

Research Letter

Hematocolpos as a complication of chronic graft-versus-host disease

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Allogeneic hematopoietic stem cell transplantation (AHSCT) is being used to treat hematological malignancies with increasing frequency. AHSCT has many complications, such as infections, veno-occlusive disease of the liver, drug reactions, and graft-versus-host disease (GvHD). Pathogenesis of GvHD is believed to be a complex immune response, primarily T-cell mediated, in which the grafted donor cells recognize the host as foreign. GvHD can involve the skin, gastrointestinal tract, lungs, and liver [1]. It is a difficult-to-diagnose disease that gynecologists may not be familiar with. Our case gives guidance on the prevention and management of the gynecologic complications of GvHD.

A 44-year-old, gravida 2, para 2 woman had been diagnosed with chronic myeloid leukemia 4 years earlier, and was treated with imatinib and hydroxyurea for 1 year. She had also suffered from dysmenorrhea 4 years earlier and had a $3 \times 2 \text{ cm}^2$ left ovarian cyst that suggested endometriosis. After entering complete remission, she underwent AHSCT. One year after the AHSCT, she developed chronic GvHD with pulmonary organ involvement and began menopause. Her laboratory findings revealed a follicle-stimulating hormone level of 49 IU and estradiol (E2) of 19. Sequential hormone replacement therapy was introduced for the menopause symptoms.

Subsequently, she presented with a 5-day history of abdominal pain. Clinical examination revealed extensive vulvar atrophy with flattening. She had almost complete obstruction of the entire vaginal canal (Fig. 1). Vaginal biopsies revealed chronic nonspecific inflammation with fibrosis. We performed the human papillomavirus (HPV) DNA chip test to screen for precancerous risk factors. The test was positive for HPV (other type) in the vagina. Vaginal stenosis limited the ability to perform a routine Papanicolaou test and

prevented coitus. Ultrasonography showed hematometra with hematocolpos (Fig. 2).

Computed tomography (CT) revealed that the vaginal canal and uterus were filled with a heterogeneous, high-density hematoma (Fig. 3). We dilated the vagina and performed a hysteroscopic-guided biopsy of the endometrium. The pathology revealed chronic nonspecific inflammation of the vagina and endometrium. Six months after vaginal dilation, a Papanicolaou test of the cervix revealed atypical squamous cells of undetermined significance. Postoperatively, she was treated with topical immunosuppressive therapy and vaginal dilators. Six months later, the Papanicolaou test revealed low-grade squamous intraepithelial lesions, and the HPV DNA chip test was positive for HPV 62. She progressed to obstruction of the vaginal canal and abdominal pain. We performed a total abdominal hysterectomy. The pathology revealed cervical intraepithelial neoplasia, grade I (HPV infection). We present a woman who developed hematocolpos as a complication of chronic GvHD after AHSCT.

GvHD remains a major complication in AHSCT patients [2]. Classically, GvHD has been classified as acute and chronic

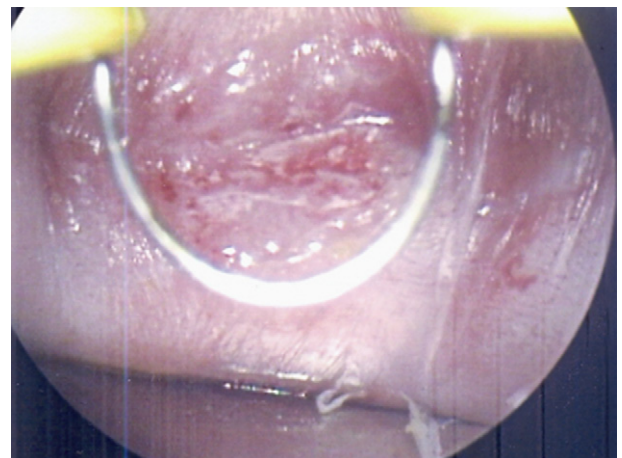


Fig. 1. Photograph shows almost complete obstruction of the entire vaginal canal.

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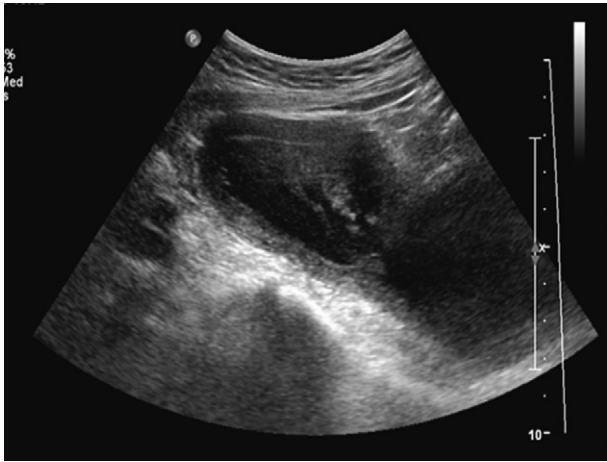


Fig. 2. Ultrasonography shows hematometra with hematocolpos.



Fig. 3. Computed tomography scan shows that the vaginal canal and uterus were filled with a heterogeneous, high-density hematoma.

GvHD, 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 [2]. Chronic GvHD is the most common complication after transplantation, described in 60–80% of patients. Chronic GvHD is more heterogeneous in its manifestations, and many of the symptoms resemble those of autoimmune disorders [3]. Skin involvement is reported in more than 90% of the cases. Gynecologic manifestations of chronic GvHD are rare and may be underestimated. Because mild chronic GvHD of the vulva or vagina may occasionally be asymptomatic and detected only on examination, gynecologic care is needed in AHSCT [4].

Regarding the gynecologic care, first, the genital area is best cleaned with warm water rather than with soap or feminine wash products [4]. Second, if symptoms such as dysuria, dryness, tenderness to touch, and dyspareunia develop, we prescribe topical estrogen therapy prophylactically to prevent

the progression of local symptoms. Third, hormone replacement therapy is recommended when menopause is confirmed, although this can contribute to the formation of hematocolpometra in the presence of vaginal synechiae progression, such as in our case. Finally, management of GvHD may require vaginal dilatation, local corticotherapy, and estrogen therapy, as in our case. Surgery is indicated in advanced cases to restore the normal anatomy [5]. In some cases, laparoscopy may be considered to exclude endometriosis that is obstructing the menstrual flow occurring as a result of vaginal stenosis [6].

Systemic immunosuppressive therapy is also indicated for vulvovaginal GvHD that progresses or fails to improve after treatment with local measures [4]. Hematologists, physicians, and oncologists are interested in chronic GvHD. Nevertheless, the gynecologist should provide counseling and examine the vagina and pelvis regularly to prevent vagina and vulvar GvHD.

References

- [1] Korngold R. Biology of graft-vs.-host disease. *Am J Pediatr Hematol Oncol* 1993;15:18–27.
- [2] Penas PF, Zaman S. Many faces of graft-versus-host disease. *Australas J Dermatol* 2010;51:1–10.
- [3] Dani KA, Stobo DB, Capell HA, Madhok R. Audit of literacy of medical patients in north Glasgow. *Scott Med J* 2007;52:21–4.
- [4] Couriel D, Carpenter PA, Cutler C, Bolanos-Meade J, Treister NS, Gea-Banacloche J, et al. Ancillary therapy and supportive care of chronic graft-versus-host disease: national institutes of health consensus development project on criteria for clinical trials in chronic graft-versus-host disease: V. Ancillary therapy and supportive care working group report. *Biol Blood Marrow Transplant* 2006;12:375–96.
- [5] Anguenot JL, Ibecheole V, Helg C, Piacenza JM, Dumps P, Bonnefoi H. Vaginal stenosis with hematocolpometra, complicating chronic graft versus host disease. *Eur J Obstet Gynecol Reprod Biol* 2002;103:185–7.
- [6] Jain SP, Henry RJ. Haematocolpos following allogeneic bone marrow transplantation for chronic myeloid leukaemia. *BJOG* 2001;108:1309–10.