Treatment of Vaginal Agglutination Complicating Chronic Graft-Versus-Host Disease: A Rare Case Report

Kronik Graft-Versus-Host Hastalığında Vajinal Aglütinasyon Tedavisi: Olgu Sunumu

Kronik Graft-Versus-Host Hastalığı / Chronic Graft-Versus-Host Disease

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Özet

Myelodisplastik sendrom tedavisi için iki yıl önce kemik iliği nakli olan 34 yaşındaki hasta vajinal aglütinasyona bağlı cinsel birlikteliği girememe şikayeti ile jinekooji kliniğimze başvurdu. Vajinal adezyonlar cerrahi yaklaşımla tedavi edildikten sonra topikal estrojen ve tibolon tedavileri başlandı. Ameliyattan iki ay sonra hasta cinsel ilişkiye girebildi. Bu olgu sunumunda graft versus host hastalığının vulvovajinal komplikasyonları, tedavisi ve önlenmesi tartışılmaktadır.

Anahtar Kelimeler

Kemik İliği Nakli; Graft-Versus-Host Hastalığı; Vajinal Aglütinasyon

Abstract

We describe a 34-year old patient with vaginal agglutination, which presented as inability to have sexual intercourse two years after bone marrow transplantation for myelodysplastic syndrome. The vaginal adhesions were freed surgically after local estrogen therapy and tibolone was started. She was able to have sexual intercourse two months after the operation. In this case report, vulvovaginal complications of graft-versus-host disease and their treatment and prevention are discussed.

Keywords

Bone Marrow Transplantation; Graft-Versus-Host Disease; Vaginal Agglutination

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Introduction

Allogenic blood or bone marrow transplantation (BMT) has become an attractive treatment alternative for various diseases, particularly for hematologic diseases. Graft-versus-host-disease (GVHD), an immunologic disorder in which immunocompetent donor T lymphocytes recognize, become sensitized to and react against histocompatibility antigens of the host is a major complication of allogenic BMT. Chronic GVHD affects approximately 25-45% of patients and occurs in >100 days after BMT. Both limited (only skin or liver) and extensive (skin, liver, oral mucosa, lacrimal glands, esophagus, and serosal membranes) forms of chronic GVHD resemble collagen vascular diseases [1]. Vulvovaginal complications such as vulvar atrophy, alopecia of the vulva, vaginal synechiae, stricture and complete obliteration leading to secondary complications such as hematocolpometra may also develop in female patients with chronic GVHD [2-3]. Here, we describe a patient who received allogenic peripheral blood stem cell transplantation (PBSCT) for myelodysplastic syndrome (MDS) and developed chronic GVHD leading to vaginal agglutination.

Case Report

A 34 year-old, gravida 2, para 2 woman with MDS underwent allogenic PBSCT in January 2012 after conditioned with busulfan and cyclophosphamide. GVHD prophylaxis consisted of cyclosporine and short-term methotrexate. On the 20th day, she developed acute GVHD with grade II skin involvement that required high dose methylprednisolone treatment. She gradually progressed to extensive chronic GVHD with skin and oral mucosa involvement. Sicca syndrome (Sjögren's syndrome) accompanied the clinical course. Extracorporeal phototherapy was initiated to reduce steroid usage, which led to serious osteoporosis with compression fractures despite prophylaxis with calcium and vitamin D.

At the end of the second year after the transplant, she came to our clinic with a complaint of inability to have sexual intercourse. She also developed secondary amenorrhea since the transplantation. Gynecologic examination revealed vulvar atrophy, alopecia of the vulva and pubis, and complete obliteration of the introitus. The uterus was atrophic, endometrial thickness was 4 mm, and both of the ovaries were also atrophic and nonfollicular according to transrectal sonographic examination. Follicle-stimulating hormone and luteinizing-hormone (LH) levels were elevated, while estradiol (E2) level was low; 132.1mIU/ml, 57.1mIU/ml, and 5.0pg/ml, respectively. After a month of local estrogen (estriol 1mg/g) usage, dense vaginal adhesions obliterating the lower half of the vagina were freed with blunt and sharp dissection up to the level where the original vaginal mucosa and cervix could be visualized under general anesthesia. The vaginal mucosa and ectocervix were atrophic and fragile. A 3x8cm vaginal dilator made of glass was placed into the vagina and left in place for two days. Tibolone (2.5mg/day, PO) was also administered. The patient continued to use the vaginal dilator and estrogen cream, and returned for pelvic examination three weeks postoperatively, which revealed normal vaginal patency. She was advised to have regular intercourse and to use the mold only during nights. At the two-month postoperative visit, the patient reported that she was able to have comfortable sexual intercourse. Therefore, she was advised to cease the vaginal dilator usage.

Discussion

In 1982, Corson et al. have first addressed gynecologic manifestations of chronic GVHD [2]. They have described four patients with chronic GVHD who developed vaginal inflammation, sicca syndrome, adhesions or stenosis requiring surgical therapy. Vaginal agglutination and its potential complications such as hematocolpometra and endometriosis, related to chronic GVHD have also been reported in six other case reports [3-8]. Our case, to our knowledge, is one of the very few cases of vaginal agglutination accompanying chronic GVHD described in the literature. Secondary amenorrhea either due to vaginal agglutination or ovarian failure due to chemo-irradiation damage often accompanies vulvovaginal problems in these patients. Our patient also had secondary amenorrhea, premature ovarian failure and dense vaginal adhesions.

The etiology of gynecologic problems in allogenic PBSCT patients is multifactorial [7]. One of the causes of premature ovarian failure in this context is the toxicity of the conditioning regimens in myeloablative doses. Abnormalities of humoral and cellular immunity associated with chronic GVHD resembling autoimmune diseases may also contribute to the ovarian failure [1]. However, the histopathologic effects of chronic GVHD itself may explain vulvar atrophy, vaginal dryness, adhesions and strictures in our patient. Hypoestrogenism as a result of concomitant ovarian failure seemed to exacerbate the vulvovaginal symptoms.

Young patients with GVHD usually have iatrogenic premature ovarian failure as well. Therefore, their treatment should include every effort to raise the quality of life, including hormone treatment. In the first case series of 5 patients with gynecologic manifestations of GVHD reported by Corson et al., it has been emphasized that therapy of vaginal manifestations of chronic GVHD should be both local and systemic [2]. We preferred tibolone, which had androgenic activity for our patient, believing that it would have a positive effect both on her mood and libido. However, the preferred type of hormone therapy for these patients needs further investigation. In another case series of 8 patients, Constantini et al. presented the importance of compliance to vaginal dilator program [9], which is in line with our case. As, Haemato-oncology subgroup of the British Committee for Standards in Haematology (BCSH) and the British Society for Bone Marrow Transplantation (BSBMT) have concluded in a joint working group the ultimate goal of the treatment, whichever one is chosen, should be the effective control of GVHD while minimizing the risk of toxicity and relapse [10].

Conclusion

Gynecologic problems may be underestimated during the late period of PBSCT especially in patients with chronic GVHD. Therefore, regular gynecologic examination may prevent complications such as vaginal agglutination, which can result in hematocolpometra, endometriosis and low quality of life due to inability to have sexual intercourse. Early diagnosis is very important since simple measurements such as local estrogen creams and vaginal dilators may be helpful. On the other hand,

for established vaginal strictures, surgery is required, which has the risk of inadvertent bladder and rectal damage due to atrophy and fibrosis.

Competing interests

The authors declare that they have no competing interests.

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