

# Vulvar and Vaginal Graft versus Host Disease: A Healthcare Clinic Initiative

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## ABSTRACT

**Objective:** In patients receiving bone marrow transplantation (BMT), their mucosa becomes altered and sclerotic changes in the female external genital organs occur. Although a few studies have specifically addressed vulvar and vaginal graft versus host disease (VVGvHD) and its repercussions on the sexual health and quality of life of patients, VVGvHD can be overlooked by health practitioners. The objective of the study is to describe the initiation of a health care clinic specializing in VVGvHD in a general tertiary hospital. **Methods:** A VVGvHD clinic was founded as a part of BMT daycare in a joint initiative of the nursing staff and the medical director of the department and a gynecologist specializing in vulva and vaginal disease. Patients were assessed for vulvovaginal symptoms, such as dryness, burning, itching, pain to touch, pain during intercourse, and dysuria. These patients might be subsequently referred to the VVGvHD clinic according to their needs assessed by daycare nurses. Treatment guidelines were developed by the specialist gynecologist.

**Results:** A total of 81 women aged 2–66 years (median age = 38 years) visited the clinic from 2009 to 2015. Of these women, 70 received an allogeneic transplant and 11 underwent autologous transplantation before consultation in our clinic. VVGvHD was detected in 54% of the patients. **Conclusions:** The VVGvHD clinic was developed to fulfill the specific needs of female patients who underwent BMT. The pioneer clinic was founded as a joint effort of the multidisciplinary team. Evidence supporting the optimum treatment for this condition is insufficient. This was the main reason for performing this study to explore the clinic that was newly based in Israel. VVGvHD may be a fluctuating condition with frequent deterioration and improvement. Therefore, regular clinical examinations are necessary.

**Key words:** Bone marrow transplantation, nursing, vulvar and vaginal graft versus host disease

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## Introduction

Bone marrow transplantation (BMT) is a complex medical process that potentially helps and cures individuals with various hematological disorders and malignant diseases, such as leukemia and lymphoma. BMT is classified as allogeneic and autologous, which, respectively, involve bone marrow cells from a donor and from oneself. However, allogeneic BMT causes side effects including graft versus host disease (GvHD), which is a reaction of the graft introduced to the human body (host). Although GvHD may help alleviate leukemia, this symptom is an overreaction and may become a disease that can cause serious or lethal conditions.

In women, GvHD may affect the genitalia including vulva and vagina. This study aimed to discuss vulvar and vaginal GvHD (VVGvHD) and describe a special multidisciplinary clinic developed for the diagnosis, treatment, and follow-up of individuals with this condition.

## Symptoms of Vulvar and Vaginal Graft vs. Host Disease

GvHD is a complex complication with acute and chronic stages, which are categorized on the basis of various symptoms developed after transplantation. The pathogenesis of GvHD is a complex T-cell-mediated immune response; in this mechanism, grafted donor cells react against histocompatibility antigens in the host.<sup>[1]</sup>

GvHD may affect various organs including skin, liver, and intestines. This condition also occurs in the female genitalia, particularly vulva and vagina, known as VVGvHD.<sup>[2]</sup> VVGvHD was first described by Corson *et al.* in 1982<sup>[3]</sup> and defined as “an abnormality of the mucosa and manifestation of sclerotic changes in the female external genital organs.” However, a few studies have specifically addressed VVGvHD and its repercussions on the sexual health and quality of life of patients.<sup>[2]</sup>

We observed that female patients do not focus on health problems involving their genital areas when they consider a serious and life-threatening procedure, such as BMT. Female patients may also feel ashamed and uncomfortable when they describe “trivial” symptoms associated with VVGvHD. Consequently, these symptoms may be overlooked by health practitioners. The lack of awareness of this aggravating condition may lead to underdiagnosis, misdiagnosis, and mistreatment.<sup>[1]</sup> Hayes and Rock<sup>[4]</sup> emphasized the importance of precise and timely diagnosis and preventive measures.

Female genital GvHD affects the vulva and vagina in approximately 25%–50% of allogeneic BMT survivors: 68% in vulva and 26% in vulva and vagina. Onset is at a median

of 7–10 months after allogeneic BMT. However, vaginal GvHD may develop after several years.<sup>[5]</sup>

The main symptoms of VVGvHD are dryness, burning, itching, pain to touch, pain during intercourse, and burning when urine touches the opening of the vagina in a condition known as vestibular dysuria.<sup>[5,6]</sup> Vaginal atrophy should be ruled out because of estrogen deficiency as most patients become menopausal, following transplantation.<sup>[6]</sup> Physical findings compatible with VVGvHD are purulent discharge, mucosal erosion, vaginal stenosis, and loss of elasticity graded from mild to severe. Vulvar GvHD may cause loss of normal vulvar anatomy, including disappearance of the small lips, adhesion of the clitoris, narrowing of the vaginal opening, and complete obliteration of the female genitalia in radical cases.<sup>[5,7]</sup>

Mild chronic VVGvHD can be asymptomatic when a woman is sexually inactive. Sexual activity is also not correlated with the severity of systemic GvHD.<sup>[1]</sup>

## Recommendations for the Treatment and Development of Special Clinics for Vulvar and Vaginal Graft vs. Host Disease

Structured care for women who received allogeneic BMT should be provided to identify and treat VVGvHD.<sup>[1,2,5,6]</sup> However, only one team of BMT ambulatory care in Australia has developed a program for female genital GvHD. In this program, one gynecological team assesses all women before transplantation to offer counseling regarding the early recognition of symptoms of genital tract GvHD and estrogen deficiency. Patients are advised to undergo vaginal examination and return to follow-up after 3 months and 6 months and each year thereafter.<sup>[7]</sup>

Several recommendations have been provided. Symptomatic patients should be evaluated and followed up by a gynecologist with experience in GvHD or by practitioners with experience in lichen planus of the genitalia.<sup>[6]</sup> Shanis *et al.*<sup>[5]</sup> supported the need for a long-term gynecological follow-up because of the risk of delayed onset of VVGvHD.

A careful gynecologic approach is essential for post-BMT female patients to detect mild asymptomatic VVGvHD.<sup>[6]</sup>

However, the implementation of these recommendations has yet to be reported. Specialty treatment care centers have yet to be developed to address this issue and to provide the standard of care to this group of patients.

This study aimed to describe the initiation of a health care clinic specializing in VVGvHD. To the best of our knowledge, no similar clinic exists in Israel.<sup>[2,5,6]</sup>

## Developing a Specialized Clinic for Vulvar and Vaginal Graft vs. Host Disease: A Multidisciplinary Approach

The VVGvHD clinic was founded as part of BMT day care in our hospital in a joint initiative of the nursing staff, the medical director of the department, and a gynecologist specializing in the vulva and vaginal disease. Gynecologic symptom assessment by nurses is included as a part of the implementation of routine work in the department and daycare. This assessment is also considered during admission and upon discharge in accordance with a structured checklist.

In 2009, specific guidelines were developed by the specialist gynecologist in the clinic to manage health care for women undergoing a transplant from a donor. A retrospective search was performed by the nursing staff in the daycare to detect post-BMT patients who might benefit from this clinic. The protocol was presented in a staff meeting to raise the awareness and commitment of the staff.

A total of 81 women aged 2–66 years (median age = 38 years) visited the clinic from 2009 to 2015. Of these women, 70 received an allogeneic transplant and 11 underwent autologous transplantation before consultation in this clinic. We detected VVGvHD in 54% of the patients, and this finding is similar to that reported in a previous study.<sup>[5]</sup> These patients attended the clinic for scheduled visits every 2–4 months according to symptom severity.

The repeated visits of these patients to our clinic were considered a long-term follow-up session. On the basis of follow-up data, we observed that VVGvHD may be a fluctuating condition with frequent deterioration and improvement. Therefore, regular examinations are necessary. With active and routine assessment, VVGvHD can be diagnosed in early stages, severe complications can be treated and prevented, and quality of life can be improved.

### Structured Nursing Care

Patients are initially assessed on their first visit to the day care clinic after they are discharged from the BMT department by daycare nurses. The assessment includes anamnesis of vulvovaginal symptoms. As needed, patients are referred to a physiotherapist to strengthen their pelvic muscles and to a sexual counselor. A relationship of trust, sharing, and openness between a nurse and a patient develops before BMT, continues during transplantation, and lasts after discharge because the nursing staff in the BMT department is the same as those in the day care. These nurses support patients and their families during their visit

to the clinic. A patient is referred to a gynecologist when anamnesis; vulvovaginal symptoms have been identified by a nurse or a physician.

A gynecologist treats patients according to the symptoms presented in Box 1. The patients visit the clinic once every 2 months as part of their post-BMT follow-up.

The nurses in the clinic asked some of the women who visited the clinic to share their personal experiences regarding VVGvHD. All of the patients consented to share the following information.

### Case Report

SF is a 46-year-old woman diagnosed with AML, married, and mother of five children. She underwent allogeneic BMT from a foreign donor in 2008. Since then, she has suffered from remission and GvHD in various locations, namely, eyes, intestines, vulva, and vagina. According to the patient, “VVGvHD caused dryness, pain that prevented me from having a normal sex life and emotional problems and frustration.”

She described her discomfort and pain to the nurses in the BMT clinic as part of the routine follow-up after BMT. The nurses assessed her condition and referred her to the VVGvHD clinic. She was treated by the gynecologist in the clinic. The treatment included steroid cream and cyclosporine cream inserted into the vagina. She visited the GvHD clinic every month for further evaluation and coordinated with the gynecologist and the nurses who encouraged her. However, her condition did not sufficiently improve. As such, she was advised to use dilators, in addition to the creams, to treat vaginal scarring. After a year, VVGvHD was alleviated, her symptoms were significantly decreased, and her sexual relationship was restored.

According to SF, “I’m finally healthy inside and out. I’m a healthy and confident wife, mother, daughter, and friend. The nursing staff helped me with their patience, laughter,

#### Box 1: Treatment for vulvar and vaginal graft versus host disease according to symptoms

Vulvar discomfort
Avoid irritants
Clean with warm water
Water-based lubricants
Vulvar graft versus host disease
Intra-vaginal immune suppressive drugs
Cortico-steroids
Cyclosporin
Tacrolimus
Vaginal scarring
Dilators
Estrogen
Severe cases
Surgical intervention followed by dilators

and dependability”The patient visits our daycare every 2–3 months. This case study revealed the importance of careful follow-up in symptom management that helps and improves the quality of life of patients.

## Discussion and Implication for Clinical Practice

The VVGvHD clinic was developed to fulfill the specific needs of female patients who underwent BMT. These patients suffer from substantial debilitating symptoms that are improperly diagnosed and untreated. The pioneer clinic was founded as a joint effort of the multidisciplinary team. However, studies regarding specialty care centers for these patients have been rarely performed. Evidence supporting the optimum treatment for this condition is also insufficient.<sup>[2,5,6]</sup>

We observed the nature of VVGvHD and its response to treatment and follow-up. With active and routine assessment, VVGvHD can be diagnosed in early stages, and severe complications can be treated and prevented.

The case report demonstrated the perceived improvement in the patient's quality of life physically and emotionally. Nurses are mainly involved in identifying patients with specific symptoms which indicate the need for referral to the VVGvHD clinic. These nurses also guide and support these patients. These factors were also evident in the case study. Considering the lack of awareness of patients with VVGvHD, we recommend further research on variables, such as social interaction, intimacy, well-being, and matching interventions, which are possibly associated with VVGvHD.

The assessment and treatment of VVGvHD in women after allogeneic BMT remain a challenge to BMT teams. To the best of our knowledge, Hadassah is the only clinic providing comprehensive care for this specific population in Israel.

## Limitations

The study was done in only one clinic in Israel, and therefore, the number of participants was limited and cannot reflect the whole population of these kinds of women.

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### Conflicts of interest

There are no conflicts of interest.

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