Case Report / *Olgu Sunumu*

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Ulcus Vulvae Acutum: Is it a Actually Rare Condition?

Ulcus Vulvae Acutum: Gerçekten Nadir Bir Durum mu?

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Abstract

Ulcus vulvae acutum (UVA) was defined by Lipschütz and is also known as primary aphthous ulcer or non-sexually transmitted reactive acute genital ulcer. Its etiology is unknown. Diagnosis is made by excluding other infectious and non-infectious causes that may be responsible for vulvar ulcer. A 12-year-old female patient presented with a rapidly growing pustule-like lesion that appeared in the genital area four days ago, progressing with swelling and tenderness. On physical examination, no pathological findings were found except a very painful ulceronecrotic lesion with purulent discharge at the entrance of the vagina at six o'clock. In complete blood count, hemoglobin level was 12.6 g/dL, white blood cell was 4.210/mm^3 and platelet count was 187.000/mm^3. Erythrocyte sedimentation rate was 14 mm/hr and C-reactive protein was 26 mg/L. Serum biochemistry analysis and complete urinalysis were normal. After all cultures were taken, the patient was started on empirical intravenous piperacillin-tazobactam and fluconazole treatment. Oral paracetamol, ibuprofen and topical lidocaine were added to the treatment in addition to antimicrobial agents. Eye consultation was requested in terms of Behçet's disease, uveitis was not seen. Pathergy test and HLA-B51 were negative. Vaginal and urine cultures were negative. Epstein-Barr virus, cytomegalovirus, herpes simplex virus (HSV) types I and II, *Toxoplasma gondii*, parvovirus B19, hepatitis B virus, hepatitis C virus, hepatitis A virus, human immunodeficiency virus and VDRL tests were negative. With the preliminary diagnosis of UVA, the patient was started on intravenous methylprednisolone (2 mg/kg/day). Topical steroids and anesthetics were applied to the lesions. After methylprednisolone treatment, the ulcer shrank rapidly and the pain was noticeably reduced. On the sixth day of her hospitalization, the dose of methylprednisolone was reduced to 1 mg/kg/day and she was discharged. No new lesions were observed in the follow-up and methylprednisolone was gradually discontinued within three weeks. No new lesion developed in the

Öz

Ulcus vulvae acutum (UVA), Lipschütz tarafından tanımlanmış olup primer aftöz ülser veya non-seksüel geçişli reaktif akut genital ülser olarak da bilinmektedir. Etiyolojisi bilinmemektedir. Tanı, vulvar ülserden sorumlu olabilecek enfeksiyöz ve enfeksiyöz olmayan diğer nedenler dışlanarak konur. On iki yaşında kız hasta dört gün önce genital bölgede ortaya çıkan, hızla büyüyen, şişlik ve hassasiyetle ilerleyen püstül benzeri lezyon şikayeti ile başvurdu. Fizik muayenede vajen girişinde saat altı pozisyonunda pürülan akıntı olan çok ağrılı ülseronekrotik lezyon dışında patolojik bulguya rastlanmadı. Tam kan sayımında hemoglobin düzeyi 12.6 g/dL, beyaz kan hücresi 4.210/mm^3 ve trombosit sayısı 187.000/mm^3 olarak bulundu. Eritrosit sedimentasyon hızı 14 mm/saat ve C-reaktif protein 26 mg/L idi. Serum biyokimya analizi ve tam idrar tahlili normaldi. Tüm kültürler alındıktan sonra hastaya ampirik intravenöz piperasilin-tazobaktam ve flukonazol tedavisi başlandı. Tedaviye antimikrobiyal ajanlara ek olarak oral parasetamol, ibuprofen ve topikal lidokain eklendi. Behçet hastalığı açısından göz konsültasyonu istendi, üveit görülmedi. Paterji testi ve HLA-B51 negatifti. Vajinal ve idrar kültürleri negatifti. Epstein-Barr virüs, sitomegalovirüs, herpes simpleks virüs (HSV) tip I ve II, *Toxoplasma gondii*, parvovirus B19, hepatit B virüsü, hepatit C virüsü, hepatit A virüsü, insan immün yetmezlik virüsü ve VDRL testleri negatif bulundu. UVA ön tanısı ile hastaya intravenöz metilprednizolon (2 mg/kg/gün) başlandı. Lezyonlara topikal steroid ve anestezikler uygulandı. Metilprednizolon tedavisinden sonra ülser hızla küçüldü ve ağrı belirgin şekilde azaldı. Yatışının altıncı gününde metilprednizolon dozu 1 mg/kg/gün'e düşürülerek taburcu edildi. Takipte yeni lezyon gözlenmedi ve metilprednizolon üç hafta içinde kademeli olarak kesildi. Dokuz aylık takipte yeni lezyon gelişmedi. Genital ülserlerin en yaygın nedeni HSV'dir ve cinsel aktiviteyle ilişkilidir. Çocuklarda vulva ülseri görüldüğünde cinsel aktivite ve cinsel istismar öyküsü dikkatle

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nine-month follow-up. The most common cause of genital ulcers is HSV and is associated with sexual activity. When vulvar ulcer is seen in children, sexual activity and sexual abuse history should be carefully questioned. If there is no history of sexual activity, UVA should be considered in the differential diagnosis after excluding all other possible causes.

Keywords: Children, genital ulcer, Lipschütz ulcer, ulcus vulvae acutum

sorgulanmalıdır. Cinsel aktivite öyküsü yoksa, diğer tüm olası nedenler dışlandıktan sonra ayırıcı tanıda UVA akla gelmelidir.

Anahtar Kelimeler: Çocuklar, genital ülser, Lipschütz ülser, ulcus vulvae acutum

Introduction

Ulcus vulvae acutum (UVA), which was first described by Austrian dermatologist Lipschütz, is also known as primary aphthous ulcer or reactive non-sexual acute genital ulcer (1,2). It is characterized by the presence of a single or multiple necrotic ulcerations which suddenly appears in young adolescent virgin girls mostly and causes severe pain impeding their lives (1,3,4). Systemic symptoms such as fever, myalgia, fatigue, loss of appetite, headache, diarrhea, oral aphthae, cervical lymphadenopathy, tonsillitis, and respiratory symptoms accompany the ulcer (3-8).

Its etiology is unknown. Diagnosis is made by excluding other infectious and non-infectious causes which can be responsible for vulvar ulcer (2,7). In some of the cases, infections caused by Epstein-Barr Virus (EBV), cytomegalovirus (CMV), *Mycoplasma*, paratyphoid, influenza A and *Toxoplasma gondii* are considered as triggering factors on the formation of ulcer, which are detected before or during the ulcer (2-9). Non-infectious causes are aphthous ulcer, Lichen planus, inflammatory bowel disease, Behcet's disease, drug reaction, systemic lupus erythematosus, pemphigus, malignancy, trauma, burns and foreign bodies (3).

Case Report

A 12-year-old girl had a pustule-like lesion which appeared on her genital region four days ago and grew rapidly with a swelling and tenderness. Her axillary body temperature was 39°C and she also had a headache. The patient went into a private hospital and herpes ulcer was considered, then she was consulted to the clinic of obstetrics and gynecology. A culture of vaginal secretion was performed and candida infection was considered. The patient was admitted to our hospital because of her ongoing symptoms on the 5th day of her complaints. Before the admission, she did not take any medication except analgesics. In patient's history, we learned that she had a similar pustular-like lesion with mild pain on her genital region, and she went to the clinic of dermatology. She was prescribed topical steroid, topical antibiotic and oral acyclovir and her symptoms reduced after five days with these drugs. Her family history was unremarkable. On physical examination, no pathological findings were observed other than a very painful ulceronecrotic lesion with purulent discharge which was on the entrance of the vagina, at six o'clock position (Figure 1). She had severe pain and could not close her legs. The pain was aggravated when she urinated.

Figure 1. A very painful ulcero-necrotic lesion with purulent discharge which was on the entrance of the vagina, at 6 o'clock position.

Complete blood count showed a hemoglobin level of 12.6 g/dL, a white blood count of 4.210/mm^3 (70% neutrophils, 24% lymphocytes, 6% monocytes), and a platelet count of 187.000/mm^3. Erythrocyte sedimentation rate was 14 mm/h and C-reactive protein was 26 mg/L. Serum biochemistry analysis and complete urinalysis were normal. Due to the fact that the lesion seemed necrotic and had a yellow-green discharge, discharge culture was performed, and intravenous piperacillin-tazobactam and fluconazole were administered empirically. Beside antimicrobial agents, oral paracetamol, ibuprofen and topical lidocaine were added to the treatment.

Because of the previous history of a similar lesion, she was consulted to the departments of ophthalmology, dermatology and pediatric rheumatology for Behçet disease. Uveitis was not observed and Pathergy test and HLA-B51 were negative. Vaginal and urine cultures were negative. On the third day of hospitalization, since necrotic appearance and purulent discharge both disappeared, the patient did not have fever anymore, and the cultures were negative, piperacillin-tazobactam and fluconazole were stopped. Serological tests for EBV, CMV, herpes simplex virus (HSV) type I and II, *Toxoplasma gondii*, parvovirus B19, hepatitis B virus (HBV), hepatitis C virus (HCV), hepatitis A virus (HAV), human immunodeficiency virus (HIV), and VDRL were found to be negative. Anti-nuclear antibody (ANA) was negative and serum immunoglobulin levels were normal according to her age. The only positive result was influenza B in the respiratory

Figure 2. The appearance of the healed lesion.

tract specimen. During follow-up examinations, it was found that there were actually two ulcers under the discharge. Biopsy was not performed due to considering that the process is painful and non-diagnostic.

The patient was started on intravenous methylprednisolone (2 mg/kg/day) with the preliminary diagnosis of UVA. Application of topical steroid and anesthetic on the lesions was continued. After methylprednisolone treatment, the ulcer rapidly shrank and the pain markedly relieved. On the sixth day of hospitalization, the dosage of methylprednisolone was reduced to 1 mg/kg/day and she was discharged. The patient was recalled for follow-up examination at our outpatient clinic. Her pain was reduced, the lesions on the vaginal region were healed. No new lesions were evident in the follow-up and the methylprednisolone was stopped gradually within three weeks. During the nine month follow-up, there were no new lesions and complaints (Figure 2).

Discussion

UVA is a rare disease. Lipschütz first defined the disease in a case of a 17-year-old in Vienna (1). The disease is also called as Lipschütz ulcer. In the United States of America, the first case was reported in a 12-year-old girl by Rostenberg in New York (10). Later cases have been reported in the literature as small series of cases and mostly as isolated single case.

UVA typically causes very painful ulcers on the vulva; the lesion is usually seen in the form of necrotic and covered with gray-yellow exudate, and the ulcer is almost always on the labia minora (11,12). Mostly systemic symptoms such as fever, fatigue, lymphadenopathy, headache, diarrhea, tonsillitis, and a flu-like illness are the accompanying symptoms (2,7). The age group it is seen most is young adolescent girls, and most of them have no history of sexual contact (13). The etiology is unknown. But it is thought that some of the infectious agents may be a triggering factor. The most related infectious agent is EBV (11-14). Among the other triggering agents are *Mycoplasma* spp., CMV, parvovirus B19, influenza A, and *Salmonella typhi* (7,15).

In the literature, the disease has been reported as single cases; meanwhile a few series of cases have also been published. Some of those series of cases include both adult and child patients. In Portugal, in a retrospective study carried out by Baptista, out of 110 women with acute genital ulcer between the ages of 10-79, 33 of them were diagnosed with Lipschütz ulcer. Half of the cases were under the age of 24 and their symptoms started 3.6 days before their application to the hospital. The most significant complaint of the patients was determined as vulvar pain, and the pain was observed in 84% of the patients. In two thirds of the patients, non-gynecologic symptoms beginning the previous week were identified. In one third of the patients, fever was monitored. While in half of the patients, granulation tissue was observed on the surface of the ulcers, necrosis was seen only in 12% of them. In 27% of the cases, a triggering factor was found; 3% of them were determined as CMV, 3% of them were *Mycoplasma*, 2% of them were EBV, and 1% of them were parvovirus B19 (7).

In another case series consisting of 13 patients reported from France in 2009, the average age was 16 years (six of the patients aged between 11 and 19 years), and 92% of the patients had no history of sexual intercourse. In 77% of the patients, more than one ulcer was detected and in 90% of the cases, the ulcer was reported to be in a bilateral symmetrical form (kissing ulcer). In four of the patients EBV serology was found to be positive, and in all of them, the lesions were observed in the kissing pattern. A biopsy was performed in five of the patients and all were found to be non-specific. Valacyclovir and beta-lactam antibiotics were given for six and four patients, respectively. While relapse was observed in three of them, one of these three patients was diagnosed as Behçet's disease in the follow-up examinations (14).

In Lehman's study, the average age was 11.5 years, and in 90% of the cases there was no history of sexual intercourse. In of the patients, a history of autoimmune disease in the family was detected. In nine patients, fever was present before the ulcer; in three of them an upper respiratory tract infection was present, in three of them acute gastroenteritis was present, one patient had streptococcal pharyngitis, one of them had influenza A infection, and in one patient, the

cause of fever could not be detected. For pain management, hospitalization was required as the pain level was too high in three of the patients. Dysuria was observed in all of the patients; and because urination caused the pain to get much worse, these patients were given intravenous (IV) opioid for pain management and urinary catheterization was applied to them. In three of the patients, EBV serology was found positive. Two of the patients' biopsies were found to be non-specific. In six of the patients, recurrence was observed (four times in two of them, three times in three of them, twice in one patient). Recurrences occurred on an average of one months later. In all the patients the ulcers healed a few weeks later. In treatment, systemic or topical steroids, systemic or topical antibiotics, local debridement, oral nonsteroidal anti-inflammatory drugs were used. In one patient with multiple recurrences, oral colchicine was used for a long time. In topical treatment, lidocaine cream and topical antacid (aluminum hydroxide and magnesium hydroxide) were used in some patients (2).

In twin sisters, vulvar ulcers occurring days after one another were reported by Truchuelo. Since the patients did not have symptoms other than a slight malaise and ulcer and no factors were detected, it was considered that a viral infection that was spread through an airborne route might have triggered the situation (16). In our case, among these infectious factors, as the only possible related one, we detected influenza type B PCR as positive in the respiratory tract specimen, and we considered the influenza B as the triggering factor.

Although UVA is actually not a disease that is hard to diagnose, clinicians must know it well in order to diagnose it and consider it in the differential diagnosis of the diseases causing acute genital ulcers. Diagnosis is made by excluding other causes of acute genital ulcers. Complete blood count, biochemistry (especially liver function tests), bacterial culture; with regard to sexually transmitted diseases, anti-HSV, VDRL, anti-HIV; and in terms of triggering factors, EBV, CMV, toxoplasmosis, parvovirus, *Mycoplasma*, influenza tests, throat culture (if tonsillitis is present) should be requested in patients with acute genital ulcer (2,4,8,17). Biopsy is not diagnostic, so it does not have to be performed definitely (3,8,14,18). In histopathological analysis, superficial edema, dilated capillaries, and ulcer containing neutrophil infiltration are seen in the dermis (3). We did not find it necessary to perform a biopsy on our patient.

UVA treatment is symptomatic (2,8,18). Genital hygiene, sitz bath, and emollients such as zinc oxide can be recommended (19). Pain is the most significant and challenging symptom for the patients. To relieve pain and prevent the formation of scars, oral analgesics, local anesthetics, and topical steroids are used. As local anesthetics, lidocaine gel or lidocaine-prilocaine mixture was used in some cases. In some cases, use of intravenous opioids for pain management was reported (8). The most challenging situation for us was that the patient's pain was rather severe. Due to the pain, she did not want to move her legs in any way, and she had much difficulty while urinating. Movement or any kind of contact with the lesion caused extreme pain. Therefore, difficulties were experienced in the application of local treatments.

In the literature, in very serious cases, systemic steroids were used. When the literature related to oral steroids was analyzed, it was seen that they were used for different durations and in different doses (3,8,11). We used intravenous 2 mg/kg/day of methylprednisolone for the first six days, and then we used oral methylprednisolone for a week. We observed that the patient's ulcer healed completely with a two-week steroid treatment. While only a single attack is observed in some patients, there may be multiple attacks in some others; and it has been reported that thalidomide and colchicine are used in recurrent cases (18,20). The prognosis of UVA is usually good, even if the disease is not cured, it gets better and heals spontaneously within a few weeks (2,3,12). It rarely leaves a scar tissue. The most basic treatment approach should be the pain relief, and systemic steroid may be helpful.

Conclusion

In conclusion, the most prevalent cause of genital ulcers is HSV, and it is related to sexual activity. When vulvar ulcer is observed in children, the history of sexual activity and sexual abuse should be carefully questioned. If there is no history of sexual activity, after excluding all the other possible causes, UVA should be considered first for the differential diagnosis.

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