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Olgu Sunumu / Case Report

Ovarian Failure Induced Labial Adhesion after Hematopoietic Stem Cell Transplantation

Hematopoetik Kök Hücre Transplantasyonu İle Tetiklenen Ovaryan Yetmezliğe Bağlı Gelişen Labial Adezyon

Mustafa Ulubay[1], Uğur Keskin[1], Ulaş Fidan[1], Fahri Burçin Firatligil[1], Rıza Efendi Karaca[1], Mustafa Öztürk[2], İbrahim Eker[3], İbrahim Alanbay[1], Ali Ergün[1].

[1]Gülhane Military Medicine Academy, Department of Obstetrics and Gynecology. 3 Department of Hematology ANKARA

[2]Etimesgut Military Hospital, Obstetrics and Gynecology Service, ANKARA

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ABSTRACT

Labial adhesion is a disease which occurs after complete or partial fusion of labium majors and / or minors. It usually originates at the posterior fourchette and sometimes progresses towards urethral opening and clitoris. Incidence of labial adhesion is most frequent in prepubescent girls with a peak incidence at the age of 13 – 23 months. The factors that cause labial adhesion remain unknown. Vaginal irritation or inflammation process with underlying hypoestrogenism can cause this disease.We present a case who developed labial adhesion due to ovarian failure after hematopoietic stem cell transplantation.

Key words: labial adhesion, hematopoietic stem cell transplantation, hypoestrogenism.

ÖZET

Labial adezyon, labium major ve / veya minör lerin tamamen veya kısmi birleşmesi sonrası oluşan bir hastalıktır. Genellikle arka forşette gelişir ve bazen de üretra ağzına ve klitorise kadar uzanım gösterebilir. Labial adezyon daha çok puberte öncesi kız çocuklarında görülürken, 13-23 aylık yaş gurubunda pik yapar. Labial adezyona sebep olan faktörler bilinmemektedir. Hipoöstrojene bağlı gelişebilen vajinal irritasyon veya inflamasyon bu duruma sebep olabilecek hipotez olarak düşünülmektedir. Bu olguda hematopoetik kök hücre transplantasyonu sonrası gelişen ovaryan yetmezliğe bağlı gelişen labial adezyon sunuldu.

Anahtar kelimeler: Labial adezyon, hematopoetik kök hücre transplantasyonu, hipoöstojenizm.

INTRODUCTION

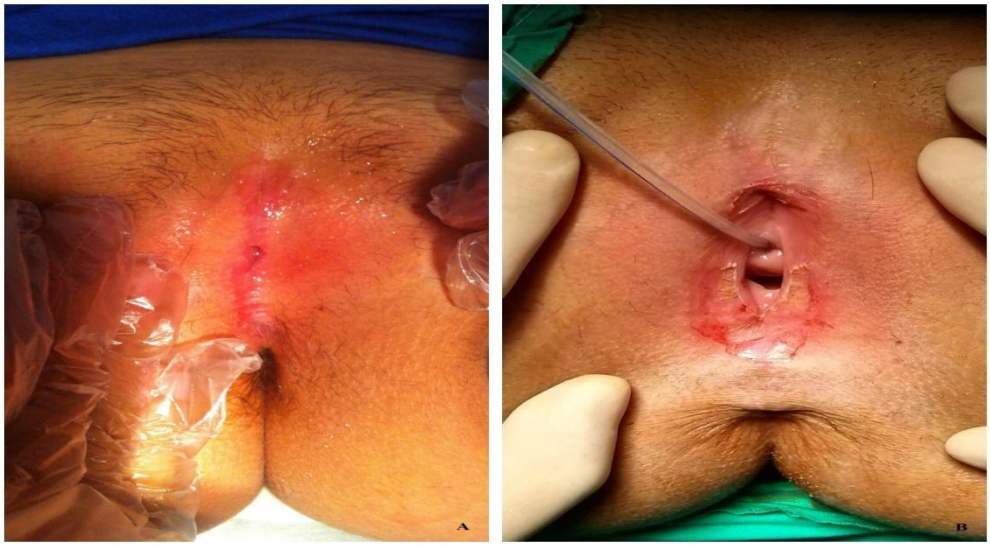
Labial adhesion is a condition which is described as complete or partial fusion of labium majors and / or minors. The incidence of labial adhesion is most frequent in prepubescent girls with a peak incidence at the age of 13 – 23 months[1]. Although the incidence is between 0.6% and 3% percentage, it is thought that the incidence is significantly higher than expected because of the asymptomatic patients[2].The factors that cause labial adhesion remain unknown. Vaginal irritation or inflammation process with underlying hypoestrogenism is thought as a hypothesis, which can cause this disease[3].However, dermatological problems, trauma, eroded vulvar epithelium, recurrent urinary tract infections may be seen in

the baseline of the process.The diagnosis of labial adhesion is easy with physical examination which is made by inspection of the external genitalia[4]. But it should be distinguished from congenital anomalies and imperforate hymen. This discrimination can be done with midline raphe sign which is seen in labial adhesions[5]. Chronic myeloid leukemia can be a life threatening disease and the treatment of this disease can cause chemotherapy induced ovarian failure. In our case, we presented a labial adhesion, which had been seen after chemotherapy induced ovarian failure.

CASE REPORT

A ten years old girl was diagnosed as chronic myelogenous leukemia (CML) by leucocytosis and systematic work-up, including Philadelphia chromosome-positive cytogenetic and molecular analysis in peripheral blood and bone marrow. Remission was achieved with imatinib treatment alone. She had received imatinib treatment until her hematopoietic stem cell transplantation (HSCT) at 12 years old from her full matched 17 years old brother, which was because HSCT from matched sibling donor is the standard of care in pediatric CML. Her hypothalamo-pituitary-gonadal axis evaluation before HSCT was prepubertal (Follicular Stimulating Hormone (FSH): 3.9 IU/mL, Luteinizing Hormone (LH): 0.9 IU/mL, Estradiol (E2): 13 pg/mL, Progesterone (P): 0.22 ng/mL, Beta-human Chorionic Gonadotrophin (β-hCG): negative), there was no evidence of stimulation of the hypothalamo-pituitary-gonadal axis. Stem cell source was bone marrow and she was conditioned with a regimen including busulfan and cyclophosphamide. She did not receive total body irradiation. She was given methotrexate and cyclosporine for graft-versus-host disease (GvHD) prophylaxis. Full engraftment and full donor type chimerism was achieved with a mean value of total 2,3 x 10^6 CD 34 + cellsper kg of patient weight without any serious complication. Acute or chronic GvHD was not developed. On the second year controls after HSCT, she had been diagnosed as hypergonadotropic hypogonadism. Her breasts were Tanner stage 3 and pubic hair Tanner 3. In the inspection of the external genitalia we saw that labium majors were attached to each other in the midline of vulva with including clitoris (figure 1A). However there was an opening over the urethra in the adhesion line. She had no history of genital malformation or genital trauma. Pelvic ultrasonography revealed blood filled endometrial cavity with the uterus 7x6x6 centimeters in diameter (hematometra) and there were no follicular activities in bilateral ovaries. FSH was 0.33 IU/mL, LH was 0.05 IU/mL, E2 was undetectable, P was 0.02 ng/mL and β-hCG was negative observed in the laboratory findings after the chemotherapy treatment. We thought primary ovarian failure depending on chemotherapy that causes labial adhesion by hypoestrogenism with our observations.

We gave her, topical estrogen cream application (Estriol ® vaginal cream) once in a day for 3 months usage and 17-β estradiol tablets (Estrofem 2 mg. ®) for oral usage. After the treatment, we proposed her, a control examination. In the control exam, we examined that, she had failed from topical estrogen treatment and continued symptoms of lower genital tracts' infection. So, that is why, an operation was performed to the patient. The patient was underwent general anesthesia and prepared for lysis of the adhesion. Firstly urine catheter was placed into urethra, than the adhesion tissue was incised from clitoris to the posterior fourchette using lancet, and then the incised tissue was sutured with 6/0 monofilament suture and the operation was ended (figure1B). Next, the area was locally infiltrated with combination of nitrofurazone pomade (Furacin ® soluble dressing pomade) and lidocaine pomade (Anestol ® pomade). The patient was discharged with topical estrogen pomade, and called for the control examination. There was no recurrence with the 6-months follow-up.



1A. Adhesioned labia majors in the midline of vulva. **1B.**After the surgery, lysis of adhesion.

DISCUSSION

Labial adhesion is a condition which is also described as complete or partial fusion of labium majors and / or minors. It usually originates at the posterior fourchette and sometimes progresses towards urethral opening and clitoris[6].

In fact, labial adhesions are so frequently than expected because of asymptomatic patients. These asymptomatic patients can urinate or have menses and they have no discomfort with them[2]. So,it is challenging to determine which patient would have medication or get surgery. After the onset of puberty, the estrogen hormone which is produced from ovaries, could fix the labial adhesions spontaneously[6]. Regarding to literature, if there is an obstruction in the outlet of perineum for urination or having menses, immediate intervention should be done like surgery. Otherwise there is no need to correct the adhesions till puberty. However there is no randomized trial about treatment of adhesions versus waiting for spontaneously in the literature. In our patient, she could urinate, but have no menses after chemotherapy treatment. The cause of labial adhesion appears to thin vulvar epithelium secondary to low estrogen levels. We also gave her treatment for hypogonadotrophic hypogonadism secondary to chemotherapy. If the hormone levels of the patient were enough about hypothalamo hypophyseal ovarian axis, maybe we wouldn't give any treatment for her. So, we would like to wait for fixing labial adhesion spontaneously by estrogen.In literature, treatment with topical estrogen has been associated with a success rate up to 47% to 100%. The rate differs, depending on usage frequency and length[4,7]. And there is an alternative topical application for estrogen, is betamethasone. The success rate of this treatment is up to 68%[8]. But we didn't use topical steroids in our case.

These topical treatments have also side-effects. Mastalgia, tenderness in breasts, vaginal pruritus and pigmentation, cervical hypersecretion and headache are the side-effects of the estrogen topical usage[7,8]. The steroid therapy may cause, skin burning and irritation, skin atrophy, striae and miliaria. But in the usage of labial adhesion treatment, these side-effects aren't seen, so steroid therapy appears safer than estrogen

therapy[8]. If the patient don't have any benefit from topical treatment, surgical separation would be tried in an option. By the time, fibrous tissue and thicken adhesions could be developed after the surgery[6]. In our opinion, by the side of the therapy, education of the patients and / or parents is very important. They are also educated for signs of urinary or genital tracts' infections and recurrence of the adhesions.

CONCLUSION

Whereas 10%–50% of women of reproductive age may have premature ovarian failure after exposure to gonadotoxic chemotherapy in a nontransplantation setting, the gonadotoxicity after HSCT is significantly greater owing to higher chemotherapy doses and possible total-body irradiation. Over 70% of patients after HSCT will have premature ovarian failure. The real incidence of ovarian damage after HSCT is difficult to assess. Series reporting ovarian function and pregnancies after HSCT vary greatly in terms of endpoints, number of patients included, age at and indications for BMT, conditioning regimens and duration of follow-up. The risk of premature ovarian failure is very high, however, and increases with age and in case of HSCT conditioning treatment with total body irradiation[9,10].

It is also important to realize that, the higher chemotherapy in HSCT could cause labial fusion because of hypoestrogenic status. Not only, immediate hormone replacement therapy for pubertal advance is necessary, but also protecting menstrual regulation and hypoestrogenic state of genital tract development is important. Although local estrogen therapy for labial fusion is successful in most of the pediatric patients, surgical intervention can rarely be necessary. Surgical intervention is easy to perform, an effective and rapid treatment for labial adhesions.

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Disclosure of Interests

The authors declare that they have no competing interests.

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Yazışma Adresi / Address for Correspondence:
Dr. Fahri Burçin Fıratlıgil
Gülhane Military Medical Academy
Department of Obstetrics and Gynecology
ANKARA
E-mail: md.fahri@gmail.com

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