Case Report
Obstet Gynecol Sci 2013;56(4):277-280
http://dx.doi.org/10.5468/ogs.2013.56.4.277
pISSN 2287-8572 · eISSN 2287-8580

Obstetrics & Gynecology Science

Gynecologic complication of chronic graft-versus-host disease: Vaginal obstruction

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Allogenic peripheral blood stem cell transplantation (Allo-PBSCT) is being used to treat hematological malignancies with increasing frequency. Graft-versus-host disease (GvHD) is a complex complication of PBSCT. A 43-year-old woman came to the gynecology clinic for amenorrhea. She had been diagnosed with acute myeloid leukemia 2 years earlier and treated with induction and consolidation chemotherapy. After developing complete remission, she underwent Allo-PBSCT. When she started chemotherapy, her menstrual cycle completely disappeared. Fourteen months after menopausal hormone replacement therapy, it was discovered that her upper vaginal canal was completely obstructed. The lower vagina had an atrophic appearance. We report a rare case of partial vaginal obstruction as a complication of chronic GvHD and review the literature. We expect that this case report provides an opportunity to remind clinician of the gynecologic complications of GvHD.

Keywords: Graft vs host disease; Hematocolpos; Peripheral blood stem cell transplantation; Vagina

Introduction

Allogenic peripheral blood stem cell transplantation (Allo-PBSCT) is being used to treat hematological malignancies with increasing frequency. Allo-PBSCT has many complications, such as infections, veno-occlusive disease of the liver, drug reactions, and graft-versus-host disease (GvHD). GvHD is a complex complication with acute and chronic stages that are categorized based on whether symptoms developed within 100 days after the transplant or later. Currently, the number of days after the transplant is not sufficient to differentiate acute from chronic GvHD. 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 [1]. Manifestations of GvHD involving the skin, gastrointestinal tract, lungs, and liver are well described [2-4]. However, involvement of the vagina has not been well characterized. Therefore, GvHD may be an unfamiliar topic to gynecologists. However, if the possible impact of GvHD on the vulva or vagina is not underestimated, diagnosis and management would not be difficult. This case provides a chance to review the gynecologic complications of GvHD.

Case report

A 43-year-old, gravida 4, para 2 woman came to the gynecology clinic for counseling about premature menopause. She had been diagnosed with acute myeloid leukemia 2 years earlier and treated with induction and consolidation chemotherapy using idarubicin and cytosine arabinoside. After developing complete remission, physician recommended patient to have gynecological examination. At the gynecology clinic office, gynecologist conducted pelvic examination with Papa-

Received: 2012.11.6. Revised: 2013.2.7. Accepted: 2013.2.8.
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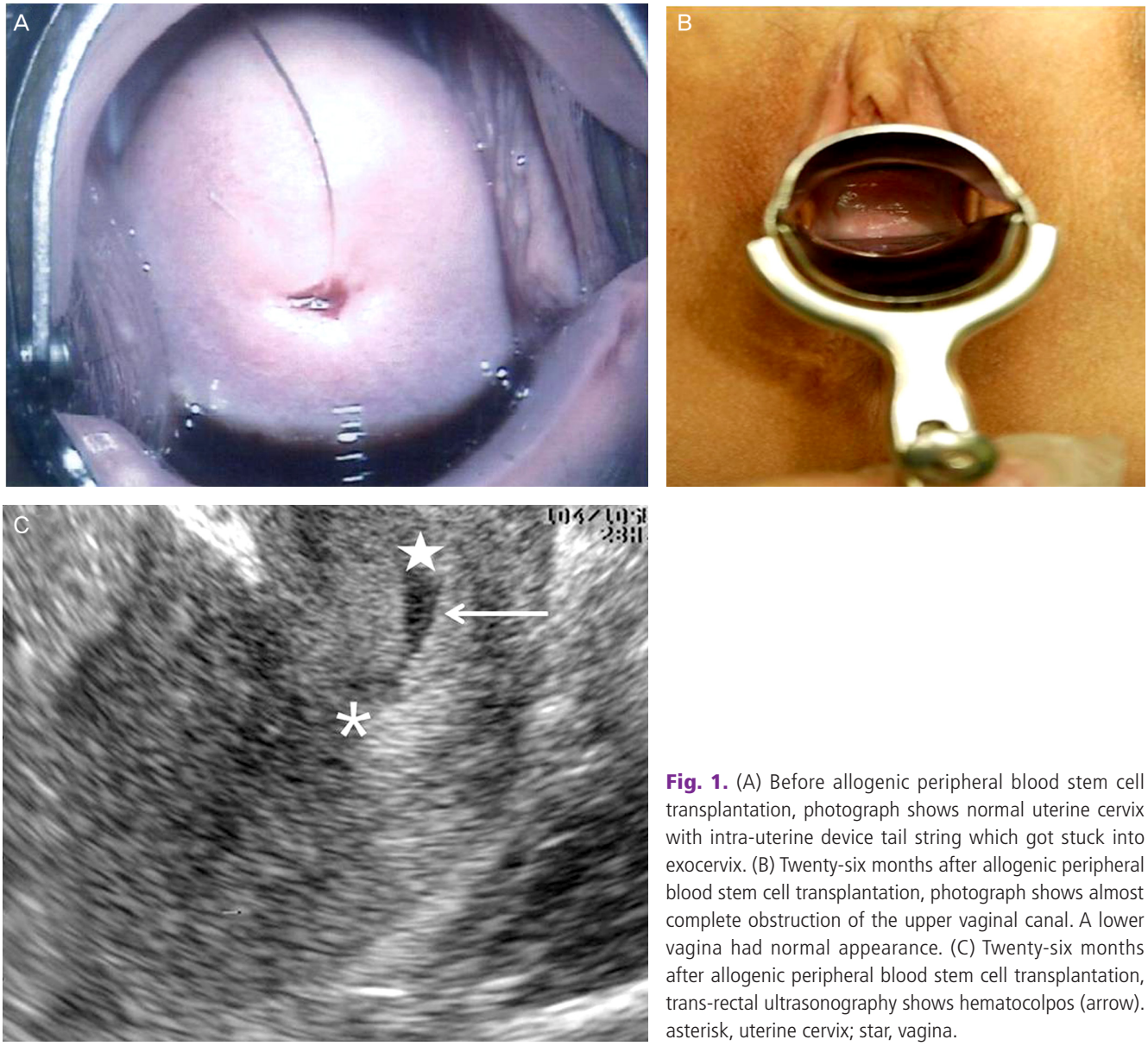

Fig. 1. (A) Before allogenic peripheral blood stem cell transplantation, photograph shows normal uterine cervix with intra-uterine device tail string which got stuck into exocervix. (B) Twenty-six months after allogenic peripheral blood stem cell transplantation, photograph shows almost complete obstruction of the upper vaginal canal. A lower vagina had normal appearance. (C) Twenty-six months after allogenic peripheral blood stem cell transplantation, trans-rectal ultrasonography shows hematocolpos (arrow). asterisk, uterine cervix; star, vagina.

nicolaou (Pap) test. The uterine cervix revealed cooper intra-uterine device (IUD) tail string which got stuck into exocervix, but otherwise non-specific finding (Fig. 1A). Of course the IUD was immediately removed. The result of Pap test was reactive cellular changes. Eleven days after gynecologic consultation, patient underwent Allo-PBSCT and the donor was her younger brother. There was no evidence of residual disease on a bone marrow biopsy performed 10 months after transplantation.

Twenty-six months after Allo-PBSCT, she revisited our gynecology clinic and it was found that her follicle-stimulating hormone level was greater than 100 IU/mL and estradiol was 4.14 pg/mL. By reviewing the patient medical record and taking a medical history, it was found that when she started chemotherapy, her menstrual cycle completely disappeared. About one year after chemotherapy, the patient tried coitus with husband, but vaginal dryness and dyspareunia were very severe, so could not have sexual intercourse. However, patient had no other menopausal symptoms like hot flush, sleep disturbance, mood swing and so on. To introduce sequential hormone replacement therapy (HRT), we performed clinical examination. The clinical examination revealed extensive vulvar atrophy with flattening but otherwise non-specific appearance including uterine cervix. After that, the patient started sequential HRT.

Fourteen months after initiation of HRT, it was discovered that her upper vaginal canal was completely obstructed (Fig. 1B). The lower vagina had a normal appearance. The human papillomavirus (HPV) deoxyribonucleic acid (DNA) chip test and Pap test were conducted in vagina not in uterine cervix because of obstruction of upper vaginal canal. The HPV DNA chip test was positive for HPV (other type) in the vagina. The Pap test was negative. Trans-rectal ultrasonographic findings were hematocolpos and atrophic uterus (Fig. 1C). We explained the results to the patient and provided reassurance. The patient is currently being treated with tibolone and we recommended non-hormonal moisturizing vaginal gel and vaginal dryness and dyspareunia were much improved.

Here, we present the case of a woman who after Allo-PBSCT, showed obstruction of the upper vagina as a chronic complication of GvHD.

Discussion

GvHD is a systemic syndrome. The commonly involved organs include the skin, mouth, liver, eyes, esophagus, and upper respiratory tract. Clinical features are similar to those of autoimmune diseases, including scleroderma, Sjögren's syndrome [5], lichen planus, and primary biliary cirrhosis [6]. However, gynecologic manifestations of GvHD in patients treated with Allo-PBSCT are rare and probably underestimated. Vaginal inflammation, dryness, stricture and stenosis have been reported, together with desquamative web formation [7].

For 80% of patients with chronic GvHD, drying of the vagina would be expected [8]. It is hypothesized that inflamed and atrophic vaginal surfaces might cause obstruction of the vaginal canal. It should be recognized that the severity of vaginal and vulvar symptoms does not correlate with the severity of GvHD found in other organ systems. That is, some women with severe vaginal stenosis have only mild chronic GvHD.

There have been some reports describing similar cases [9-13]. Corson et al. [9] first reported vaginal involvement in five women with sclerosing vaginitis and stricture formation in 1982. Since then, several cases have been reported with complete vaginal obliteration [10-13]. Vaginal obstruction limits the ability to perform a routine Pap test and prevents sexual intercourse. However, most cases show mild chronic GvHD of the vulva or vagina that may be asymptomatic and detected only on examination. Because of this, careful gynecologic approach is needed in Allo-PBSCT [14]. Management of vulvovaginal lesions is based on the onset of therapy at early stages of the disorder and maintenance of sexual activity. HRT is recommended when menopause is confirmed, but its local beneficial effects are limited in advanced disease. Sequential HRT may contribute to the formation of hematocolpometra in the presence of vaginal synechiae. It has been reported that HRT does not influence the severity or activity of GvHD and can be safely used as a prophylactic measure to treat ovarian failure [15].

Management of the early stages of anatomical distortion of the external and internal genitalia includes vaginal dilatation, local corticotherapy, and estrogen therapy to help prevent stenosis. Surgery is indicated in advanced cases to restore normal anatomy. Progression or recurrence of lesions may be observed, despite treatment, in cases of extensive GvHD. Vulvar and vaginal GvHD seems to be a discrete entity in the continuum of chronic GvHD. As more studies are performed, women who experience these complications can promptly and effectively be treated.

We report a rare case of partial vaginal obstruction as a complication of chronic GvHD and review the literature. We expect that this case report provides an opportunity to remind clinician of the gynecologic complications of GvHD.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

Acknowledgements

This work was supported in part by the Soonchunhyang University Research Fund.

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