur after allogeneic bone marrow transplantation (BMT). GVHD is a rather common complication that happens in 25% to 70% of patients in spite of receiving prophylaxis medications (1). The pathogenesis of GVHD is believed to be a complex, primarily T-cell-mediated, immune response in which the grafted donor cells react against histocompatibility antigens in the host. It could happen after hematologic allogeneic stem cell transplantation for hematologic disorders such as myelodysplastic syndrome. Myelodysplastic syndrome is a group of disorders, specifically malignant hematopoietic stem cells, that are characterized by dysplastic and ineffective blood cell production. GVHD can affect the skin, gastrointestinal tract, lungs, liver, and vulvovaginal areas. Manifestations of GVHD involving the skin, gastrointestinal tract, lungs, and liver are well described. Common gynecologic manifestations include vulvovaginal pain, vaginal fusion, and stenosis. Approximately one-third of GVHD patients can develop vaginal stenosis. These symptoms can be treated with: Topical anesthetics, topical steroids, topical immunosuppressants, vaginal dilators,

and surgery (2). Genital tract GVHD is a significant, complex, under-diagnosed complication of allogeneic stem cell transplantation. It is not an uncommon condition (24% - 35%) and can happen at a median time of 13 months after transplantation. It has adverse effects on a woman's lifestyle and sexual health (3, 4). It is classified into acute (aGVHD) and chronic (cGVHD). Chronic GVHD (cGVHD) is a multi-system disease that significantly deteriorates functional status, quality of life, and survival (5). The incidence of symptomatic cGVHD requiring medication is 40% to 70%. However, there are reasons that symptomatic genital cGVHD is considered an underdiagnosed and underestimated cGVHD (6). The risk of pelvic organ prolapse is extremely rare in GVHD patients possibly due to the high risk of vaginal stenosis.

Pelvic floor disorders are common health issues with the prevalence of one out of four American women reporting a wide range of symptoms of urinary incontinence, constipation, sexual dysfunction, pelvic organ prolapse (POP), or fecal incontinence (7).

Management of POP in symptomatic patients includes conservative or surgery according to the patient's preferences. Surgery is usually considered when conservative

treatment options like insertion of pessaries, pelvic floor muscle exercises, hormone therapy, and other strategies fail (8). The lifetime risk of surgery for pelvic organ prolapse for women in the US is 13% and it's estimated that 50% of women will require reconstructive surgery for POP by 2050 (9).

## 2. Case Presentation

After obtaining consent from our patient the case is reported. The patient was a 65-year-old multiparous patient with myelodysplastic syndrome. She previously underwent a vaginal hysterectomy for a benign disease. Her past medical history includes myelodysplastic syndrome (MDS) and hypertension. The patient underwent an allogeneic stem cell transplant from her sister in 2011. After the transplant, the patient developed chronic GVHD with sclerodermatous changes. She has been treated with tacrolimus 0.5 mg once a day for continuous immunosuppression. After developing chronic GVHD, she was referred to the urogynecology service and was diagnosed with stage III post-hysterectomy vaginal vault prolapse. The patient chose to undergo definitive surgical management, and underwent an anterior and posterior repair and uterosacral ligament suspension. Surgery was uncomplicated, estimated blood loss was 60 cc's, lasting approximately 90 minutes. Post-operatively, the patient exhibited mild disorientation with upper extremity shaking. Her primary hematologist was consulted. Despite being afebrile with a normal white blood cell count, sepsis was still suspected and broad-spectrum antibiotics were initiated. Final blood and urine cultures were negative. Other lab abnormalities included alkaline phosphatase 198 U/L, alanine transaminase 145 U/L, aspartate aminotransferase 136 U/L, uric acid 7 mg/dL, and elevated liver enzymes. These all normalized within 10 days.

Three days postoperatively the patient had a complete return of normal mental status. Due to increasing abdominal distention, a CT scan was performed and was negative. She was hospitalized for eight days and managed conservatively. All her post-operative symptoms including neurological symptoms, abnormal lab tests, and abdominal distention were likely due to an exacerbation of GVHD.

## 3. Discussion

Graft-versus-host disease (GVHD) commonly occurs after allogeneic bone marrow transplantation (BMT). It affects 25 % of all women who receive hematopoietic stem cell transplantation (HSCT). The pathogenesis of GVHD is believed to be a complex, primarily T-cell-mediated, immune response in which the grafted donor cells react

against histocompatibility antigens in the host. GVHD can affect the skin, gastrointestinal tract, lungs, liver, and vulvovaginal areas. It was reported that 65% to 85% of patients with chronic GVHD have skin involvement, 60% mouth involvement, 40% to 55% liver involvement, 25% to 45% eye involvement, 20% to 30% nutritional problems, and 10% to 15% have lung manifestations (10). Female genital GVHD usually happens 7 - 10 months after HSCT and therefore it is considered a chronic manifestation. The symptoms of vulvovaginal involvement are sensitivity, fusion, stenosis, dryness, burning, pruritus, dysuria, dyspareunia, and sexual dysfunction. In 68% of cases, the symptoms affect the vulva only, while in 26% both the vulva and the vagina are affected. The most common complaints are vulvar dryness (80%) and dyspareunia, affecting sexual activity (50%). Other reported signs of genital involvement are vulvar erythema, vulvar fissures or erosions, fusion of the clitoris in three, vaginal synechiae, and total obstruction of the vagina (11). In the majority of cases, symptoms like dryness and dyspareunia were stabilized with local steroids and estrogen treatment, and most patients could resume sexual activity after treatment. However; they are at low risk for developing urinary incontinence and prolapse (12).

We performed a PubMed search using the keywords: "GVHD", "prolapse", and "post-operative complications" and found no case of pelvic organ prolapse after diagnosis of GVHD. There is also no reported case of post-operative complication in patients with genital GVHD, either. Gynecological manifestations in GVHD patients include vulvovaginal pain, dyspareunia, vaginal stenosis, and fusion. The clinical armamentarium for the treatment of these symptoms includes topical anesthetics, topical steroids, topical immunosuppressants, vaginal dilators, and surgery. The risk of developing severe pelvic organ prolapse is extremely rare among GVHD patients. Our patient had stage III prolapse and underwent native tissue repair with uterosacral ligament suspension and anterior and posterior repair. We did not offer her mesh repair such as abdominal sacrocolpopexy, because the risk of mesh complication in patients with GVHD is unknown. To date, she is still satisfied with her repair with no evidence of recurrent prolapse.

GVHD is a complicated illness to treat, as it often involves many organ systems. Therefore, we hope through this case presentation, awareness of the post-operative clinical presentations in patients with GVHD be increased. The early involvement of a hematologist and oncologist in managing these patients is important.

## Footnotes

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