



FREQUENCY OF BALANITIS XEROTICA OBLITERANS AMONG BOYS WITH PHIMOSIS

UČESTALOST BALANITIS XEROTICA OBLITERANS-A KOD DJEČAKA SA FIMOZOM

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ABSTRACT

Introduction: Balanitis xerotica obliterans (BXO) is an inflammatory disease of unknown etiology and pathogenesis, that represents genital form of lichen sclerosus. Disease is located on foreskin, glans of penis and on urethra. It was discovered that BXO is common cause of phimosis. There is evidence of connections between balanitis xerotica obliterans and appearance of squamous cell carcinoma. The diagnosis of the disease can be clinical and pathohistological. Therapy can be conservative and surgical.

The Aim: Determining the frequency of BXO among the boys with phimosis in the light of increasing number of evidence about importance of this clinical entity in development of many complications of urogenital system.

Material and methods: Our research contained 470 male patients aged from 1 to 18 years. All the patients who were included in the study were surgically treated in period from 1. January 2014. till 1. January 2017. in University Children's Hospital and all of them had diagnosed phimosis. All the patients underwent circumcision. Foreskins that were suspicious of BXO diagnosis, but could not be diagnosed clinically, were sent to pathohistological analysis. Statistical methods used for measuring central tendency and for determining frequency of BXO were methods of descriptive statistics, or frequency analysis in IBM SPSS Statistics 22 program.

Results: Patients with phimosis were in average age of 9.12 ± 4.46 (1-18) years. After data analysis, it was established that in the group of 470 patients there are 48 with BXO diagnosis (10.21%). Patients with BXO were in average age of 10.33 ± 3.14 (6-18) years.

Conclusion: Our research has shown that the frequency of BXO among boys with phimosis population is coherent with results of other studies. We concluded that pathohistological analysis of the foreskin is necessary to avoid false negative results after clinical examination.

Keywords:

balanitis xerotica obliterans,
lichen sclerosus,
phimosis



SAŽETAK

Uvod: Balanitis xerotica obliterans (BXO) je inflamatorna bolest nepoznate etiologije i patogeneze, koja predstavlja genitalnu varijantu lichen sclerosus-a. Bolest zahvata prepucijum, glans penisa i uretru. Ustanovljeno je da je BXO čest uzročnik fimoze. Dokazana je povezanost između balanitis xerotica obliterans-a i pojave skvamocelularnog karcinoma. Dijagnoza bolesti može biti klinička i patohistološka. Terapija se dijeli na konzervativnu i hiruršku.

Cilj: Utvrđivanje učestalosti BXO kod dječaka sa fimozom u svjetlu sve većeg broja dokaza o značaju ovog kliničkog entiteta u razvoju mnogobrojnih komplikacija urogenitalnog trakta.

Materijali i metode: Naše istraživanje je obuhvatilo 470 pacijenata muškog pola uzrasta od jedne do 18 godina. Svi pacijenti uključeni u studiju su u periodu od 1. januara 2014. do 1. januara 2017. bili hirurški liječeni u Univerzitetnoj dečjoj klinici i svi su imali postavljenu dijagnozu fimoze. Kod svih pacijenata urađena je cirkumcizija. Preparati kože prepucijuma koji su bili suspekti na dijagnozu BXO, a kod kojih se dijagnoza nije mogla klinički postaviti su poslani na patohistološku analizu. Od statističkih analiza za određivanje mjera centralne tendencije i za određivanje učestalosti BXO korišćene su metode deskriptivne statistike, odnosno analiza frekvenci u programu IBM SPSS Statistics 22.

Rezultati: Pacijenti sa fimozom su bili prosječnog uzrasta od $9,12 \pm 4,46$ (1-18) godina. Analizom podataka je ustanovljeno da se u grupi od 470 pacijenata nalazi 48 sa dijagnozom BXO (10,21%). Pacijenti sa BXO su bili prosječnog uzrasta od $10,33 \pm 3,14$ (6-18) godina.

Zaključak: Naše istraživanje je pokazalo da je učestalost BXO u populaciji dječaka sa fimozom u skladu sa rezultatima drugih istraživanja. Zaključili smo da je patohistološka analiza preparata prepucijuma neophodna da bismo izbjegli lažno negativne nalaze nakon kliničkog pregleda.

Ključne reči:

Balanitis xerotica obliterans, lichen sclerosus, fimozza

Introduction

Balanitis xerotica obliterans (BXO) is a disease first described by Stuhmer in 1928. BXO is now considered to be the male genital variant of lichen sclerosus et atrophicus. This disease can involve the prepuce, the glans or the urethra, either individually or in any combination. BXO was regarded as an exclusively adult disease, until a case was documented in a 7-year-old boy in 1962. Later, during the 1970s it is recognized as a common cause of acquired phimosis and meatal stenosis in schoolboys (1). BXO represents a chronic inflammatory process of an unknown etiology (2), although it is believed to be a multifactorial disease. It has been noticed that the disease occurs in monozygotic twins, which may suggest a genetic basis of disease (3). Genetic factors have been implicated in association with HLA subtypes among male members of the family. Publications showed an incidence of disease with other auto-immune type conditions (e.g. diabetes, vitiligo, alopecia). An infective etiology has also been considered (on viruses, spirochetes and acid-fast bacilli) (1) but the connection was not proven.

The pathogenesis is unclear. Lichen sclerosus can occur anywhere on the body, regardless of gender and age of the patient, but most frequently the outer genitals. It is manifested with areas of skin paleness, polygonal papules or plaques with thinned, atrophic, fragile skin, sometimes with telangiectasia, purpura, erosion or soft fissures. Hyperkeratosis and sclerosis can be seen on affected areas. The frenulum often becomes contracted and followed by

scarring of the prepuce that leads to a phimosis, characterized by the typical whitish discoloration (4). Changes on the penis can also be manifested as ulcers on the glans. The above mentioned changes on the penis can lead to disturbances in urination and impairment of sexual function (5). BXO is also associated with the risk for malignant transformation. Guidelines of European Association of Urology (EAU) classify BXO among high-risk factors for the development of squamous cell carcinoma of the penis (6).

The diagnosis of lichen sclerosus (BXO) is usually clinical. In the case when clinical signs of the disease are expressed clearly, histopathologic examination is normally not required. Making a diagnosis in the early stage of the disease can be complicated. In clinically unclear cases, biopsy and histological analysis of the prepuce are recommended. Third of men with clinical signs and symptoms of the disease have non-specific results, after histological analysis of the prepuce after circumcision. Non-specific biopsy results do not rule out the disease, while specific findings after a biopsy confirm the diagnosis (7). Histologically, the typical cases of lichen sclerosus show lichenoid dermatitis with vacuolization of the basal layer of the epidermis and with homogenization and sclerosis of superficial dermis (4). Differential diagnosis includes lichen planus, scleroderma, leukoplakia, vitiligo and erythroplasia of Queyrat (5).

Treatment options can be divided into conservative and surgical. BXO conservative therapy proposes the use of topical corticosteroids. Corticosteroids which are

used as a therapy for BXO represent ultra potent corticosteroids, such as Clobetasol, Diflorasone and Betamethasone (8). Surgical treatment depends on the progression of the disease. Circumcision is the most common and can be a definite treatment method for disease confined to the glans and prepuce. Surgical treatment used for more complex cases of BXO, when urethral meatus is affected and includes procedures such as meatoplasty, urethrotomy, urethral dilatation or complicated procedures such as urethroplasty with buccal mucosa or mucosa of the bladder as a graft, or excision of the affected regions with the use of skin grafts, if the BXO affect glans, coronary sulcus and penile skin (5).

The aim of this study is to determine the incidence of balanitis obliterans xerotica in the population of boys with phimosis, in light of increasing evidence of the importance of this clinical entity in the development of many complications of the urogenital tract.

Material and methods

Our retrospective study included 512 male patients, aged from one to 18 years, who had to meet the appropriate diagnostic criteria to be included in the study and who were surgically treated in the period from 1 January 2014 to 1 January 2017 in the University Children's Hospital. To be included in the study, patients had to have been diagnosed with phimosis as a diagnostic criterion.

The data were gathered from electronic medical records of inpatients and outpatients in hospital informational system Heliant of University Children's Hospital. The selection of patients was carried out so that all patients who were performed circumcision surgery in the observed period, were initially selected and after analyzing the data obtained, a number of patients were excluded because they did not fit the diagnostic criteria, set in our study. Basic demographic data on the age structure of the patients was also received by gathering data from the medical history. After processing the data, the observed group included 470 patients of which 463 of them had a diagno-

sis of phimosis, including three who had an associated diagnosis of testicular retention, and one had an associated diagnosis of varicocele. Beside the patients with phimosis, due to the similarity of the clinical picture, five more patients were included in the study diagnosed with buried penis, one patient who was diagnosed with paraphimosis and one in which the circumcision was performed due to stenosis of the urethra, which is believed to have been caused by balanitis xerotica obliterans, as one of the most severe complications of the disease.

Circumcision involves the surgical removal of excess skin of prepuce. In the case of suspected findings and inability to clinically diagnose BXO, the sample of the prepuce skin is sent for histopathologic analysis preceded by an adequate preparation.

The samples were prepared by fixation in buffered - 10% formalin solution, dipped into the paraffin, and then they were stained with hematoxylin and eosin solution (HE), Van Gieson reagent (EVG) for detection of the elastic fibers and the Schiff's reagent for staining of the basal membrane.

Statistical analysis

The results are shown graphically, as a mean value (standard deviation) and as percentages.

For the determination of the incidence of balanitis xerotica obliterans in the group of patients with phimosis and for determining the measure of central tendency (the median, the mode, the mean and standard deviation) in the group of patients with and in the group of patients without balanitis xerotica obliterans, methods of descriptive statistics were used, ie the frequency analysis in software IBM SPSS Statistics 22.

Results

Patients with phimosis were an average age of 9.12 ± 4.46 (1-18) years. The highest incidence of phimosis was observed in 7-year-old patients (10.4%) (**Figure 1**).

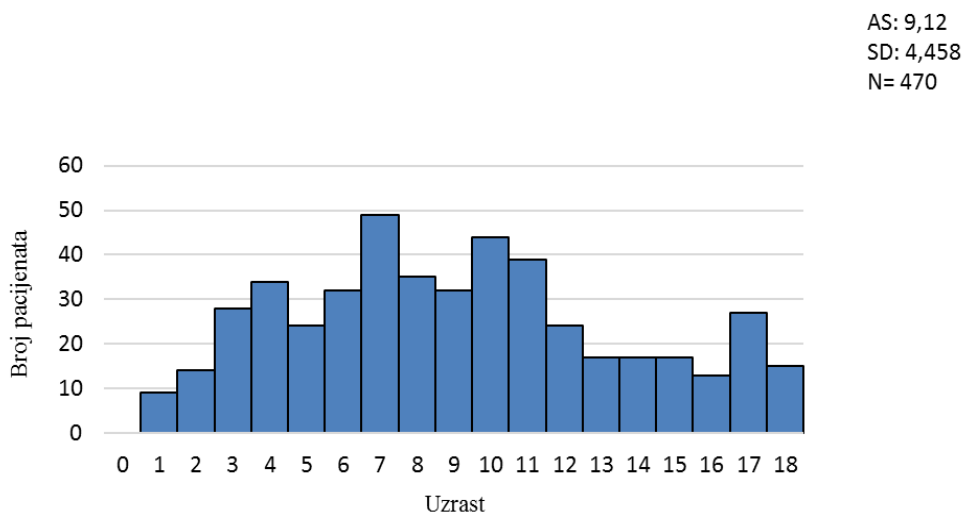


Figure 1. The age structure of the patients with phimosis

Data analysis showed that in a group of 470 patients there is a number of 48 patients diagnosed with balanitis obliterans xerotica-a (10.21%) (Figure 2).

Patients with BXO were an average age of 10.33 ± 3.14 (6-18) years. It was found that the highest incidence of BXO was in a group of patients aged 7 years (16.7%) and 11 years (14.6%) (Figure 3).

BXO diagnosis was clinically confirmed in 31 patients (64.58%), and histopathologically in 17 patients (35.42%). Results of histopathological analysis showed thinner epidermis with parakeratosis and focal hyperkeratosis in some places, which is missing in some places, infused with lymphocytic infiltrate. Vacuolar degeneration of the epidermis is present. In the lamina propria is noticed dense inflammatory infiltrate consisting of lymphocytes, as well as low level of edema. Focally, dermal sclerosis was observed. All of the above corresponds to the diagnosis of lichen sclerosus et atrophicus (BXO), (Figure 4).

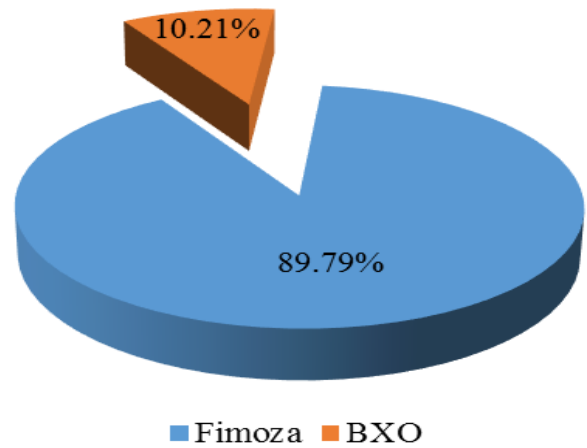


Figure 2. Incidence of BXO in the group of patients with phimosis

AS: 10,33
SD: 3,144
N= 48

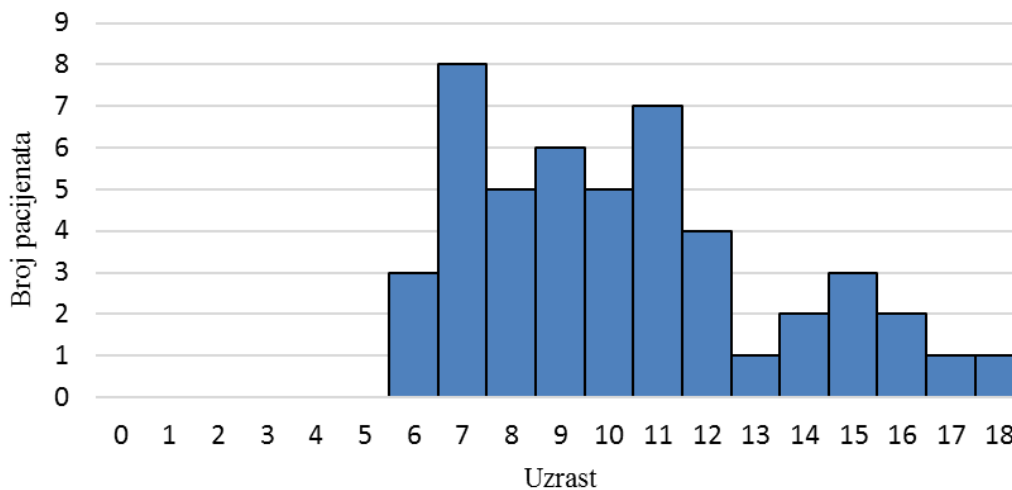


Figure 3. The age of patients with BXO

Discussion

The genital form of lichen sclerosus et atrophicus, which is common in men and is called balanitis xerotica obliterans, is a disease of an unknown etiology and frequency. By reviewing available scientific literature, we concluded that the incidence of the disease is variable and there are drastic differences in the results of different studies on the incidence of BXO. The scientific literature describes BXO frequency in the range from 5% to 52% of (9). Our research has established that the incidence of BXO is 10.21%, which approximately corresponds to the findings of the research conducted by Irkilata et al. Their study included 140 boys, out of which 79 had phimosis and 61 boys did not. Patients with phimosis were divided into groups with partial and full phimosis. Calculated frequen-

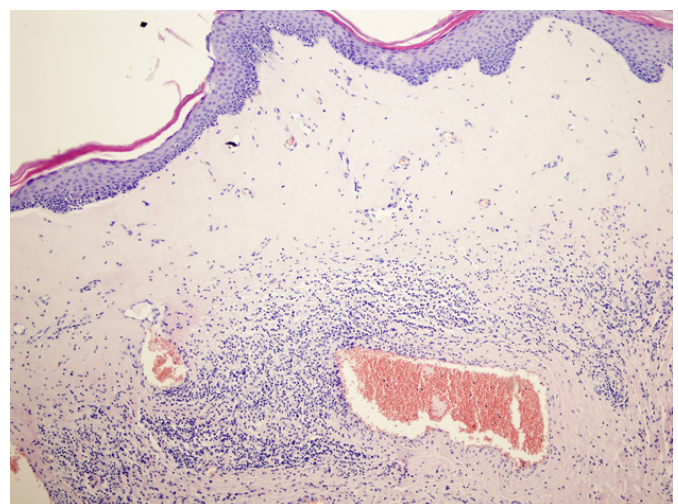


Figure 4. Histology findings of BXO obtained after pathohistological examination of the prepuce

cy of patients with phimosis was 12.6% (10). Kiss et al. after ten years of a prospective study, which involved 1178 boys with phimosis, came to the result that the incidence of BXO in the observed population is 40%, which is significantly higher incidence than the one which is obtained by our research (11). The result of this study, which included a large number of patients over ten years, indicates the possible need for more detailed and longer-term research on a larger sample of patients, in order to get relevant results. Our study included patients aged one to 18 years, but in the group of patients with BXO there was no patient younger than six years old. This result does not correspond with the results of research conducted by Jayakuma et al. The study in which they histologically examined prepuce skin parts obtained with circumcision, showed that the frequency of BXO in patients under the age of five years is 19.3% (12). By reviewing literature on the basis of a lower incidence of BXO in our study, in which only 17 out of 48 (35.42%) prepuce skin parts were examined histologically, the question arises about the necessity of routine sending of prepuce skin on histopathologic analysis after circumcision. Assertion about the necessity of sending prepuce skin on histopathologic analysis confirms the research conducted by Bochove-Overgaauw et al. which included 135 patients between the ages of one and 16 years, and where BXO was found in 37 patients (27%) after histopathological analysis. In 19 of 37 patients (51%) diagnosis BXO matched the clinical diagnosis made after a physical

examination, and in 18 patients (49%) the findings were false negative after a physical examination (13). The results obtained by histopathologic analysis of the prepuce skin in this study correspond to the results obtained in other studies. (4, 14).

Based on the results of this study, we concluded that the routine histopathological examination of the prepuce skin after circumcision would contribute to higher incidence of BXO in our study. The lack of this study is in the fact that patients with phimosis were not classified appropriately in relation to the level of phimosis, or on the basis of whether it is congenital or acquired phimosis.

Conclusion

In our research we came to the conclusion that BXO is present in the population to the extent of frequency range described in other studies. Based on results of our, as well as other studies, we can conclude that the routine histopathological analysis of prepuce after circumcision is necessary in all clinically suspicious cases, which would result in more accurate diagnosis of the disease and in avoiding possible false negative or false positive diagnosis of BXO.

Proper and timely diagnosis is crucial, because BXO is a significant risk factor for developing complications of the urogenital tract, including the development of cancer.

References

1. Depasquale I, Park AJ, Bracka A. The treatment of balanitis xerotica obliterans. *BJU Int.* 2000 Sep; 86(4):459-465.
2. Holbrook C, Tsang T. Management of boys with abnormal appearance of meatus at circumcision for balanitis xerotica obliterans. *Ann R Coll Surg Engl.* 2011 Sep; 93(6):482-484.
3. Fallick, ML, Faller G, Klauber GT. Balanitis xerotica obliterans in monozygotic twins. *Br J Urol.* 1997 May; 79(5):810.
4. Jasaitiene D, Valiukeviciene S, Vaitkiene D, Jievaltas M, Barauskas V, Gudnaviciene I, et al. Lichen sclerosus et atrophicus in pediatric and adult male patients with congenital and acquired phimosis. *Medicina (Kaunas).* 2008; 44(6):460-466.
5. Hartley A, Ramanathan C, Siddiqui H. The surgical treatment of Balanitis Xerotica Obliterans. *Indian J Plast Surg.* 2011 Jan-Apr; 44(1): 91-97.
6. Philippou P, Shabbir M, Ralph DJ, Malone P, Nigam R, Freeman A, et al. Genital lichen sclerosus/balanitis xerotica obliterans in men with penile carcinoma: a critical analysis. *BJU Int.* 2013; 111:970-976.
7. Fistarol SK, Itin PH. Diagnosis and Treatment of Lichen Sclerosus An Update. *Am J Clin Dermatol.* 2013 Feb; 14(1): 27-47.
8. Garzon MC, Paller AS. Ultrapotent Topical Corticosteroid Treatment of Childhood Genital Lichen Sclerosus. *Arch Dermatol.* 1999 May; 135(5):525-528.
9. Celis S, Reed F, Murphy F, Adams S, Gillick J, Abdelhafeez AH, et al. Balanitis xerotica obliterans in children and adolescents: a literature review and clinical series. *J Pediatr Urol.* 2014 Feb; 10(1):34-39.
10. Irkilata L, Bakirtas M, Aydin HR, Aydin M, Demirel HU, Adanur S, et al. Pathological Investigation of Childhood Foreskin: Are Lichen Sclerosus and Phimosis Common? *J Coll Physicians Surg Pak.* 2016 Feb; 26(2):134-137.
11. Kiss, Király L, Kutasy B, Merksz M. High incidence of balanitis xerotica obliterans in boys with phimosis: prospective 10-year study. *Pediatr Dermatol.* 2005 Jul-Aug; 22(4):305-308.
12. Jayakumar S, Antao B, Bevington O, Furness P, Ninan GK. Balanitis xerotica obliterans in children and its incidence under the age of 5 years. *J Pediatr Urol.* 2012 Jun; 8(3):272-275.
13. Bochove-Overgaauw DM, Gelders W, De Vylder AM. Routine biopsies in pediatric circumcision: (non) sense? *J Pediatr Urol.* 2009 Jun; 5(3):178-180.
14. Naji H, Jawad E, Ahmed HA, Mustafa R. Histopathological examination of the prepuce after circumcision: Is it a waste of resources? *Afr J Paediatr Surg.* 2013 Apr-Jun; 10(2):164-166.