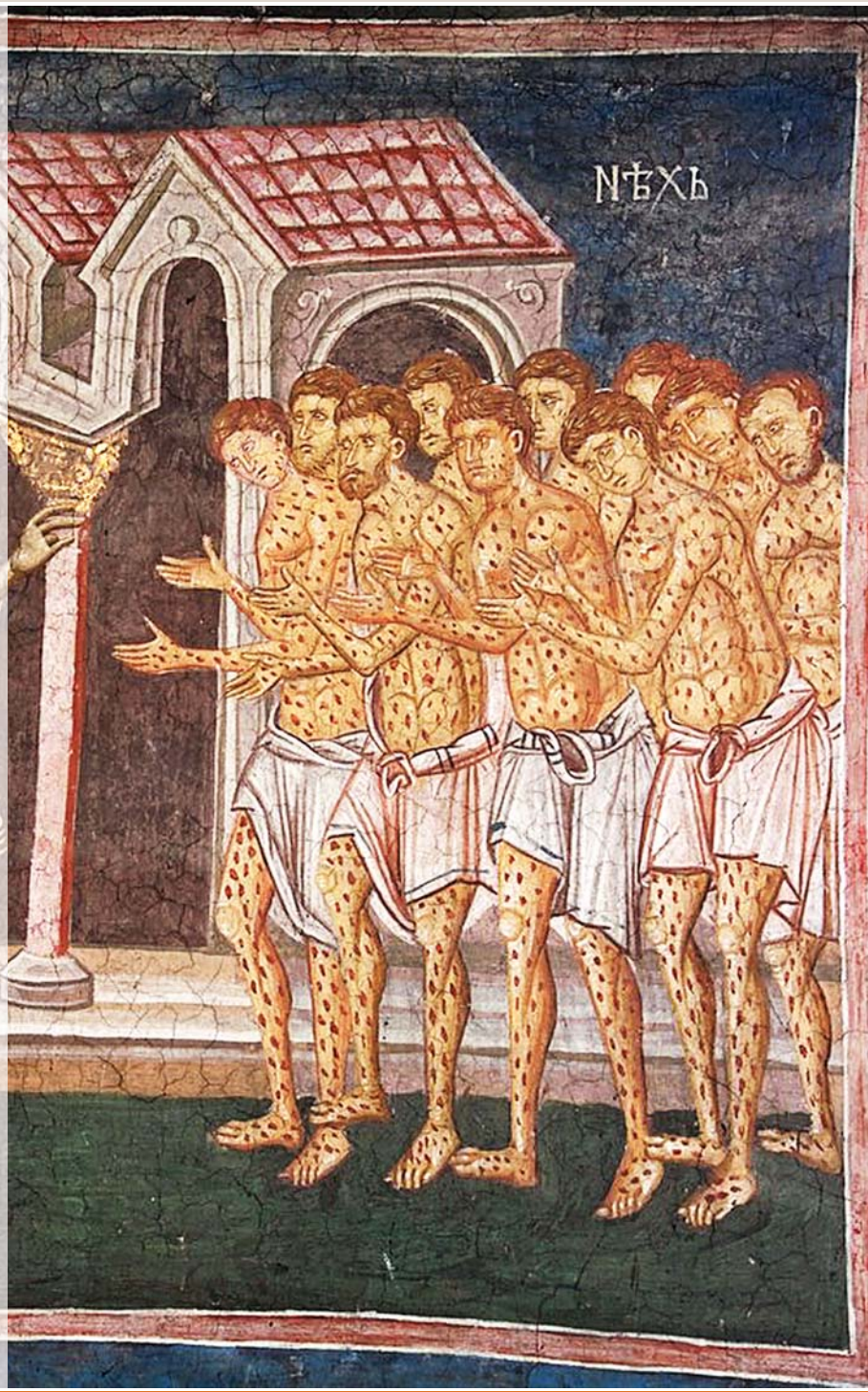
Serbian Journal of Dermatology and Venereology

ISSN 1821-0902 UDC 616.5(497.11) Volume 5, Number 4, December 2013



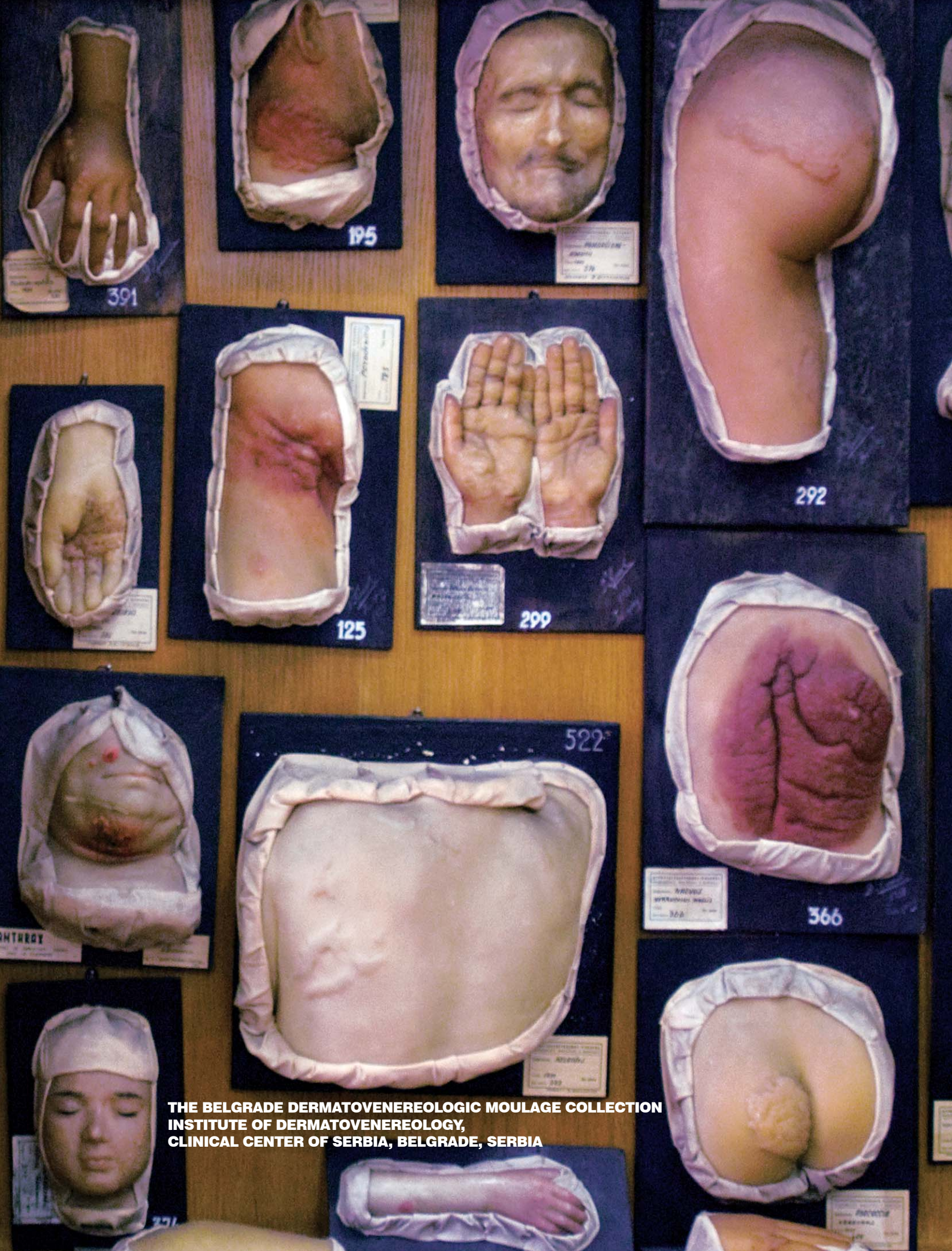
Published by the
Serbian Association of Dermatovenereologists

The Journal is published four times a year with the circulation of 360. Manuscripts are to be submitted to the Editor-in-Chief: Prof. Dr. Marina Jovanović, Klinički centar Vojvodine, Klinika za kožne i venerične bolesti, 21000 Novi Sad, Hajduk Veljkova 1-7
E-mail: serbjdermatol@open.telekom.rs, Tel: +381 21 484 3562; +381 21 451 781.
Open access: www.udvs.org

Published on behalf of The Serbian Association of Dermatovenereologists by Zlatni presek, Beograd

CONTENTS

Serbian Journal of Dermatology and Venereology 2013; 5 (4):161-196



THE BELGRADE DERMATOVENEREOLOGIC MOULAGE COLLECTION
INSTITUTE OF DERMATOVENEREOLOGY,
CLINICAL CENTER OF SERBIA, BELGRADE, SERBIA

Artificial Penile Nodules: a Case Series of Three Patients

Milan BJEKIĆ[1*]

[1]City Institute for Skin and Venereal Diseases, Belgrade, Serbia

*Correspondence: Milan Bjekić, E-mail: milinkovski@gmail.com

UDC 616.66-089.843-06

Abstract

Artificial penile nodules are inert objects inserted beneath the skin of the penis. Objects placed underneath the skin of the penile shaft may include plastic beads made from toothbrushes, silicon, metal pellets, glass, ivory, precious metals, marbles or pearls. The penile bead implantation is performed largely due to the belief that it will enhance sexual performance and pleasure of female or male sexual partners during intercourse.

In this article, three cases with artificial penile nodules made of toothbrushes and dice are presented. All three men have implanted foreign bodies underneath the dorsal aspect of the penile skin during their prison stay and implantations were not followed by any side effects. However, insertion of foreign bodies may be followed by early and late complications and transmission of blood-borne viruses.

Penile implants are important for dermatological consideration, because they make condom use more difficult and may represent a risk factor for sexually transmitted infections.

Key words

Penis; Foreign Bodies; Body Modification, Non-Therapeutic; Sexual Behavior

Artificial penile nodules are inert objects inserted beneath the skin of the penis. Objects placed underneath the skin of the penile shaft may include plastic beads made from toothbrushes, silicon, metal pellets, glass, ivory, precious metals, marbles or pearls (1). The penile bead implantation is performed largely due to the belief that it will enhance sexual performance and pleasure of female or male sexual partners during intercourse (2). Historically, most reports on penile implantation of foreign bodies originate from North and Southeast Asia (2, 3). The occurrence of this phenomenon is much less common in non-Asian groups, but it has been reported in Romania (4), among Fijians (5) as well as Russian immigrants in Israel (6). However, it has also been reported in Western Europe (7) and in the USA (8).

Herein, three patients with artificial penile nodules are reported. All of them were referred to the City Institute for Skin and Venereal Disease in Belgrade due to some other skin or venereal complaints.

Case reports

Case 1

A 28-year-old man presented with folliculitis unrelated to artificial penile nodules. Physical examination accidentally revealed 5 asymptomatic penile nodules, four of them on dorsal part of the penis and one at the prepuce edge (Figure 1). Careful personal history gave insight into the etiology of nodules. These were capsule shaped artificial self-implanted plastic pearls, inserted two years ago by piercing the penile skin with a sharp iron rod, without a local anesthetic.

The beads were made from a toothbrush by using sandpaper. The patient was in prison at that time, and suffered no serious side effects after insertion. The aim was to enhance the patient's sexual pleasure and the pleasure of his sexual partners.

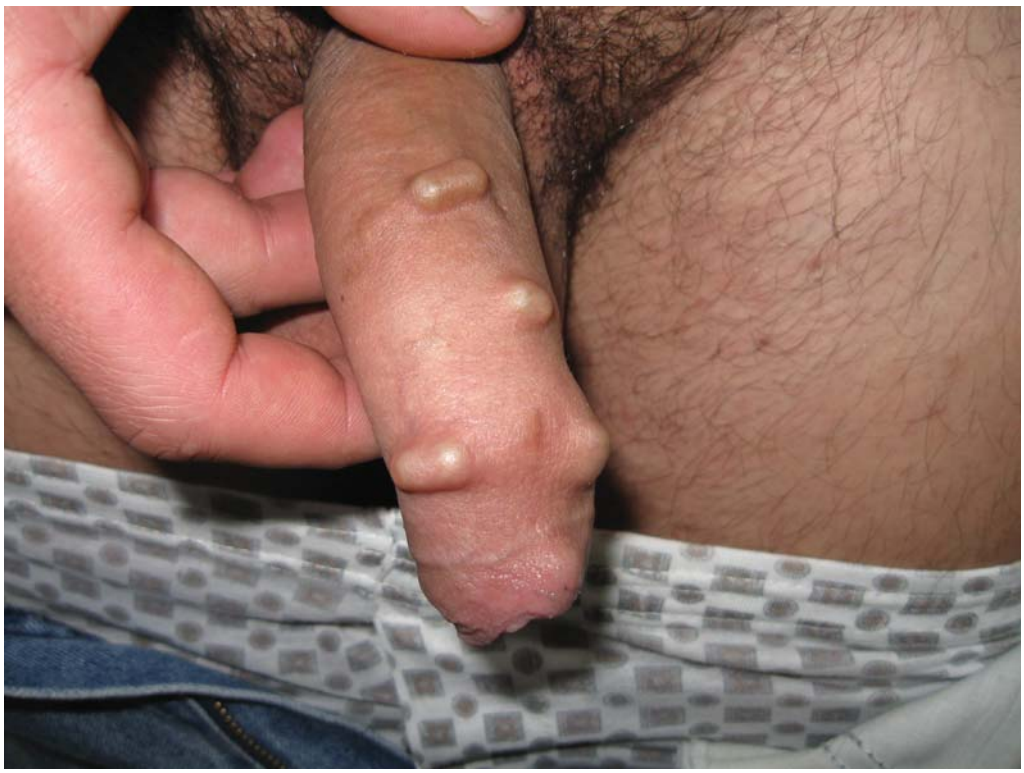


Figure 1. Case 1: four capsule shaped penile implants on the dorsal aspect of the penis; the fifth pearl is implanted at the edge of the prepuce

Case 2

A 30-year-old man was referred to our Institute for routine screening for sexually transmitted infections. The examination showed an oval, hard, subcutaneous nodule on the dorsal aspect of the prepuce. The overlying skin was normal, and the nodule moved freely with preputial retraction (Figure 2). No other abnormalities were found in the genital region and the regional lymph nodes were not enlarged. All performed laboratory tests were negative for venereal diseases. Further questioning showed that the foreign body was self-implanted while he was in prison five years before. The implant was made from plastic (toothbrush) in the same way as in the previous case. The implantation was not followed by any side effects.

Case 3

A 21-year-old man visited a dermatologist because of genital warts. Physical examination revealed two small, skin colored, fleshy warts on the dorsal aspect of penis. A hard, mobile nodule was noticed below the warts on the penile shaft. It was a self-made small niche made with a sharp spoon, two years before when he was in prison. According to the patient's description, the procedure was a little painful with slight bleeding. A pyramid-shaped foreign body made from a dice, by rubbing it against the concrete, was pushed under the penile skin. Before insertion the patient cleaned the implant with an "after-shave" lotion. The implant moved freely under the skin (Figures 3a and 3b). The healing occurred within days without any adverse events. He noticed that his girlfriend was much more stimulated during intercourse since he inserted "a dolphin" under the penile skin.

Discussion

The phenomenon of penile bead implantation is not uncommon in other cultures, but is new and rather peculiar in our society. In this paper we present three Serbian ex-prisoners with self-made artificial penile nodules.

The origins of the custom of inserting penile implants, especially among prisoners, dates back to

Figure 2. Case 2: an oval hard nodule on the dorsal part of the penile shaft

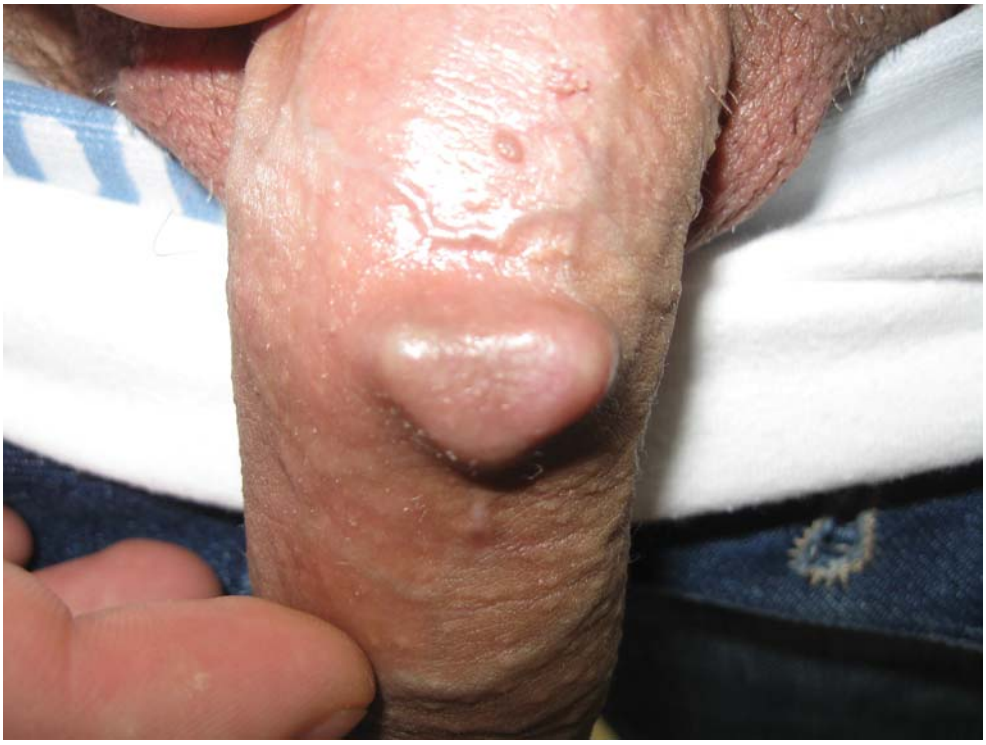


Figure 3a. Case 3: a pyramid-shaped foreign body (with a pyramidal basis) beneath the penile skin. Genital warts are above the implant.

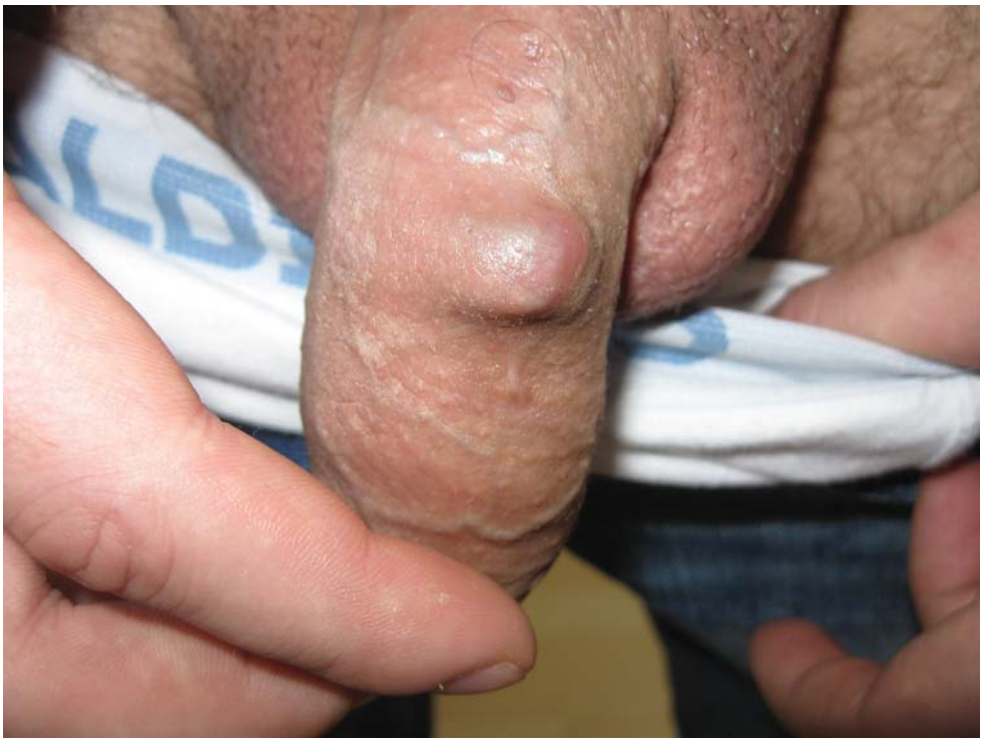


Figure 3b. Case 3: the penile nodule has turned, so the top of the pyramidal base is beneath the penile skin

the 18th century in Japanese gangsters, members of the criminal organization Yakuza (3), who practiced it to demonstrate their loyalty to the clan (9).

Several case reports and studies of prisoners and ex-prisoners worldwide, suggest that this population gradually adopted the practice (7, 8, 10). However, the practice has also said to be more common among seamen, soldiers, drug addicts and those with lower socioeconomic backgrounds (6, 7, 11).

Data regarding the prevalence of this phenomenon vary among different cultures. Serour in his study reported the prevalence of 0.63% among Russian immigrants who participated in a circumcision program in Israel (6). In the study of Tsunenari et al, 22% of prisoners in Japan had penile implants and most of them belonged to the Yakuza organization (3). A study conducted in Taiwan among male heroin abusers has shown that 40% of respondents had artificial penile nodules (11). Among one hundred young amphetamine users in Thailand, Thomson et al, found that 51% had penile modifications, the most common being inlaying with muk(s) in 61% (12).

Implants are made from different materials – plastic, metal, glass, ivory, silicon, wood, marbles and pearls. In Japan, implants are called "Tancho nodules" after glass bottles of popular "Tancho" Japanese hair pomade, either melted or polished which is used to smooth beads for implantation (13). Other terms for insertion are "fang muk" in Thailand, China, Singapore, Malaysia, Vietnam and Cambodia; chagan balls in Korea; bulleetus in Philippines, penis marbles in Fuji, "goli" in India and RuJu in Taiwan (5, 11, 14, 15). Artificial penile nodules in our country are called "dolphins".

In prison, the beads are made out of spoons, toothbrushes, dominoes, chopsticks, melted toothpaste tube caps, buttons or deodorant roller balls (3, 16, 17). Outside the prison, there are glass balls, pearls or precious stones being used for implantation (3). Our two patients made implants from toothbrushes and the third patient made it from a dice. By making, polishing and subcutaneously inserting penile beads in the foreskin, prisoners combat prison boredom and provide income from selling and inserting finished implants to other prisoners (18).

Implantation procedures in prison are usually performed under primitive conditions without using anesthesia and antiseptics. The procedure of bead

implantation is simple. The penile skin is penetrated with a sharp pointed object (a ballpoint pen, sharpened piece of plastic, iron rod, spoon, knife or razor), and the foreign body is pushed under the penile skin through the small incision (1). Implants may be inserted at different parts of the penis, but the dorsum is the most common site (2), as described in our cases.

The penile shaft is covered by thin and very mobile skin. The loose adherence of the skin to the underlying tissues allows insertion of implants and accounts for their mobility within the subcutaneous layers. Once implanted the bead, becomes movable underneath the penile skin during intercourse.

Though the prevalence of complications during implantation of penile implants seems to be low, the true incidence and severity of early or delayed complications are probably underreported (1). One study has shown that 96.6% of sixty interviewed implant bearers had no complications even eight years after implantation (19). On the other side, early complications, including penile erythema and edema, inflammation, infections and abscesses were reported by others (8, 10, 19).

Penile implantation may certainly increase transmission of hepatitis B virus, hepatitis C virus and human immunodeficiency virus (HIV). Insertion of penile implants in prison, without proper measures of protection against infection (lack of sterile instruments, sterile gloves, use of shared and inadequately cleaned incision instruments and exposure to other's blood), is associated with several potential risks such as getting infections at the site of insertion with blood borne viruses.

Among male heroin users in Taiwan, penile bead implantation, called RuJu, was an independent risk factor (OR=2.47, 95% CI 1.40, 4.36, $p<0.01$) for HIV infection (11). This could be explained by facts that having implants underneath the penile skin may dissuade bearers from using condoms, because the fixed beads would lead to painful intercourse, or condom failure. Moreover, beads may cause abrasion of male or female genital organs. Lesions of genital mucosa may be sites for HIV entry. On the other hand, sharing instruments used for implant insertion, medical complications during bead implantation and condom leakage are risk factors for HIV transmission (11, 16).

However, other complications of penile insertion, such as superinfections, rejection, functional impotence, urethral stenosis, sepsis and well-differentiated squamous cell carcinoma of the penis, have been reported (7, 20). The female sexual partners of men with artificial penile nodules reported dyspareunia, bleeding and injuries of vagina and cervix, which also put them at risk for sexually transmitted infections (18).

The reasons for penile foreign body implantation are certainly manifold and culture related. Some do it because of peer influence or as a symbol of affiliation to a certain group, others as a symbol of manhood and potency, or even on demand from a female partner, but in majority of cases because of the belief that beads will produce more friction during sexual intercourse and enhance sensuality and sexual pleasure (10, 15, 21).

The diagnosis is usually straightforward, and the hardness of the implanted beads is pathognomonic. These objects are usually palpable as non-tender, hard subcutaneous nodules and when followed with details from the patient's history, should pose no diagnostic problem for dermatologists. However, these may cause diagnostic confusion in certain patients if they are associated with genitourinary complaints.

Even in our country, all physicians must be familiar with this practice when assessing certain groups of men. Penile implants are important for dermatologists and venereologists, because these make condom use more difficult and may represent a risk factor for sexually transmitted infections.

Conclusion

To the best of our knowledge, these cases are the first men reported with penile implants in Serbia.

Acknowledgement

This study was supported by the Ministry for Science and Technology of Serbia, through Contract No. 175042 (2011-2014).

Abbreviations

HIV - human immunodeficiency virus

References

1. Fischer N, Hauser S, Brede O, Fisang C, Muller S. Implantation of artificial penile nodules – a review of literature. J Sex Med 2010;7:3565-71.
2. Wilcher G. Artificial penile nodules – a forensic pathosociology perspective: four case reports. Med Sci Law 2006;46:349-56.
3. Tsunenari S, Idaka T, Kanda M, Koga Y. Self-mutilation. Plastic

spherules in penile skin in yakuza, Japan's racketeers. Am J Forensic Med Pathol 1981;2:203-7.
4. Wolf P, Kerl H. Artificial penile nodules and secondary syphilis. Genitourin Med 1991;67:247-9.
5. Norton SA. Fijian penis marbles: an example of artificial penile nodules. Cutis 1993;51:295-7.
6. Serour F. Artificial nodules of the penis. Report of six cases among Russian immigrants in Israel. Sex Transm Dis 1993;20:192-3.
7. Rothschild MA, Ehrlich E, Klewno WA, Schneider V. Self-implanted subcutaneous penile balls – a new phenomenon in Western Europe. Int J Legal Med 1997;110:88-91.
8. Hudak SJ, McGeady J, Shindel AW, Breyer BN. Subcutaneous penile insertion of domino fragments by incarcerated males in Southwest United States prisons: a report of three cases. J Sex Med 2012;9:632-4.
9. Tsunenari S, Yonemitsu K, Kanbe T, Kanda M. How to identify the Yakuza, Japanese racketeers-their sociology, criminology and physical characteristics. Ann Acad Med Singapore 1984;13:25-31.
10. Yap L, Butler T, Richters J, Malacova E, Wand H, Smith AM, et al. Penile implants among prisoners – a cause for concern? PLoS ONE 2013;8:e53065.
11. Lee TS. Penile bead implantation in relation to HIV infection in male heroin users in Taiwan. J AIDS Clin Res 2012;3(Suppl):1.
12. Thomson N, Sutcliffe CG, Sirirojn B, Sintupat K, Aramrattana A, Samuels A, et al. Penile modification in young Thai men: risk environments, procedures and widespread implications for HIV and sexually transmitted infections. Sex Transm Infect 2008;84:195-7.
13. Sundaravej K, Suchato C. Tancho's nodules. Australas Radiol 1974;18:453-4.
14. Sugathan P. Bulleetus. Int J Dermatol 1987;26:51.
15. Stankov O, Ivanovski O, Popov Z. Artificial penile bodies-from Kama sutra to modern times. J Sex Med 2009;6:1543-8.
16. Loue S, Loarca LE, Ramirez ER, Ferman J. Penile marbles and potential risk of HIV transmission. J Immigr Health 2002;4:117-8.
17. Hull TH, Budiharsana M. Male circumcision and penis enhancement in Southeast Asia: matters of pain and pleasure. Reprod Health Matters 2001;9:60-7.
18. Kelly A, Kupul M, Nake Trumb R, Aeno H, Neo J, Fitzgerald L, et al. More than just a cut: A qualitative study of penile practices and their relationship to masculinity, sexuality and contagion and their implications for HIV prevention in Papua New Guinea. BMC Int Healh Hum Rights 2012;12:10.
19. Marzouk E. Implantation of beads into the penile skin and its complications. Scand J Urol Nephrol 1990;24:167-9.
20. Kakinuma H, Miyakawa K, Baba S, Suzuki H, Kawada N, Takimoto Y. Penile cancer associated with an artificial penile nodule. Acta Derm Venereol 1994;74:412-3.
21. Murty OP. Male genital ornaments: penis pearls. J Forensic Leg Med 2008;15:96-100.

Arteficijalni penilni nodusi: prikaz tri slučaja

Sažetak

Uvod: Arteficijelni penisni nodusi su inertni objekti koji se postavljaju ispod kože penisa u cilju povećanja seksualnog zadovoljstva kako osobe koja ih je implantirala, tako i njenih budućih seksualnih partnera. Objekti koji se postavljaju pod kožu su obično od plastike, silikona, metalnih loptica, stakla, drveta, mermera ili dragocenih metala.

Prikaz sučaja: U radu su prikazana tri pacijenta koji su tokom boravka u zatvoru pod kožu dorzalne strane penisa sami implantirali strana tela koja su napravili od plastike držača četkica za zube i od kockice za jamb. Proces implantacije je prošao bez neželjenih efekata.

Diskusija: Iako ni u jednom od tri prikazana slučaja nije bilo neželjenih efekata, poznato je da se posle intervencija ove vrste mogu razviti rane i kasne komplikacije. Takođe je poznato na osnovu sluačjeva objavljenih u svetskoj literaturi, da postoji povišeni rizik za prenošenje virusa hepatitisa i HIV-a tokom ove prakse.

Pacijente prikazujemo sa ciljem da dermatovenerologe upoznamo sa ovom praksom koja je sve više prisutna i u našoj sredini, kao i sa problemima koje ona nosi, kao što je, između ostalog, otežana upotreba kondoma tokom seksualnih odnosa, što vlasnike implantata dovodi u povećani rizik za polno prenosive infekcije.

Zaključak: Na osnovu podataka iz nama dostupne literature, tri slučaja opisana u ovom radu predstavljaju prve slučajeve arteficijalnih penisnih implantata u Srbiji.

Ključne reči

Penis; Strana tela; Telesna modifikacija, neterapijska; Seksualno ponašanje

Extramammary Paget's Disease in the Pubic Region: a Case Report

Slobodan STOJANOVIĆ[1,4*], Nada VUČKOVIĆ[2,4], Pavle JEREMIĆ[3,4], Biljana JEREMIĆ[1]

[1]Clinic of Dermatovenereology Diseases, Clinical Center of Vojvodina, Novi Sad, Serbia
[2]Center for Pathology and Histology, Clinical Center of Vojvodina, Novi Sad, Serbia
[3]Clinic of plastic and reconstuctive surgery, Clinical Center of Vojvodina, Novi Sad, Serbia
[4]Faculty of Medicine, University of Novi Sad, Serbia

*Correspondence: Slobodan STOJANOVIĆ, E-mail: slobodanstojanovicns@sbb.rs

UDC 616.5 :618.16]-006.6-091.8

Abstract

The authors present a case of a patient with extramammary Paget's disease in the pubic region treated by a dermatologist with a private practice for almost 4 years before incisional biopsy was performed. A thorough examination showed no evidence of malignancies of internal organs, whereas definite diagnosis was made by excision of the entire skin lesion and histopathological analysis.
With regard to multiple criteria, findings in our patient were consistent with current literature data, but interestingly, the primary extramammary Paget's disease has not spread into deeper tissues.

Key words

Disease, Extramammary; Skin Neoplasms; Genitalia, Female; Reconstructive Surgical Procedures; Histological Techniques

Extramammary Paget's disease (EMPD) is a rare cutaneous malignancy characterized by intraepithelial adenocarcinoma outside the mammary gland. Mammary Paget's disease (MPD) is almost always associated with a ductal carcinoma (1, 2). EMPD mostly occurs in older people with a predilection for the apocrine-rich anogenital skin and less commonly for the axilla (1). The disease usually manifests as a sharply defined erythema with polygonal borders (1, 2), but centrifugal tumor growth is also possible (1, 2). The disease is rare, with an unclear pathogenesis, so there is no standard treatment algorithm; it commonly requires wide excision over the clinically visible borders (2, 3, 4). Long-term monitoring is recommended due to common recurrence (1). The diagnosis of EMPD is usually made histopathologically and it has a few stages (1, 5).

Case Report

An 80-year-old female patient presented with skin lesions in the pubic region, over labia majora, with slightly elevated erythema, small erosions and slight oozing. At the beginning, the condition was not associated with pain or itching. The patient visited a private dermatologist. The submitted documentation showed that the patient had a sharply demarcated erythematous plaque of 30 x 30 mm in diameter; local therapy included betamethasone dipropionate 0.05% in combination with clotrimazole tablets 1%, and 0.1% gentamicin sulfate cream. Since then, the patient visited the same dermatologist seven times; she was treated under the clinical diagnosis of candidomycetic dermatitis of the pubic region, but without satisfactory results.

After more than half a year of unsuccessful treatment and development of severe itching, the patient visited another dermatologist, but after 3 months, there was no improvement. Over the next year, she experienced moderate itching and burning once a month. She used mometasone furoate 0.1% cream in the evening, for 5-6 days at least once a month. As the disease was progressing, the patient

presented with a burning sensation even when using water.

In October 2010, the patient visited the Dermatovenereology Department of the Clinical Center of Vojvodina in Novi Sad for the first time. Physical examination revealed a skin lesion in the pubic region at about 1 cm above the anterior commissure of the labia majora of 60 x 50 mm in diameter. It was a sharply demarcated, erythematous dry plaque, without oozing, associated only with slight burning sensation.

The patient visited her private dermatologist again and underwent incisional biopsy (performed for diagnostic purposes, in order to plan reconstructive surgery - which is usually done in all major procedures). The sample (Figure 1) was sent for histopathological examination, under suspicion of Bowen's disease, and the result was superficial melanoma (Clark 2, Breslow 0.5 mm).

The patient was referred to the Clinic of Plastic and Reconstructive Surgery, Clinical Center of Vojvodina, Novi Sad, considering the fact that the above histopathological analysis indicated complete excision of the lesion. The internist examination showed that there were no contraindications for surgery. All relevant preoperative laboratory and other findings, including gynecological and gastroenterological ultrasound and X-rays, were within the reference values.

Under general anesthesia, the patient underwent total excision of the lesion, with vacuum drainage, local skin transposition flap, and a protective lining of 2.5 cm. The removed tissue included the skin with subcutaneous fat tissue, 8,3 x 6,6 cm in diameter, with the brown lesion and the clinically unaffected surrounding area, which was sent for histopathological analysis. The obtained findings showed that the lesion comprised grouped cubic and polygonal cells within the epidermis, individual cells at all levels of the epidermis, and adenoid formations on the dermoepidermal border; tumor cells were HMB45 negative and CK7 positive; the base of the tumor consisted of connective tissue – pointing to the previous incisional intervention; the tumor tissue was entirely removed. Based on this description, the diagnosis of extramammary Paget's disease (EMPD) was made (Figures 2 and 3). Analysis of histopathological findings was done at the Institute of Pathology and Histology, Clinical Center of Vojvodina, Novi Sad, Serbia, including revision of the first biopsy, performed at the private clinic, and both confirmed the diagnosis of EMPD.

There were no complications during the postoperative period, and the postoperative wound healing was uneventful. At check-ups, all results were within normal values without regional lymph node

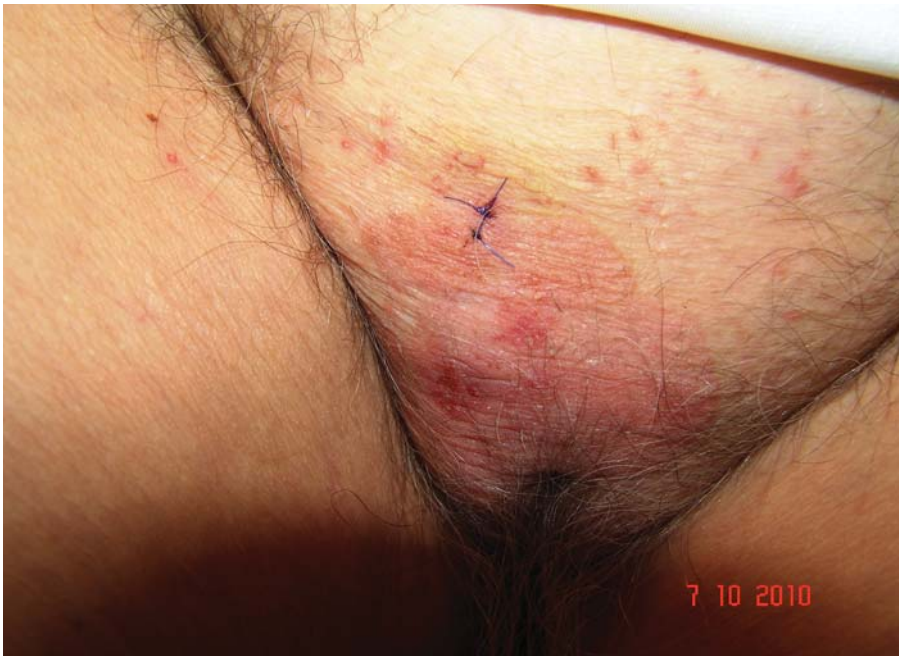


Figure 1. Paget's disease of the pubic region with a visible locus of the first incisional biopsy

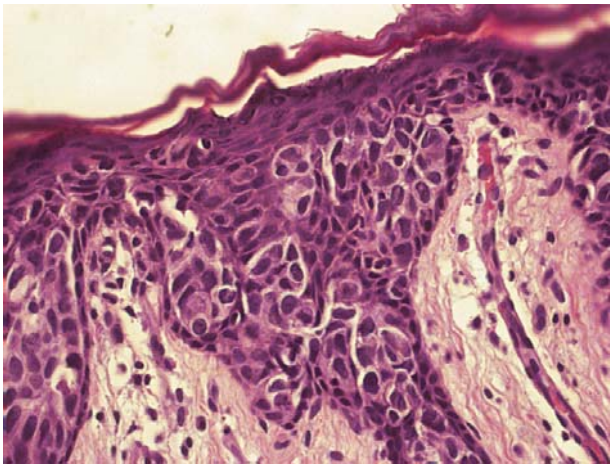


Figure 2. Electron micrograph of multiple Paget cells in the epidermis (HEx400)

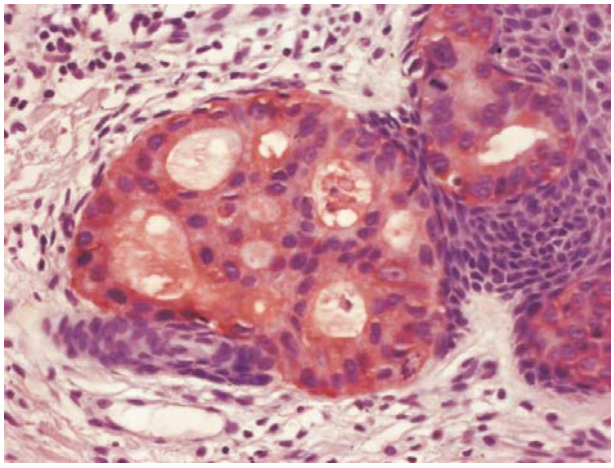


Figure 3. Electron micrograph of Paget cells forming an adenoid pattern (CK7x 400)

involvement or other complications. Gynecological and gastroenterological examination and ultrasound findings, as well as extensive double contrast irigography, showed that EMPD was not associated with any other genital or anorectal disease.

The patient's medical history showed that she had three gynecological surgical interventions for benign tumors of the vulva, endometritis, and uterine cervical polyps at the age of 41, 44 and 48, respectively; at the age of 71, the patient underwent surgery for urethral polyps; bougienage of urethral stenosis was performed at the age of 77; two surgeries were also performed for removal of facial basal cell carcinoma at the age of 79 and 84, respectively.

Discussion

In 1874, Sir James Paget reported a case series of 15 patients with chronic, eczematoid ulcerations of the nipple in association with breast cancer (6). Sir Paget suggested that these lesions were initial or associated with breast cancer (6). In contrast, in 1889, Henry Radcliffe Crocker was first to describe a case of EMPD of the scrotum and glans penis (7). The first detailed histopathological description of Paget's disease was given by Ferdinand-Jean Darier in 1889 (8).

In the early 20th century, there was a conceptual hypothesis about two forms of Paget's disease (PD): first - as a precancerous condition without a direct connection to the tumor, and second - intraepithelial metastasis of already existing breast cancer. Although this conceptual hypothesis has not been proven as true for PD, it provides a basis for understanding the pathology of primary EMPD form resulting in skin adnexal glandular structures (apocrine gland carcinoma), as well as its potential secondary manifestations, that is intraepithelial epidermotropic metastatic malignancies from the adjacent or internal organs (2).

The incidence of EMPD is very low, and it can be indirectly evaluated based on the number of new cases of breast cancer in women, because PD accounts for 0.7 - 4.3% (9), whereas EMPD accounts for 6.5% of all forms of PD (2). EMPD is more common in women than in men, the sex ratio ranges from 3 - 4.5 : 1, and it most often affects the elderly (10, 11). The average age at the time of diagnosis is 64 - 72 years, and 90% of patients are over 50 years of age (11). As for the age distribution, one should keep in mind that the disease is often present for years or even decades before it is manifested (11).

Clinical EMPD affects parts of the skin with apocrine glands. Predilection sites include the anogenital region, rarely axillae, and least rarely both anogenital region and axillae (12). The most commonly affected site is the vulva (11) and labia majora. Taking into account the centrifugal tumor growth, the entire anogenital region may be infiltrated, so in advanced stages of the disease it is often impossible to identify the origin of the primary neoplasm. This may be significant, because EMPD may also occur as an expression of the primary tumor, which affected some internal organs of the body. The risk of associated

malignancy and EMPD in the perianal area is 25 - 35%, which is significantly higher than in relation to a possible malignancy in the genital area, which is approximately 4 - 7% (13, 14), being the case in in our patient. Other possible sites of EMPD include eyelids, outer ear canal, the umbilical region, trunk and limbs (15, 16).

Depending on the site and duration of the disease, the clinical appearance of EMPD varies significantly. Large, extended lesions may be irregular with poorly defined borders, but the centrifugal growth pattern leads to the formation of polygonal borderline, providing a diagnostic clue as in our case. Some of the rare morphological characteristics of EMPD include neoplastic alopecia, sclerodermiform macular and lichenoid papules (17). Metastasis of primary EMPD is characterized by per continuitatem, lymphatic, or more rarely hematogenous spread. Out of the 76 patients with primary EMPD, Hatta and associates reported metastases in 17% of cases (18). Secondary EMPD, excluded in our patient, is an intraepithelial metastasis of internal organ tumors: colonic cancer, uterine cervix cancer, urinary bladder, urethral and prostatic cancer (11).

Like in our patient, the diagnosis of EMPD is usually made after a few years, due to a variety of clinical presentations and the rarity of the disease. On average, the disease is diagnosed two years after the appearance of initial symptoms (11). There are some reports about EMPD existing up to 30 years before they were diagnosed (12). The diagnosis of EMPD is confirmed by the presence of Paget's cells (PCs). They are usually about two times larger than the surrounding keratinocytes, round-shaped, with clear cytoplasm and large pleomorphic nuclei. With a few exceptions, PCs contain a high percentage of mucin, which can be proved by periodic acid–Schiff (PAS) and Alcian blue staining, depending on the content of mucopolysaccharides, used for differential diagnosis (18). PCs are usually isolated cells or form irregular groups: the so-called epidermal-Paget pattern. If other malignancies develop within the epidermis, such as malignant melanoma, adenocarcinoma or mycosis fungoides, it is known as Paget's phenomenon (19). If PCs are only intraepidermal, like in our patient, or found in the adnexal epithelium, the tumor is considered to be carcinoma in situ. However, penetration of the basal membrane is associated with adnexal carcinoma (20).

Histogenesis of EMPD is not fully understood. Electron microscopy studies indicate to gland origin of PCs (e.g., a large Golgi apparatus and numerous mitochondria, as well as the presence of microvilli and secretory vacuoles) (20). Immunohistochemical studies are of utmost importance for histogenesis, but also for the diagnosis and classification of PCs, and in differential diagnosis. Cytokeratin 7 (CK-7) is a very useful antibody for confirming the diagnosis of MPD as well as EMPD. As in our patient, tumor cells in the EMPD stained consistently for this antibody, while the surrounding epidermis was negative (18). Apart from low molecular weight cytokeratin, such as CK 7, other antigens present in apocrine and eccrine sweat glands, can be routinely identified in PCs, e.g. CEA (carcinoembryonic antigen) (21, 22). Detection of these antigens confirms the glandular origin of PCs. Although there is a growing body of evidence in favor of histogenetic origin of PCs from apocrine sweat glands, pluripotent stem cells have also been considered as possible origin (10).

Based on clinical, histopathological and immunohistochemical analyses, it is now a common belief that there are two different forms of EMPD in regard to pathogenesis and prognosis. Primary EMPD develops in the epidermis and it is considered to be *carcinoma in situ*. Secondary EMPD is less frequent, with intraepithelial spreading of the primary tumor (17). Just as Paget's breast cancer, EMPD may also originate from a primary cancer of the apocrine sweat glands, or the neighboring anorectal or urogenital organs. Nevertheless, some authors suggest that the lack of evidence, particularly in cutaneous adnexal cancers (possibly as a result of inadequate histological analysis) may indicate focal changes in the apocrine sweat glands. Histologically, it is impossible to distinguish the course of disease progression, especially in advanced stages (2). Associated neoplasms include cutaneous adnexal carcinomas, as well as rectal, colonic, bladder, prostatic, urethral, and cervical malignancies.

A typical differential diagnosis of EMPD includes: contact or seborrheic dermatitis, inverse psoriasis, perianal streptogenic dermatitis, mycotic infections (positive mycological finding does not exclude EMPD

in case of a secondary fungal infection), lichen simplex (severe lichenification), lichen planus, lichen sclerosus et atrophicus, circumscribed morphea, benign pemphigus (Hailey-Hailey disease), histiocytosis, necrolytic migratory erythema and genital warts (17, 23, 24). In regard to skin neoplasms, differential diagnosis of EMPD includes: Bowen's disease (of the anal/perianal/vulvar area), and vulvar intraepithelial neoplasia (17, 24). Melanoma, squamous cell carcinoma, intraepidermal sebaceous carcinoma, secondary Paget's disease and adenocarcinoma should be ruled out histopathologically (25).

Surgical excision remains the treatment of choice in primary EMP. Considering the age of patients, complicated surgical procedures are often not recommended due to the location or size of the tumor. Required surgical interventions in the anogenital area are often associated with a decreased quality of life. Apart from this, there is a high rate of postoperative recurrence. Literature data indicate to 8% recurrence after surgical excision of EMPD, performed with 2 cm margins (10). Other studies, of conventional excision procedures and safety margins of 1-2 cm, reported recurrence of 15 - 50% in the vulvar region (11). The average recurrence rate for all sites is 35 - 44% (26). Lower recurrence rates have been reported after Mohs microscopic surgery (8 - 26%) (27). Other forms of therapy of EMPD include: radiotherapy, carbohydrate laser therapy, photodynamic therapy, topical use of 5-fluorouracil, and so on. Treatment options for secondary EMPD are basically the same as for the primary form of the disease (2, 28). It is of utmost importance to treat the associated visceral malignancy.

The prognosis for the primary EMPD is generally favorable, although it may depend on the duration of the disease. The mortality rate is 13 - 18% (12), and 5-year survival is 72% (29). However, the prognosis is much worse if invasive growth is present at the time of diagnosis. The prognosis of secondary EMPD, associated with cancer of adjacent organs, depends on the prognosis of the primary visceral tumor. The median survival among patients with secondary EMPD is only 3 years (30).

Conclusion

This is a case report of a patient with extramammary Paget's disease without visceral malignancy and successful surgical management.

Abbreviations

EMPD - extramammary Paget's disease
MPD - mammary Paget's disease
HMB45 – human melanoma, black-45
CK7 – cytokeratin7
PD - Paget's disease
PCs - Paget cells
PAS - periodic acid-Schiff
CEA - carcinoembryonic antigen

References

1. Wagner G, Sachse MM. Extramammary Paget disease: clinical appearance, pathogenesis, management. J Dtsch Dermatol Ges 2011;9:448–54.
2. Kyriazanos ID, Stamos NP, Miliadis L, Noussis G, Stoidis CN. Extra-mammary Paget's disease of the perianal region: a review of the literature emphasizing the operative management technique. Surg Oncol 2011;20:e61-71.
3. Ekwueme KC, Zakhour DH, Parr NJ. Extramammary Paget's disease of the penis: a case report and review of the literature. J Med Case Rep 2009;3:4.
4. Juang GD, Lin MY, Hwang T ShI. Extramammary Paget's disease of the scrotum. J Chin Med Assoc 2011;74:325-8.
5. Venkatesh RR, David HH. Extramammary Paget's disease. Com Oncol 2004;1(2):109-15.
6. Paget J. One disease of the mammary areola proceeding cancer of the mammary gland. St Barth Hosp Rep 1874;10:87–9.
7. Crocker HR. Paget's disease, affecting the scrotum and penis. Trans Pathol Soc Lond 1889;40:187-91.
8. Darier FJ. Sur un nouvelle forme de psorrospermose cutanee: la maladie de Paget du reammelon. C R Soc Biol. 1889;41:294–8.
9. Kanitakis J. Mammary and extramammary Paget's disease. J Eur Acad Dermatol Venereol 2007;21:581–90.
10. Jones RE Jr, Austin C, Ackerman AB. Extramammary Paget's disease. A critical reexamination. Am J Dermatopathol 1979;1:101–32.
11. Shaco-Levy R, Bean SM, Vollmer RT, Jewell E, Jones EL, Valdes CL, et al. Paget disease of the vulva: a study of 56 cases. Eur J Obstet Gynecol Reprod Biol 2010;149:86–91.
12. Hatta N, Yamada M, Hirano T, Fujimoto A, Morita R. Extramammary Paget's disease: treatment, prognostic factors and outcome in 76 patients. Br J Dermatol 2008;158:313–8.
13. Zollo JD, Zeitouni NC. The Roswell Park Cancer Institute experience with extramammary Paget's disease. Br J Dermatol 2000;142:59–65.
14. Neuhaus IM, Grekin RC. Mammary and extramammary Paget disease. In: Wolff K, Goldsmith LA, Katz SI, Gilchrest BA, Paller AS, Leffell DJ, editors. Fitzpatrick's dermatology in general medicine. 7th ed. New York: McGraw-Hill; 2008. p. 1094–8.
15. Worthon CM, Patterson JB. Carcinoma of Moll's glands with extramammary Paget's disease of the eyelid. Cancer

1955;8:1009–15.
16. Gonzales-Castro J, Iranzo P, Palou J, Mascaró JM. Extramammary Paget's disease involving the external ear. Br J Dermatol 1998;138:914–5.
17. Lloyd J, Flanagan AM. Mammary and extramammary Paget's disease. J Clin Pathol 2000;53: 742–9.
18. Hatta N, Yamada M, Hirano T, Fujimoto A, Morita R. Extramammary Paget's disease: treatment, prognostic factors and outcome in 76 patients. Br J Dermatol 2008;158:313–8.
19. Calonje E. Tumours of the skin appendages. In: Burns T, Breathnach S, Cox N, Griffith SC, editors. Rook's textbook of dermatology. 8 th ed. Oxford: Blackwel Publishing; 2010. p. 53.1-44.
20. Lupton G, Graham JH. Mammary and extramammary Paget's disease. In: Friedman RJ, Rigel DS, Kopf AW, Harris MN, Baker D, editors. Cancer of the skin. Philadelphia: WB Saunders; 1991. p. 217–36.
21. Ordonez NG, Awalt H, Mackay B. Mammary and extramammary Paget's disease: An immunocytochemical and ultrastructural study. Cancer 1987;59:1173–83.
22. Lautier R, Achtelik WV, Wolff HH. Immunhistochemische Untersuchung bei mammären und extramammären Morbus Paget weisen auf eine apokrine Differenzierung hin. Z Hautkr 1990;65:571–4.
23. Kanitakis J. Mammary and extramammary Paget's disease. J Eur Acad Dermatol Venereol 2007;21:581–90.
24. Honda Y, Egawa K. Extramammary Paget's disease not only mimicking but also accompanying condyloma acuminatum. A case report. Dermatology 2005;210:315–8.
25. Hilliard NJ, Huang C, Andrea A. Pigmented extramammary Paget's disease of the axilla mimicking melanoma: case report and review of the literature. J Cutan Pathol 2009;36:995-1000.
26. Zollo JD, Zeitouni NC. The Roswell Park Cancer Institute experience with extramammary Paget's disease. Br J Dermatol 2000;142:59–65.
27. Hendi A, Brodland DG, Zitelli JA. Extramammary Paget's disease: surgical treatment with Mohs micrographic surgery. J Am Acad Dermatol 2004;51:767–73.
28. Kitagawa KH, Bogner P, Zeitouni NC. Photodynamic therapy with methyl-aminolevulinate for the treatment of double extramammary Paget's disease. Dermatol Surg 2011;37:1043–6.
29. Siesling S, Elferink MAG, van Dijck JA, Pierie JP, Blokx WA. Epidemiology and treatment of extramammary Paget disease in the Netherlands. Eur J Surg Oncol 2007;33:951–5.
30. Zhu Y, Ye DW, Yao XD, Zhang SL, Dai B, Zhang HL, et al. Clinicopathological characteristics management and outcome of metastatic penoscrotal extramammary Paget's disease. Br J Dermatol 2009;161:577–82.

Ekstramamarna Padžetova bolest u pubičnoj regiji – prikaz slučaja

Sažetak

Autori prikazuju slučaj bolesnice sa ekstramamarnom Padžetovom bolesti u pubičnoj regiji koja je lečena kod dermatologa u privatnoj praksi skoro dve godine pre incizione biopsije promene. Detaljnom pretragom nije utvrđeno istovremeno prisustvo maligniteta unutrašnjih organa, a definitivna dijagnoza je postavljena ekscizijom kožne promene u celosti i odgovarajućom patohistološkom analizom.

Po mnogim kriterijumima naša bolesnica odgovara navodima u savremenoj literaturi, ali je u ovom slučaju bilo zanimljivo to da nije došlo do širenja neoplazme sa mesta primarnog ekstramamarnog M. Padžet u dubinu tkiva.

Ključne reči

Ekstramamarna Padžetova bolest; Kožne neoplazme; Ženske genitalije; Rekonstruktivne hirurške procedure; Histološke tehnike

Cheilitis Glandularis Apostematosa in a Female Patient – a Case Report

Mirjana PARAVINA*

Faculty of Medicine, University of Niš, Serbia

*Correspondence: Mirjana Paravina, E-mail: mirjanaparavina@gmail.com

UDC 616.317-002-092-08

Abstract

Cheilitis is an inflammatory condition of the vermilion border of the lips, which is the junction between the skin and the mucosa. Cheilitis may arise as a primary disorder of the vermilion zone; the inflammation may extend from the nearby skin, or less often from the oral mucosa. Primary cheilitis lesions are either superficial or deep. Deep types include cheilitis glandularis (inflammatory changes and lip gland swelling), and granulomatous cheilitis (chronic swelling of the lip due to granulomatous inflammation mostly of unknown origin). Cheilitis glandularis is a rare condition that mostly affects the lower lip and it is characterized by nodular enlargement, reduced mobility and lip erosion. Based on clinical presentation, cheilitis glandularis may be classified into three subtypes: simplex (described as Puente and Acevedo), superficial suppurative (described by Baelz-Unna), and the most severe type – deep suppurative, also known as cheilitis glandularis apostematosa (Volkmann's cheilitis) characterized by deep-seated inflammation forming abscesses and fistulous tracts.

This is a case report of a female patient with a deep suppurative type of cheilitis affecting both lips. Treatment with systemic antibiotics (using antibiogram tests), corticosteroids and topical therapy resulted in significant improvement.

Key words

Cheilitis + diagnosis + etiology + classification + therapy; Disease Progression; Prognosis; Treatment Outcome

Cheilitis is an inflammatory condition of the vermilion border of the lips, which is the junction between the skin and the mucosa. Cheilitis may arise as a primary disorder of the vermilion zone, the inflammation may extend from the nearby skin, or less often from the oral mucosa (1, 2). Cheilitis may represent a focal inflammatory process or a manifestation related with diseases of other systems or organs (3). The primary cheilitis lesions are either superficial or deep (4). Superficial cheilitis can be classified into: exfoliative (factitious); postmenopausal; actinic (solar); allergic (contact); eczematous; angular and abrasive precancerous (Manganotti's). Deep types of cheilitis include glandular and granulomatous C.

Glandular cheilitis (GC) is a rare condition characterized by inflammatory changes and swelling of salivary glands in the lips. It commonly affects the lower lip with clinical manifestations of nodular enlargement, reduced mobility and lip inversion (5). It is most commonly seen in adult males (6), but it has also been described in females (7, 8), and children (9). Cases involving the upper (10) or both lips (11) have also been reported.

The etiological factors are sometimes hard to determine. Some causes or predisposing factors include bacterial infections (mostly *Staphylococcus aureus*), syphilis, actinic radiation, smoking, poor oral hygiene, compromised immune system, but also genetic transmission (autosomal dominant transmission is suggested) (11, 12, 13). Leao (14) described a case of GC in a HIV-infected patient, with an explanation that it was probably a coincidence.

Based on clinical presentation, glandular cheilitis can be classified into subtypes: simplex (described by

Puente and Acevedo) (15), superficial suppurative (described by Baelz-Unna) (16, 17), and a more severe deep suppurative type, also known as myxadenitis labialis or cheilitis glandularis apostematosa (Volkmann's cheilitis) (18), characterized by deep-seated inflammation forming abscesses and fistulous tracts.

Von Volkmann (18) was the first to describe cheilitis glandularis apostematosa in 1870, as a chronic suppurative inflammation of the lower lip characterized by swelling of the mucus glands and the mucopurulent discharge through the dilated ductal openings.

We report a patient with deep suppurative type of cheilitis of both lips. The treatment with systemic antibiotics (using antibiogram tests), corticosteroids and topical therapy resulted in significant improvement.

Case Report

A 61-year-old village housewife claimed that the first changes occurred on the right half of her lower lip at the age of 56 in the form of prominent redness, bumps and wetting. During the next year, the changes affected the entire lower lip. At the age of 60, the initial wetting was followed by purulent discharge, with scales and squamous lesions. She was treated by a dermatologist, a dentist and an ENT (ear, nose and throat) specialist. Various drugs were applied, mostly topically: antibiotics, antimycotics, interferon and acyclovir. The treatment provided only mild, temporary improvement.

Clinical status at first examination (the first contact with the patient)

Both lips and the vermilion border were covered with thick, adherent scales and squamous crusts; purulent hemorrhagic discharge was seen under pressure (Figure 1); lesions were painful, especially sensitive to touch, while normal functions such as speaking, eating and chewing were compromised.

Clinical status after crust removal

Both lips were enlarged, extremely erythematous, infiltrated, with erosions and superficial shallow ulcerations and fissures; the erythema and infiltration spread along the vermilion; the corners of the mouth were not affected (Figure 2); the lips were of hard-elastic consistency to touch and granular in structure; extreme sensitivity caused hemorrhagic or purulent discharge; the regional lymph nodes were not enlarged; the tongue was unaffected, while the teeth were neglected and mostly missing.

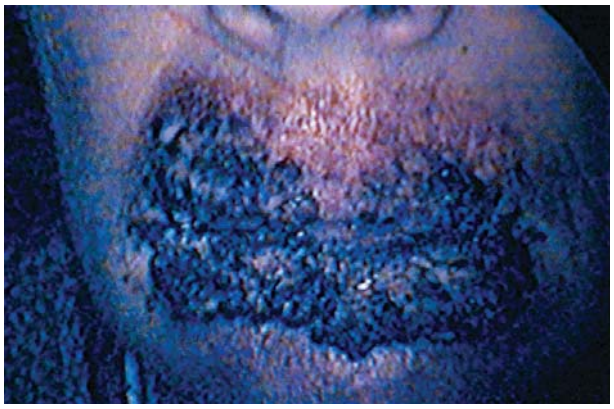


Figure 1. Both lips and the vermilion border are covered with thick, adherent scales and squamous crusts with purulent hemorrhagic lesions underneath

Internist examination

The internist examination showed normal findings.

Laboratory tests

The relevant hematological and biochemical parameters were within physiological levels; the serologic test for syphilis and enzyme-linked immunosorbent assay

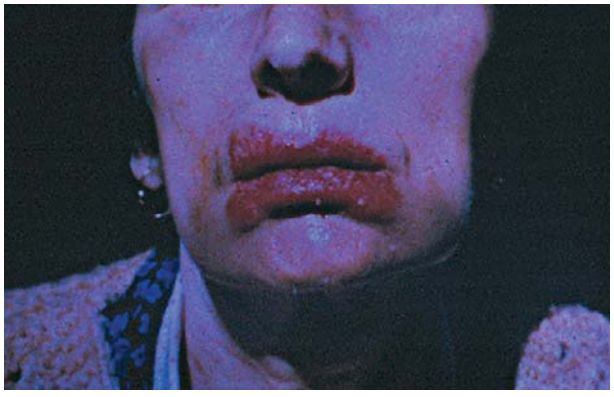


Figure 2. Both lips are enlarged, extremely erythematous, infiltrated, with erosions and superficial shallow ulcerations and fissures; erythema and infiltration spread along the vermilion; corners of the mouth not affected

(ELISA) for human immunodeficiency virus (HIV) antibodies were negative; bacteriological examination of lesion specimens showed *Staphylococcus alpha haemolyticus* and *Neiseria catharalis*.

Histopathological analysis

Probatory excision was performed 5 years earlier at the Ear, Nose and Throat Clinic in Belgrade: histological findings were consistent with inflammatory leukoplakia; the affected area showed folliculitis, and there were erosions of the vermilion lip. Repeat biopsy was rejected by the patient.

Treatment

The therapy included oral ciprofloxacin (500 mg twice a day) according to antibiogram during 10 days; 15 mg prednisone per day during 3 months; boric acid and antiseptic solutions were used to remove crusts and squamous lesions, which was followed by application of antibiotic ointments (garamycin and later chloramphenicol).

Local status after therapy

The lips were less infiltrated and erythematous without layers of crusts and squamous lesions with some erosions of the central lower lip (Figure 3); repeated antibiotic and corticosteroid therapy resulted in significant improvement (Figure 4).

Discussion

The classification of GC into three subtypes was done regarding the severity of inflammation, presence of bacterial infection and lip enlargement (5, 7, 19, 20). The simplex GC is characterized by multiple painless lesions with central depression and dilated canals, as well as mucous secretion which may occur spontaneously or under pressure. The superficial suppurative type of GC presents swelling of the lip, induration and areas of ulcerations and crusting with secretion of clear or viscous exudates from the salivary duct openings. Deep suppurative type of glandular cheilitis or cheilitis glandularis apostematosa is characterized by formation of deep abscesses and fistula tract that eventually heal by scarring. Episodes of suppurative discharge are spontaneous.

Many believe these subtypes probably represent a continuation of the same disease process, i. e., if the simple type is not treated properly, it becomes secondarily infected and progresses to the next type and then to the next (3). It is possible that the excessive salivary secretion from minor salivary glands represents an unusual response to irritation of the lip caused by other reasons, for example actinic damage or repeated licking (2). The disease progression in our patient has proven this assumption. The first symptoms were typical for GC simplex, probably caused by actinic irritation without data on hereditary

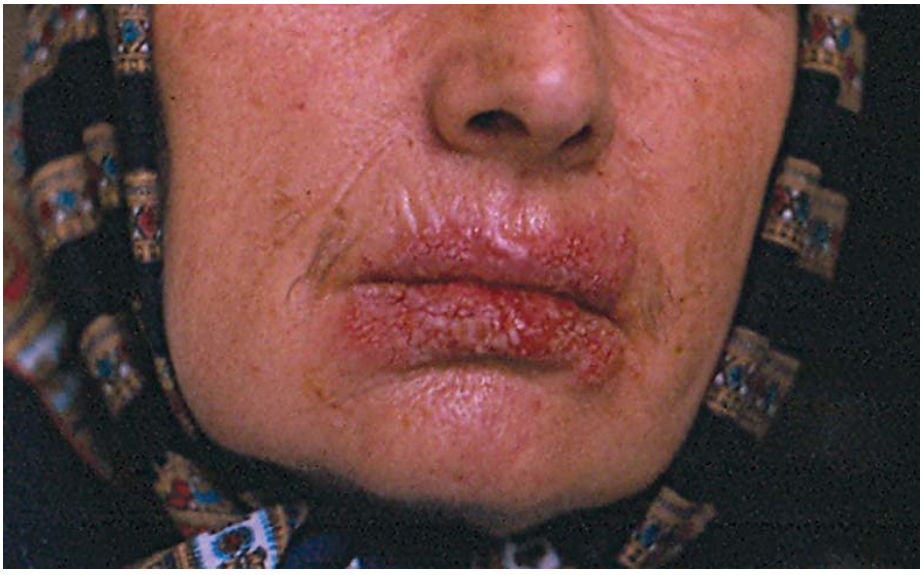


Figure 3. After treatment, lips are less infiltrated and erythematous without layers of crusts and squamous lesions with some erosions of the central lower lip

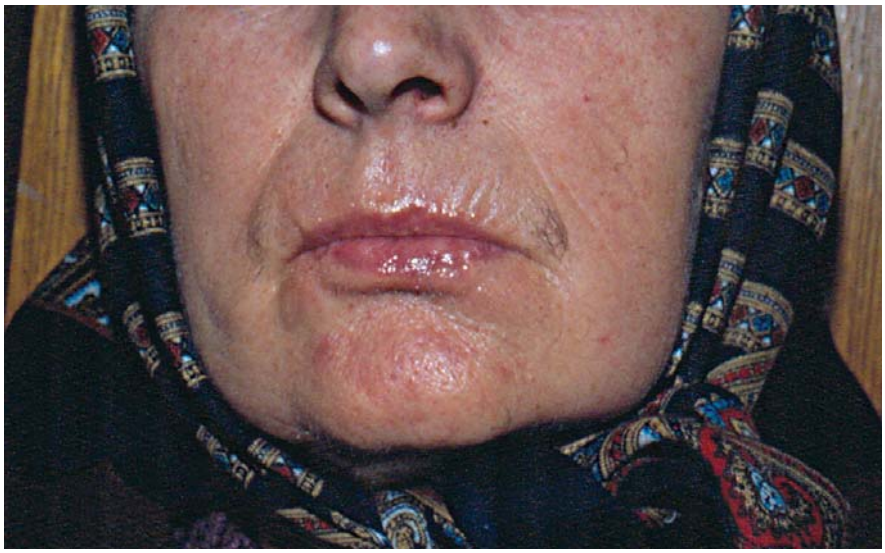


Figure 4. Repeated antibiotic and corticosteroid therapy resulted in significant improvement

burden. The subsequent bacterial infection, probably caused by poor oral hygiene, led to the development of GC apostematosa.

Based on literature data, there is a difference in the definition of the disease. There is a disagreement regarding the obligatory hyperplasia of local salivary glands. While Von Volkmann (14) described cheilitis as swelling of the mucous glands, many authors (4, 6, 8, 11) point to the hyperplasia of minor salivary glands or dilated ductal canals, and some others point to inflammation and swelling (3, 13, 20, 21). This disagreement is based on different histopathological findings: some authors (6, 7, 11) found hyperplasia of minor salivary glands, whereas others did not (3, 9, 12, 14, 21 -29). Based on histopathological findings, it prevails that hyperplasia of salivary glands in GC is not typical; chronic sclerosing sialadenitis and scarring are predominant, whereas ductal ectasia is a dominant histopathological and clinical finding (3). In general, histopathological findings of dense chronic inflammatory infiltrate are found only in more severe types of GC, while genuine hyperplasia of salivary glands or/and ductectasia are rather rare (2).

Differential diagnosis includes angioedema (no swelling between attacks), exfoliative C (persistent scaling), granulomatous C (histological changes are not always conspicuous or specific), elephantiasis nostras (3), irritant or contact cheilitis as well as plasma cell cheilitis (circumscribed, flat or elevated patches of erythema with dense plasma cell infiltrates) (29).

The treatment of GC depends on the type; it may include systemic corticosteroids, but also extensive surgical resections (3). The reduction or elimination of predisposing factors (sun or wind exposure) is the first step in the treatment, followed by photoprotection and use of emollients (30). Apart from topical use, corticosteroids may be used as intralesional and systemic. The treatment may also include anticholinergics, antihistamines and antibiotics (3, 9, 29, 31, 32, 33). Radiation therapy and surgical procedures: cryosurgery, vermilionectomy and/or labial mucosal stripping, may be used as well (33).

After application of local antiseptic and antibiotic ointments, our patient received systemic corticosteroids and antibiotics (according to an antibiogram), which led to initial improvement. Due to some deterioration, the therapy was repeated resulting in significant improvement.

The prognosis for *quo ad sanationam* was unfavorable. Although cases of spontaneous remission (11) have been reported, the treatment outcome is uncertain. The possibility of malignant alteration should not be ignored. Patients with GC, especially those with deep suppurative type, should be followed-up due to the risk of squamous cell carcinoma (SCC) (21, 31). Nico et al. evaluated 22 patients diagnosed

with CG and reported three cases of superficially invasive carcinoma on the lower lip, out of which two were albino. This points to the adverse effects of sun exposure on the development of CG and the possibility of malignant alteration (19, 22), especially in cases of deep suppurative type of CG (30, 31). In some series, 18 – 35% of cases progressed to SCC (22). The reason for this probably lies in the higher susceptibility of the inverted lip to all risk factors for the development of SCC, rather than in GC being a premalignant condition *sui generis*. The majority of reported cases had deep suppurative type of the disease requiring surgical intervention and regular follow-up (3).

Conclusion

This is a report of a female patient with a severe type of glandular cheilitis affecting both lips, with a progressive course and good response to combined antibiotic and corticosteroid therapy.

Abbreviations

C - cheilitis
GC - glandular cheilitis
HIV - human immunodeficiency virus
ENT – ear, nose and throat
Elisa - enzyme-linked immunosorbent assay
SCC - squamous cell carcinoma

References

1. Stanojević M. Bolesti usana, jezika i usne duplje. U: Paravina M, Spalević Lj, Stanojević M, Tiodorović J, Binić I, Jovanović D. Dermatovenerologija, drugo dopunjeno izdanje. Medicinski fakultet Niš. Niš: Prosveta AD; 2006. str. 277-85.
2. Stoopler ET, Carrasco L, Stanton DC, Pringle G, Sollecito TP. Cheilitisglandularis: an unusual histopathologic presentation. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2003;95:313-7.
3. Orlov S, Kojović D, Mirković B. Oralna medicina. Niš: Europrint; 2001. str. 27-37.
4. Louren SV, Gori LM, Boggio P, Nico MMS. Cheilitis glandularis in albinos: a report of two cases and review of histopathological findings after therapeutic vermilionectomy. JEADV 2007;21:1265-7.
5. Taneja P, Singh N. Cheilitis glandularis: a clinical report. Int Chin J Dent 2002;2:2-4.
6. Weir TW, Johnson WC. Cheilitis glandularis. Arch Dermatol 1971;103:433-7.
7. Hillen U, Franckson T, Goos M. Cheilitis glandularis: a case report. Acta Derm Venereol 2004;84:77-9.
8. Yacobi R, Brown DA. Cheilitis glandularis: a paediatric case report. J Am Dent Assoc 1989; 118:317-8.
9. Matsumoto H, Kurachi Y, Nagumo M. Cheilitis glandularis: report of a case affecting upper lip. Showa Shigakkai Zasshi 1989;9:441-5.
10. Yanagawa T, Yamaguchi A, Harada H, Yamagata K, Ishibashi N, Noguchi M, et al. Cheilitis Glandularis: two case reports of Asian-Japanese men and literature rewiew of Japanese cases. ISRN Dentistry 2011; Article ID 457567, 6 pages doi: lo.5402/2011/457567.
11. Lederman DA. Suppurative stomatitis glandularis. Oral Surg Oral Med Oral Pathol 1994; 78:319-22.
12. Mirowski GW, Parker ER. Biology and pathology of the oral cavity. In: Wolf K, Goldsmith LA, Katz SI, Gilchrest BA, Paller AS, Leffel DJ, eds. Fitzpatrik's dermatology in general medicine. 7th ed. New York: McGraw Hill Medical; 2008. p. 641-53.
13. Leao JC, Ferreira AMC, Martins S, Jardim ML, Barret W, Sculi C, et al. Cheilitis glandularis: an unusual presentation in a patient with HIV infection. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2003;95:142-4.
14. Von Volkmann R. Einigefallevon Cheilitisglandularisapostematosa. Arch Pathol Anal 1870;50:142-4.
15. Carrington PR, Horn TD. Cheilitis glandularis: a clinical marker for both malignancy and/or severe inflammatory disease of the oral cavity. J Am Acad Dermatol 2006;54:336-7.
16. Binić I, Janković A. Heilitisi: etiologija i mogućnosti lečenja. U: Karadaglić Đ, Jovanović M, ur. Bolesti sluzokože usne duplje: šta je novo? Beograd: Monografije naučnih skupova AMN SLD; 2010;1(2):37-53.
17. Nico MMS, de Melo JN, Lourenco SV. Cheilitis glandularis: a clinicopathological study in 22 patients. J Am Acad Dermatol 2010;62:233-8.
18. Butt FM, Chindia ML, Ashani A. Cheilitis glandularis progressing to squamous carcinoma in an hiv-infected patient: case report. East Afr Med J 2007;84(12):595-8.
19. Swerlick RA, Cooper PH. Cheilitis glandularis: a reevaluation. J Am Acad Dermatol 1984;10 466-72.
20. Rada DC, Koranda FC, Katz FS. Cheilitis glandularis: a disorder of ductal ectasia. J Dermatol Surg Oncol 1985;11:372-5.
21. Neville B, Damm D, Alen C, Bouquet J. editors. Oral and maxillofacial pathology. 2nd ed. Philadelphia: W.B. Saunders; 2002. p. 389-435.
22. Stuller CB, Schaberg SJ, Stokos J, Pierce GL. Cheilitis glandularis. Oral Surg 1982;53: 602-5.
23. Winchester L, Scully C, Prime SS, Eveson JW. Cheilitis glandularis: a case affecting the upper lip. Oral Surg Oral Med Oral Pathol 1986;62:654-6.
24. Williams HK, Williams DM. Persistent sialadenitis of the minor glands - stomatitis glandularis. Br J Oral Maxillofac Surg 1989;27:212-6.
25. Bender MM, Rubenstein M, Rosen T. Cheilitis glandularis in an African-American woman: reponse to antibiotic therapy. Skinme 2005;4(6):312-7.
26. Michalowski R. Cheilitis glandularis, heterotopic salivary glands and squamous cell carcinoma of the lip. Br J Dermatol 1962;72:445-9.
27. Rogers RS, Bekic M. Diseases of the lips. Semin Cutan Med Surg 1997;16:328-36.
28. Haldar B. Cheilitis glandularis treated by injection of intralesional triamcinolone. Indian J Dermatol 1976;21:53-4.
29. Verma S. Cheilitis glandularis: a rare entity. Br J Dermatol 2003;148:3.

Cheilitis glandularis apostematosa kod osobe ženskog pola – prikaz slučaja

Sažetak

Heilitis *(Cheilitis*) inflamatorno je oboljenje rumene zone usana (vermiliona) koja se nalazi na prelazu kože u sluzokožu. Heilitisi koji nastaju kao samostalna oboljenja mogu biti površni ili duboki. Duboki su *Cheilitis glandularis* i *Cheilitis granulomatosa*. *Cheilitis glandularis* (CG) retka je bolest koja najčešće zahvata donju usnu i karakteriše je nodularno uvećanje, redukovani mobilitet i everzija usne. Kliničke varijante su *CG simplex* (*Puente and Acevedo*), *CG suppurativa superficiallis* (*Baelz-Unna*) i *CG suppurativa profunda seu CG apostematosa* (*Von Volkmann*).

Mi prikazujemo bolesnicu sa dubokom supurativnom formom heilitisa na obema usnama, kod koje je sistemska primena antibiotika, prema antibiogramu, i kortikosteroida, uz lokalnu terapiju, dovela do znatnog poboljšanja.

Ključne reči

Cheilitis + dijagnoza + etiologija + klasifikacija + terapija; Tok bolesti; Prognoza; Ishod lečenja

Perianal Allergic Contact Dermatitis from Benzocaine – a Case Report

Malena GERGOVSKA[1], Kristina SEMKOVA[1], Jana KAZANDJIEVA[1], Nikolay TSANKOV[2]

[1]Department of Dermatology and Venereology, Medical Faculty, Medical University - Sofia, Bulgaria
[2]Clinic of Dermatology and Venereology, Tokuda Hospital Sofia, Bulgaria

*Correspondence: Jana Kazandjieva, Email: janaderm@abv.bg

UDC 616.35-031.63-002:615.211

Abstract

A large number of contact allergic reactions to benzocaine have been reported since its introduction to the pharmaceutical market as an active ingredient in different over-the-counter anesthetic ointments. Benzocaine is used as a key ingredient in many pharmaceuticals, such as products for oral ulcers, wound and burn preparations, sunburn remedies, hemorrhoidal preparations, oral and gingival products, sore throat sprays/lozenges, callous and wart remedies, creams for treatment of poison ivy dermatitis, tooth ache and denture irritation products.

We present a 56-year-old Caucasian male with chronic rash, accompanied by intense itching in the perianal area. The lesions occurred two months earlier and the patient was treated with a wide range of topical antifungals, antibiotics and corticosteroids, with temporary improvement. The skin lesions were consistent with chronic allergic contact dermatitis. The patient denied using any topical preparations other than those prescribed by his dermatologist. Patch testing with the European baseline series was performed. A strongly positive reaction to benzocaine was identified on reading days 2 and 3. Targeted history showed intermittent use of benzocaine anti-hemorrhoidal cream to treat concomitant hemorrhoids.

Benzocaine was discontinued and treatment with methylprednisolone aceponate 0.1% was initiated, resulting in significant improvement. No relapse was observed at 3-month follow-up.

In conclusion, patients with confirmed benzocaine allergy should pay special attention to product labels and avoid products that contain benzocaine and its related substances. All products labelled as “anaesthetic” or “caine” should be suspected of containing benzocaine or related compounds. Patient education and awareness are critical to avoid further episodes and relapses.

Key words

Benzocaine + adverse effects; Dermatitis, Allergic Contact; Anesthetics, Local; Pruritus Ani

Benzocaine is a local anesthetic, commonly used as a topical pain reliever (1). Local anesthetics are widely used in clinical practice and adverse effects are not uncommon. A large number of contact allergic reactions to benzocaine have been reported since its introduction to the pharmaceutical market as an active ingredient in different over-the-counter anesthetic ointments. Benzocaine is used as a key ingredient in many pharmaceuticals, such as products for oral ulcers, wound and burn preparations, sunburn remedies, hemorrhoidal preparations, oral and gingival products, sore throat sprays/lozenges, callous and wart remedies, creams for treatment of poison ivy dermatitis, tooth ache and denture irritation products (2).

Case report

A 56-year-old Caucasian male presented with chronic rash, accompanied by intense itching in the perianal region. The lesions occurred two months earlier and the patient was treated with a wide range of topical antifungals, antibiotics and corticosteroid with temporary improvement. Physical examination

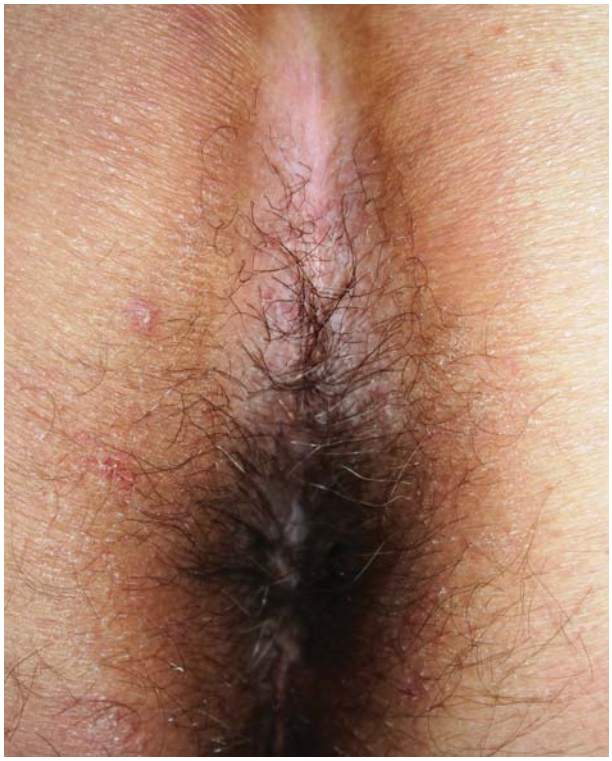


Figure 1. Perianal erythema, mild lichenification of the skin and small erythematous firm papules spread in the anogenital region

revealed perianal erythema, mild lichenification of the skin and small erythematous firm papules spread in the anogenital region (Figure 1). The skin lesions were consistent with chronic allergic contact dermatitis. The patient denied using any topical preparations other than those prescribed by his dermatologist. Routine laboratory findings were within normal ranges. Bacterial and fungal tests were negative. Patch testing with the European baseline series (Chemotechnique Diagnostics, Vellinge, Sweden) was performed. The allergens were placed on the skin of the upper back for 48 hours (day 2). A strongly positive reaction to benzocaine with vesicles and erythema was identified on readings days 2 and 3 (Figure 2). Targeted history showed intermittent use of benzocaine anti-hemorrhoidal cream to manage his concomitant hemorrhoids.

Benzocaine was discontinued and treatment with methylprednisolone aceponate 0.1% was initiated resulting in significant improvement. No relapse was observed at 3-month follow-up.

Discussion

Benzocaine was first synthesized in 1890 by the German chemist Eduard Ritsert (1859-1946) (3) and

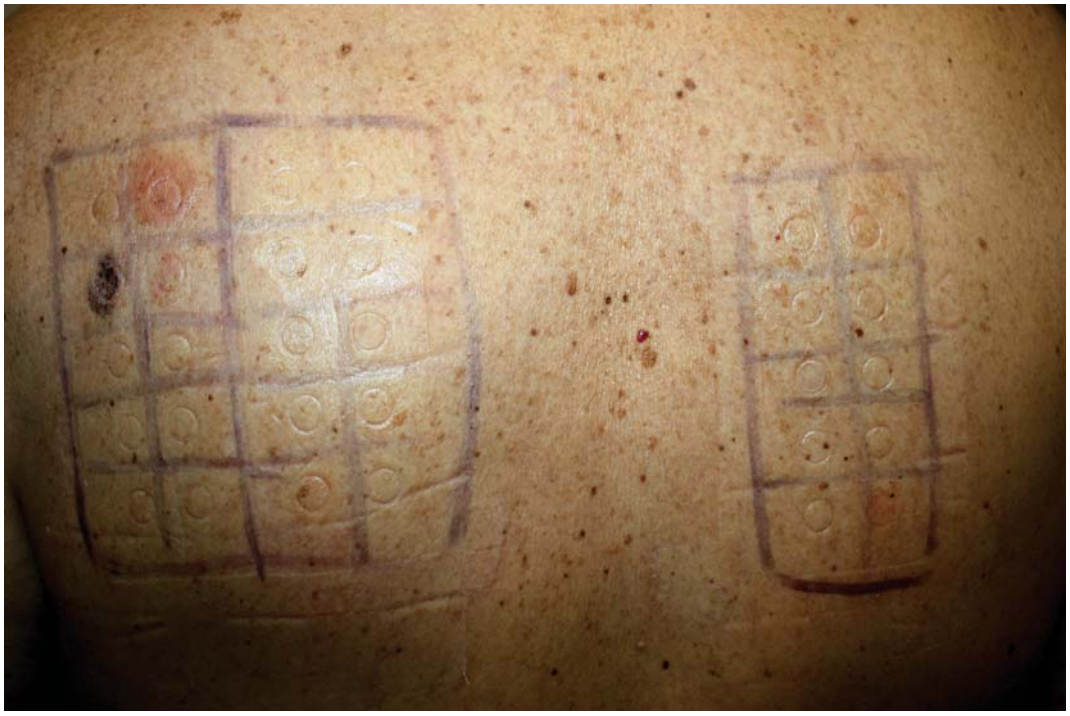


Figure 2. A strongly positive reaction to benzocaine with vesicles and erythema identified at reading on D2 and D3

introduced to the market in 1902 under the name ”Anästhesin”, according to Auterhoff (4) and Demare and Regla (5). It is also known under several other names: ethyl aminobenzoate, ethyl 4-aminobenzoate, 4-aminobenzoic acid ethyl ester, and p-aminobenzoic acid ethyl ester.

Benzocaine is a topical anesthetic, an ethyl ester of p-aminobenzoic acid (PABA). Benzocaine acts to inhibit the voltage-dependant sodium channels (VDSCs) on the nerve membrane, stopping the propagation of the action potential and blocking the local nerve impulses. It is absorbed in very small quantities by the membrane and is hydrolyzed by plasma pseudocholinesterases to metabolites containing PABA, which is highly allergenic and responsible for anaphylactic reactions (5).

Benzocaine is used in many pharmaceutical preparations and rarely in cosmetics. It is also found in antihemorrhoidal creams, some oral suspensions, and cough tablets and can be applied topically to the oral mucosa during dental procedures before injecting the local anesthetic.

Allergic reactions to local anesthetics are frequent. Amide anesthetics (eg., mepivacaine, bupivacaine, lidocaine, and prilocaine) are better tolerated, whereas ester anesthetics (eg., benzocaine, procaine, tetracaine, and chloroprocaine) are more allergenic. Benzocaine yields the greatest number of positive patch test reactions in patients with allergy to ester anesthetics who tolerate amide anesthetics (6). Regarding amide and ester anestethics, the reactivity, if positive to both (amide and ester), is more likely the result of concomitant sensitization than cross-reaction between them (7, 8). Benzocaine can cross-react with other benzoic acid-derived local anesthetics (both topical and injectable forms), as well as parabens. Parabens are alkyl ester derivatives of para-hydroxybenzoic acid and are the most commonly used preservatives in the cosmetic industry. Cross-reactions with para-amino compounds, namely, benzocaine and para-phenylenediamine (PPD), have been reported but are thought to be extremely rare (8).

Paraphenylendiamine (PPD) is found in permanent hair dyes, sulfonamides, sulfonylureas, PABA-based suncreens, and thiazide-related diuretics. Possible explanations for cross-reactions include the presence of common antigenic determinants or transformation to chemically related metabolites in the skin. Benzocaine, parabens, PPD, 2,5-diaminotoluene sulfate, 2-nitro 1,4-PPD, and the azo dyes used in textiles belong to the same group. They have in common the presence of an amino substituent at the para-position of the benzene ring. This structural similarity may explain the frequency of cross-reactions (9).

Adverse effects of topical anesthetics, such as benzocaine, are various and frequent and they can be of immediate-type or delayed. Topical products containing anesthetics are increasingly applied and have the potential to cause allergic contact dermatitis. Skin patch testing for allergy should always be considered in recalcitrant cases and in cases with suspected allergic induction (10). It is estimated that 5% of patients who use topical benzocaine preparations may become sensitized to it and, thus, long-term use can result in increased incidence of hypersensitivity reactions (<1% of all adverse reactions) (11). Most of these reactions are T cell-mediated type IV delayed hypersensitivity reactions, including allergic contact dermatitis confirmed by skin patch tests. Other types of hypersensitivity reactions (type I) IgE-mediated immediate-type reactions (urticaria, angioedema, or anaphylaxis) are very rare (12).

Conclusion

Patients with confirmed benzocaine allergy should pay special attention to product labels and avoid products that contain benzocaine and its related substances. All products labelled as “anaesthetic” or “caine” should be suspected of containing benzocaine or related compounds. Patient education and awareness are critical for avoiding further episodes and relapses.

Abbreviations

PABA - para-aminobenzoic acid
VDSCs - voltage-dependant sodium channels
PPD - paraphenylendiamine

References

1. Schwarz HD. Ritsert, Eduard. In: Neue Deutsche Biographie 2003. p. 653-4. [cited 2014 Jan 15]. Available from: www.deutsche-biographie.de/pnd139207848.html
2. Auterhoff H. Lehrbuch der pharmazeutischen hemie. Stuttgart: Wissenschaftliche Verlagsgesellschaft; 1968.
3. Ritsert E. Über den Werdegang des Anästhesins [On the development of anästhesin]. Pharm Ztg 1925;60:1006-8.

4. Auterhoff H. Lehrbuch der pharmazeutischen chemie. Stuttgart: Wissenschaftliche Verlagsgesellschaft; 1980.
5. Demare P, Regla I. Synthesis of two local anesthetics from toluene: an organic multistep synthesis in a Project-Oriented Laboratory Course. J Chem Educ 2012;89:147.
6. Warshaw EM, Schram SE, Belsito DV, DeLeo VA, Fowler JF Jr, Maibach HI, et al. Patch-test reactions to topical anesthetics: retrospective analysis of cross-sectional data, 2001 to 2004. Dermatitis 2008;19:81-5.
7. Jovanovic M, Karadaglic D, Brkic S. Contact urticaria and allergic contact dermatitis to lidocaine in a patient sensitive to benzocaine and propolis. Contact Dermatitis. 2006;54:124-6.
8. Turchin I, Moreau L, Warshaw E, Sasseville D. Cross-reactions among parabens, para-phenylenediamine, and benzocaine: a retrospective analysis of patch testing. Dermatitis 2006;17(4):192-5.
9. Vu AT, Lockey RF. Benzocaine anaphylaxis. J Allergy Clin Immunol 2006;118: 534-5.
10. Finucane BT. Allergies to local anesthetics: the real truth. Can J Anaesth 2003;50:869-74.
11. Melamed J, Beaucher WN. Delayed-type hypersensitivity (type IV) reactions in dental anesthesia. Allergy Asthma Proc 2007;28:477-9.
12. Thyssen JP, Menné T, Elberling J, Plaschke P, Johansen JD. Hypersensitivity to local anaesthetics - update and proposal of evaluation algorithm. Contact Dermatitis 2008;59:69-78.

Perianalni alergijski kontaktni dermatitis izazvan benzokainom – prikaz slučaja

Sažetak

Uvod. U svetskoj stručnoj literaturi opisan je veliki broj slučajeva kontaktne senzibilizacije izazvane lokalnom upotrebom benzokaina. Ovo se može objasniti velikim brojem lokalnih farmaceutika prisutnih na farmaceutskom tržištu koji se bez lekarskog recepta mogu nabaviti, a koji u svom sastavu sadrže lokalni anestetik. Benzokain predstavlja ključnu aktivnu supstanciju u mnogim preparatima koji se koriste za lečenje oralnih ulceracija, promena na desnima, bolnih upala zuba i grla, opekotina, rana, hemoroida. Nalazi se u velikom broju preparata za ispiranje usta, ali i lokalnih pripravka za lečenje kalusa i klavusa.

Prikaz slučaja. Prikazujemo 56 godina staru pacijentkinju čija je glavna tegoba bila intenzivan svrab u perianalnom predelu. Dva meseca pre pregleda kod nas, pored osećaja svraba, na koži perianalne regije pojavilo se intenzivno crvenilo. U tom vremenskom periodu, u terapiju je uvođen veći broj različitih preparata za lokalno lečenje: antimikotici, antibiotici, kortikosteroidi. Poboljšanje je bilo privremeno, tako da su u momentu pregleda promene odgovarale kliničkoj slici kontaktnog dermatitisa. Pacijentkinja je negirala upoterbu bilo kojeg lokalnog preparata osim navedenih koje joj prepisao dermatolog. Sprovedeno je alergološko testiranje epikutanim testom na kontaktne standardne alergene iz Evropske standardne serije alergena (*Chemotechnique Diagnostics, Vellinge, Sweden*). Utvrđen je ekcemski tip reagovanja (eritem, vezikule, otok) na benzokain. Ciljanom anamnezom otkrili smo da je pacijentkinja povremeno aplikovala na kožu obolele regije krem za lečenje hemoroida. Utvrđeno je da se u sastavu tog krema nalazio benzokain. Po prestanku upotrebe navedenog krema, uz kratkotrajnu primenu kortikosteroidnog krema (*methylprednisolon aceponate* 0,1%) promene su se povukle. Na kontroli obavljenoj posle tri meseca nakon saniranja promena nije dijagnostikovan recidiv.

Diskusija. Za razliku od farmaceutske industrije, kozmetički preparati retko u svom sastavu sadrže benzokain. Pored navedenog, benzokain se nalazi i u tabletama protiv kašlja, a takođe ga aplikuju u vidu spreja za vreme dentalnih procedura (ukoliko se može izbeći davanje parenteralnog lokalnog anestetika).

Neželjene reakcije (nealergijske) na sistemski primenjene lokalne anestetike su česte. Amidska grupa lokalnih anestetika (npr. mepivakain, mupivakin, lidokain, prilkain) bolje se podnose dok veći broj neželjenih efekata izaziva estarska grupa anestetika (npr. benzokain, prokain, tetrakain, hloroprokain). Benzokain je poznat kao kontaktni alergen koji izaziva najveći broj pozitivnih epikutanih reakcija i to kod pacijenata koji pritom ne pokazuju reaktivnost na amidske anestetike, ali ni na ostale pripadnike grupe estarskih anestetika. Benzokain može unakrsno reagovati sa drugim loklanim anesteticima koji predstavljaju derivate benzoeve kiseline (lokalni i parenteralni pripravci) i parabenima. Parabeni predstavljaju alkil-estarske derivate para-

hidroksibenzoeve kiseline, koji se često koriste kao konzervansi u kozmetičkoj industriji. Unakrsno reagovanje parabena sa susptancijama koje u svom sastavu imaju para-amino grupu, npr. benzokainom ili para-fenilendiaminom izuzetno je retko opisano u stručnoj literaturi.
Zaključak. Sve osobe kod kojih je utvrđena preosetljivost na bezokain mogu da koriste samo one preparate koji u svom sastavu nemaju benzokain ili njemu hemijski slične supstancije. U sastavu svakog proizvoda koji u svom nazivu sadrži reč „anestetik" ili „kain" treba isključiti prisustvo benzokaina i njemu hemijski srodnih supstancija. Edukacija pacijenta je preduslov kako bi se izbegli recidivi neželjenih reakcija.

Ključne reči

Benzokain + neželjena dejstva; Alergijski kontaktni dermatitis; Lokalni anestetik; Analni pruritus

Euromelanoma Campaign 2013 in Serbia

Clinic of Dermatovenereology, Clinical Ceneter of Serbia, Faculty of Medicine, University of Belgrade, Department of Dermatovenereology, Belgrade, Serbia

Euromelanoma Campaign in Serbia 2013 was organized by the Serbian Association of Dermatovenereologists and Euromelanoma Europe, under the auspices of the Ministry of Health of the Republic Serbia, supported by Beiersdorf Eucerin Company. This year, Euromelanoma Monday was set for May 13th 2013. The motto for all participating European countries included in the Campaign was "Skin cancer can be seen. See it, stop it!"

The aim of the Campaign was to identify as many people at risk for skin cancer as possible, as early as possible, provide information about risk factors and symptoms of melanoma in early stages and alert the public to dangers of sun exposure.

Intense media promotion was organized a month prior to the screening day: radio and TV announcements, informative posters in public areas, newspaper advertisements and PR articles on melanoma and Euromelanoma Day. Poster advertisements and an open line center were founded to provide information about participating dermatologists, addresees and so forth. Websites: www.udvs.org and www.euromelanoma.org/serbia provided basic information about the prevention,

Figure 1. Press Conference - Participants: Prof. Dr. Ljiljana Medenica, campaign coordinator for Euromelanoma and the National Euromelanoma team, member of the Executive Committee of the European Academy of Dermatology and Venereology, Director of the Department of Dermatology, Clinical Center of Serbia, Belgrade; sitting on the left is Prof. Dr. Miloš Nikolić, member of the National Euromelanoma team, President of the Association of Serbian Dermatologists; sitting on the right: Dr. Jugoslav Kelečević, Ministry of Health of the Republic of Serbia Advisor, and T. A. Dr. Dušan Škiljević, member of the National Euromelanoma team, teaching assistant at the Department of Dermatology, School of Medicine in Belgrade

screening, diagnosis and treatment of melanoma and other skin cancers.

In order to take part in the Campaing, people could get information on participating dermatologists (their addresses and phone numbers) and make appointments through free of charge phone calls (from 7th to 9th May, 2013; call center: 0800 222 888 from 08:00-20:00).

A unique anonymous Euromelanoma questionnaire (approved by the Ethic Committee of the Serbain Association of Dermatovenereologists) was translated into Serbian and sent to the participating dermatologists after the list of appointments was closed.

Dermatologists from all over Serbia participated in the Euromelanoma Campaign. One hunderd and twenty dermatologists (~50% of all dermatologists of the Serbian Association of Dermatovenereologists) performed skin screening of patients on their lists; there were 114 dermatologists from public hospitals and 6 dermatologists from private practice. Free-of-charge screening was performed in 1.494 subjects. The screening took place at Dermatology Clinics of Medical Centers, Outpatient Clinics or Private Offices.

The majority of screened subjects were female; 986/1.494 (67.1%) females and 484/1.494 (32.9%) males participated in the Campaign. There was a wide spectrum of ages. Over 65% of individuals were sensitive phototypes II or III. A significant percentage (17%) reported outdoor jobs. More impressively, 20.1% of individuals reported sunburns before adolescence, and this may correlate to the fact that most individuals belonged to sensitive phototypes. Also, 6.6% used solarium, ≤ 20 sessions per year, and 0.8% >20 sessions per year, which would be worth comparing with other European countries, given its implication in skin cancer risk.

The clinical screening results revealed that 25.8% of subjects had dysplastic nevi, 24.0% actinic keratoses (AKs), 3.9% basal cell carcinomas (BCCs), 0.5% squamous cell carcinomas (SCCs), while 13.2% were diagnosed with melanoma. Statistical analysis was performed for patients with melanoma, BCC, SCC and suspected lesions. Statistical analysis was also performed for patients with melanoma, BCC, and SCC - suspected lesions.

Euromelanoma Day Campaign team from Serbia was represented by Prof. Lj. Medenica, Prof. M. Nikolić, Assist. Prof. D. Škiljević.

Ljiljana MEDENICA
Clinic of Dermatovenereology
Clinical Center of Serbia, Belgrade, Serbia
*Correspondence: Ljiljana MEDENICA
E-mail: medenicaljiljana@yahoo.com

FORTHCOMING EVENTS

Dermatology and Venereology Events 2014

DATE	MEETINGS, CONGRESSES, SYMPOSIA	ABSTRACT SUBMISSION DEADLINE	MORE INFORMATION AT
28 February, 2014	Symposium on Psoriasis, Military Medical Academy, Belgrade, Serbia	No abstract submission	www.sld.org.rs
7 March, 2014	Meeting of the Serbian Medical Society's Section of Dermatology and Venereology, Clinical Center of Serbia, Belgrade, Serbia	No abstract submission	www.sld.org.rs
28 March, 2014	Symposium on Melanoma Update, Military Medical Academy, Belgrade, Serbia	No abstract submission	www.sld.org.rs
8-10 April, 2014	Dubai World Dermatology & Laser Conference 2014, Dubai, United Arab Emirates	31 December, 2013	www.dubaiderma.com
11 April, 2014	Symposium on Autoimmune Bullous Diseases, Military Medical Academy, Belgrade, Serbia	No abstract submission	www.sld.org.rs
11 April, 2014	Meeting of the Serbian Medical Society's Section of Dermatology and Venereology, Military Medical Academy, Belgrade, Serbia	No abstract submission	www.sld.org.rs
23-26 April, 2014	9th European Lupus Meeting, Athens, Greece	15 January, 2014	www.lupus2014.org
24-26 April, 2014	European Workshop on Skin Immune Mediated Inflammatory Diseases, Verona, Italy	16 February, 2014	www.simid2014.org
7-10 May, 2014	10th EADO Congress, Vilnius, Lithuania	1 February, 2014	www.eado2014.com
10 May, 2014	Meeting of the Serbian Medical Society's Section of Dermatology and Venereology, Clinical Center of Niš, Prolom Banja, Serbia	No abstract submission	www.sld.org.rs
22-25 May, 2014	11th EADV Spring Symposium, Belgrade, Serbia	17 January, 2014	www.eadvbelgrade2014.org
4-7 June, 2014	6th Summer Academy Practical and Aesthetic Medicine, Sofia, Bulgaria	No deadline information	www.summerdermatology.com
9-12 June, 2014	2014 STD Prevention Conference in Collaboration with the 15th IUSTI World Congress and the 2nd Latin American IUSTI-ALACITS Congress, Atlanta, Georgia USA	15 April, 2014	www.cdc.gov

Prepared by: Dr. Tatjana Roš, Clinic of Dermatovenereology Diseases, Clinical Center of Vojvodina, Novi Sad, Serbia, E-mail: t.rosh@nscable.net

AUTHOR GUIDELINES

Serbian Journal of Dermatology and Venereology is a journal of the *Serbian Association of Dermatologists and Venereologists*. The journal is published in English, but abstracts will also be published in Serbian language. The journal is published quarterly, and intended to provide rapid publication of papers in the field of dermatology and venereology. Manuscripts are welcome from all countries in the following categories: editorials, original studies, review articles, professional articles, case reports, and history of medicine.

Categories of Manuscripts

1. Editorials *(limited to 5 pages) generally provide commentary and analyses concerning topics of current interest in the field of dermatology and venereology. Editorials are commonly written by one author, by invitation.*

2. Original studies *(limited to 12 pages) should contain innovative research, supported by randomized trials, diagnostic tests, outcome studies, cost-effectiveness analysis and surveys with high response rate.*

3. Review articles *(limited to 10 pages) should provide systemic critical assessment of literature and other data sources.*

4. Professional articles *(limited to 8 pages) should provide a link between the theory and practice, as well as detailed discussion or medical research and practice.*

5. Case reports *(limited to 6 pages) should be new, interesting and rare cases with clinical significance.*

6. History of medicine *(limited to 10 pages) articles should be concerned with all aspects of health, illness and medical treatment in the past.*

7. Short Communications *(limited to 3 pages) should disseminate most current results and developments in the shortest possible time. They will be reviewed by expert reviewers and evaluated by the Editor.*

The journal also publishes book reviews, congress reports, as well as reports on local and international activities, editorial board announcements, letters to the editor, novelties in medicine, questions and answers, and "In Memoriam". All submitted manuscripts will undergo review by the editor-in-chief, blind review by members of the manuscript review panel or members of the Editorial Board. Manuscripts submitted to this journal must not be under simultaneous consideration by any other publisher. Any materials submitted will NOT BE RETURNED to the author/s.

All manuscripts should be submitted to the **Editor in Chief: Prof. Dr. Marina Jovanović***, Clinic of Dermatovenereologic Diseases, Clinical Center of Vojvodina, Hajduk Veljkova 1-3, Novi Sad, Serbia, by mail to: serbjdermatol@open.telekom.rs.*

Manuscripts for submission must be prepared according to the guidelines adopted by the International Committee of Medical Journal Editors (www.icmje.org). Please consult the latest version of the Uniform Requirements for Manuscripts Submitted to Biomedical Journals.

1. Manuscript Preparation Guidelines

The manuscript should be written in English, typed in double spacing throughout on A4 paper, on one side only; Use Times New Roman, font size 12, with 30 lines and 60 characters per line. Articles must be written clearly, concisely and in correct English. Accepted manuscripts in need of editing will be returned after editing to the corresponding author for approval. When preparing their manuscripts, authors should follow the instructions given in the *Categories of Manuscript:* the number of pages is limited (including tables, figures, graphs, pictures and so on to 4 (four)), and all the pages must be numbered at the bottom center of the page.

For manuscript preparation, please follow these instructions:

1.1. Title page

The title page should include the following information:

- The title of the article, which should be informative, without abbreviations and as short as possible;

- A running title (limited to 30 characters);

- Authors' names and institutional affiliations;

- The name, mailing address, telephone and fax numbers, and email of the corresponding author responsible for correspondence about the manuscript. Furthermore, authors may use a footnote for acknowledgements, information and so on.

1.2. Abstracts

A structured abstract in English *(limited to 150 words) should follow the title page. The abstract should*

provide the context or background for the study, as well as the purpose, basic procedures, main findings and principal conclusions. Authors should avoid using abbreviations.

- An **abstract in Serbian language***, (limited to 150 words) should follow the second page. It should contain a briefing on the purpose of the study, methods, results and conclusions, and should not contain abbreviations.*

1.3. A list of abbreviations

Use only standard abbreviations, because use of non-standard abbreviations can be confusing to readers. Avoid abbreviations in the title, abstract and in the conclusion. A list of abbreviations and full terms for which they stand for should be provided on a separate page. All measurements of length, height, weight, and volume should be reported in the metric units of the International System of Units – SI, available at http://www.bipm.fr/en/si/.

1.4. Cover Letter

Manuscripts must be accompanied by a cover letter, which should include a date of submission, statement that the manuscript has been read and approved by all the authors and that the authorship requirements have been met. It should also include the name, address, and telephone number of the corresponding author, who is responsible for communicating with other authors about revisions and final approval of the proofs. The original copy of the cover letter, signed by all authors, should be enclosed with the manuscript.

2. Tables and illustrations

Tables *should capture information concisely and precisely. Including data in tables, rather than in the text, reduces the length of the article itself.*

- Submit tables in separate files, not included in the manuscript. Tables are to be double spaced and numbered sequentially, with Arabic numbers (Table 1, Table 2, etc.), in order of text citation. Each column, including the first, must have a heading. Provide a brief title for each table. Put all explanatory matter in footnotes, including any nonstandard abbreviations used in the table.

- **Figures** should be submitted in a separate file, not included in the manuscript document. Cite figures consecutively, as they appear in the text, with Arabic numbers (Fig. 1, Fig. 2, Fig. 3, etc.). Each figure must be assigned a title, as well as a legend. Legends should appear on a separate page, not with each figure. The **Legend Page** is to be numbered in sequence after the last page of the references list. Figures should be professionally drawn, as sharp black-and-white or color photographs. If photographs of persons are used, either the subjects must not be identifiable, or their pictures must be accompanied by written permission to use them.

3. References

References in the text, tables and legends should be identified by Arabic numerals in parentheses. Number references consecutively in the order in which they are first mentioned in the text. The *Vancouver System* of referencing should be used. List each author's last name and initials; full first names are not included. List all authors, but if the number exceeds six, give the first six followed by „et al." National journals, which are not indexed in *Index Medicus*, should be abbreviated according to the style in the *List of Abbreviated Titles of Yugoslav Serial Publications* available on http://vbsw.vbs.rs. For further information please visit www.ICMJE.org.

4. Additional information

Accepted manuscripts are edited and returned to the corresponding author for approval. Then a final version of the manuscript will be requested in a defined period of time. Authors will be notified of acceptance or rejection by email, within approximately 4 weeks after submission.

- Open access: Every article published in the **Serbian Journal of Dermatology and Venereology** will immediately be accessible on **www.udvs.org** to everyone at no charge.

For further information please contact the Editorial Office (Tel: +381 21/484 35 62) or visit our web site: **www.udvs.org**.

CIP – Каталогизација у публикацији
Народна библиотека Србије, Београд

616.5(497.11)

SERBIAN Journal of Dermatology and Venerology / editor-in-chief Marina Jovanović. - Vol. 1, no. 1 (january 2009)- . - Belgrade (Pasterova 2) : The Sebian Association of Dermatovenereologists, 2009- (Beograd : Zlatni presek). - 30 cm

Tromesečno
ISSN 1821-0902 = Serbian Journal of Dermatology and Venerology
COBISS.SR-ID 156525836

KOMPLEMENTARNA MEDICINSKA NEGA KOJA DELUJE NA SVA 4 UZROKA ZBOG KOJIH NASTAJU AKNE

Eucerin istraživački tim formulisao je jedinstveni, patentom zaštićeni kompleks aktivnih principa koji deluju na glavne uzroke nastanka akni:
L-karnitin reguliše produkciju sebuma
Dekandiol deluje antibakterijski
Likokalkon A deluje antiinflamatorno

U saradnji sa dermatolozima, formulisana je dnevna krema koja rešava probleme koji se često javljaju kao posledica medicinskog tretmana akni, a to su dehidrirana koža i fotosenzitivnost.

Eucerin DermoPURIFYER komplementarna hidratantna krema SPF 30

Osim patentom zaštićenog kompleksa protiv akni ova krema sadrži:

- Gliko-glicerol koji stimuliše stvaranje akvaporin kanala i obezbeđuje dubinsku hidrataciju kože
- Visoku UVA/UVB zaštitu

Efikasnost i veoma dobra podnošljivost na koži dokazana je kliničkom studijom.
Klinička studija Eucerin DermoPURIFYER Komplementarna hidratantna krema[1]:

- Procena podnošljivosti od strane lekara i pacijenata: veoma dobra
- Preporuka (od strane lekara): 93%
- Želja za ponovnim korišćenjem (pacijenti): 85%

Eucerin DermoPURIFYER preparati mogu da se koriste zajedno sa uobičajenim medicinskim tretmanima akni. Svi preparati su nekomedogeni i pogodni su za svakodnevnu upotrebu.

[1] Eksterna klinička in-use studija, 29 pacijenata koji su na nekoj medicinskoj terapiji akni (na primer retinoidi, benzoil peroksid); nakon 8 nedelja korišćenja preparata, vizuelna procena na početku tretmana, nakon 4. i 8. nedelje, fokus na dobroj podnošljivosti

Cover figure: Christ Healing Ten Lepers, Christ's Miracles, 14th century, The monastery Visoki Dečani, Serbia, Kosovo

Published by the
Serbian Association of Dermatovenereologists