

Balanitis xerotica obliterans: An observational, descriptive and retrospective clinical study

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Abstract. Lichen sclerosus is a chronic disease of unknown etiology that can occur in the genital area of both sexes. Balanitis xerotica obliterans (BXO) occurs only in the genital area of men and typically affects the foreskin, penile glans, and/or the meatus. In the present report, an observational, descriptive, and retrospective epidemiological clinical study of available data between January 2006 and December 2020 in patients diagnosed with BXO from the casuistic of CMI DERMAMED (Târgu Mureș, Romania) was performed. During this 15-year period, 164 patients were diagnosed with BXO, of whom 70 (42.8%) were in the 51-60-year-old age group. They presented at the medical consultation at 3-9 months after onset of symptoms, where 124 (75.6%) the patients were found to be with stage III of the disease. The most important comorbidities were found to be diabetes mellitus and obesity, who were treated with potent steroids (betamethasone and clobetasol) with favorable results, with only nine (5.48%) cases necessitating surgical treatment. In general, BXO is a rare, acquired, non-infectious and chronically inflammatory (autoimmune) skin disease that has an unknown etiology. Although the risk of developing this condition is particularly high in patients in the 40-60-year-old age group, it can occur at any age. In the present report, the majority of the patients presented

after a long period of disease development, such that they were already in advanced stages of the condition with clinically subjective symptoms and severe sexual problems. This delay in diagnosis has several causes, including misdiagnosis, psychological issues, and sexual behavior. Diabetes mellitus and overweight/obesity tended to be important comorbidities of BXO since the majority of the patients were also affected by these conditions. These comorbidities can exert an important pathophysiological influence on BXO. The first-line treatment option for this condition is the local application of potent steroids, with favorable effects. Due to the risk of malignant transformation as a result of BXO, it is recommended that these patients should be followed up for a longer period.

Introduction

Lichen sclerosus is a chronic disease of unknown etiology that can affect both sexes and commonly occur in the genital area. By contrast, balanitis xerotica obliterans (BXO) occurs only in the genital area of men and typically affects the foreskin, penile glans and/or the meatus (1). In terms of etiology, it has been previously proposed that infections, especially sexually transmitted ones, trauma of the penis or chronic inflammatory conditions in the genital area can all cause or at least increase the risk of this condition (2). However, accumulating evidence suggests that autoimmune mechanisms in association with other diseases, such as diabetes, genetic predispositions and/or inflammatory states of different causes, such as bacterial infections can all lead to the development of the disease (3-5). As such, *borrelia* infection has been mentioned to be a possible etiological agent (6). In addition, the lack of circumcision has been previously reported to be a risk factor for developing BXO. Although there is no race predilection, several studies have reported higher rates of this condition in African American and Hispanic populations due to lower rates of circumcision (1,7). The prevalence rate in England of lichen sclerosus is 0.1-0.3%, whereas that of BXO in addition to the epidemiological data remains scarce (8,9). This is likely to be due to the initial presentation of the patients to physicians from a wide array of medical specialty backgrounds (7,8).

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Clinically, this disease typically remains asymptomatic initially. Over time, physical examinations frequently reveal erythematous changes or white hypopigmented lesions on the glans penis or foreskin (10). These erythematous changes can develop further into more defined lesions around the coronal sulcus and can progressively invade the urethral meatus and other anatomical regions (10). The balanitis, as a form of generalized inflammation, can lead to phimosis, which can cause disruptions in micturition and disorders in sexual dynamics (10). In advanced stages, erosions and ulcerations in the genital area can occur, which can be accompanied by local pruritus and/or pain, followed by local bacterial and/or fungal infections (10,11). The differential diagnosis includes neoplastic processes, autoimmune diseases, contact dermatitis, psoriasis, Zoon balanitis, leukoplakia, and fixed drug reaction (10). Malignant transformation, especially to squamous cell carcinoma, occurs in 3-6% of women and 2-8% of men (10,12). For treatment, asymptomatic BXO does not require therapy (12). For symptomatic lichen sclerosus, the main treatment method is the topical administration of potent steroids, including Betamethasone, Clobetasol, and Triamcinolone (13). The surgical treatment option is circumcision, though this is only an option for severe phimosis reticent to local treatment (13,14).

The aim of the present observational, descriptive, retrospective study was to describe and analyze the clinical, epidemiological, and evolutionary characteristics of BXO in patients examined in daily practice. It is hoped that it reveals common characteristics of this condition that can deepen the understanding of this disease.

Materials and methods

Patients. An observational, descriptive, retrospective epidemiological clinical study was performed on data obtained from patients diagnosed with BXO between January 2006 and December 2020 from the casuistic of CMI DERMAMED (Târgu Mureș, Romania). Over this 15-year period, 164 patients were diagnosed with BXO in total. Written informed consent from the patients and ethics approval from CMI DERMAMED were obtained for the processing of personal patient data. Only one patient aged <18 years was included in the present study. Informed consent signed by both parents was obtained for this patient. The average age was 47.52 ± 10.00 years, ranging between 14 and 90 years. All patients were caucasian males and uncircumcised.

Diagnostic criteria. The diagnosis was established by dermatological clinical examination. The severity of this disease was defined by GLF, using the following criteria: i) Stage I, defined as clinical lesions without reported disturbances in sexual dynamics; ii) stage II, defined as clinical lesions with disorders in sexual dynamics; iii) stage III, defined as clinical lesions with sexual dynamic disorders and presence of phimosis, erosions and/or ulcerations. Patients were then assigned into clinical stages I, II, or III according to these criteria established. The exclusion criteria were: people without a diagnosis of BXO, and patients who have not signed the informed consent.

Study protocol. In the present study, GLF evaluated patients and collected data, including general data, disease onset,

disease stage, sexual behavior, key personal history, present comorbidities, quality of life data, prescribed treatments, and disease progression. By contrast, other investigators, who were blinded to the clinical cases and treatment options, performed data analysis and the evaluation of the results. Due to data from the literature concerning a possible link between this disease and diabetes (15), diabetes (blood glucose >126 mg/dl) in patients previously known to be without diabetes were screened. All patients had their body mass index (BMI) calculated (normal, $18-24.9$ kg/m², overweight: $25-29.9$ kg/m², obese >30 kg/m²) and were followed up for 2 years after the diagnosis of BXO by clinical examination and/or telephone interview. For collecting and analyzing the data, Excel program version 2016 (Microsoft Corporation) was used. The data are presented as case numbers, SD, and percentages.

Results

Demographic data. The cases were first categorized by age groups. In the 21-30 years age group, 10 (6.1%) cases were found, whereas in the 31-40 years age group, 18 (10.9%) cases were found. In the 41-50 years age group, 60 (36.6%) cases were found. In the 51-60 years age group, there were 70 (42.8%) cases, whilst 4 (2.4%) cases were found in the 61-70 years age group. In total, one case (0.6%) was seen in the ≤ 20 years age group with one case (0.6%) also observed in the ≥ 70 years age group (Table I).

Time between symptom onset and diagnosis. Regarding the time elapsed between the onset of first symptoms of the disease and clinical diagnosis, 3 (1.8%) patients presented after 3 months, 15 (9.1%) patients presented after 4 months, 44 (26.8%) presented after 5 months, 51 (31.2%) presented after 6 months, 33 (20.2%) presented after 7 months, 13 (7.9%) patients presented after 8 months and 5 (3%) patients presented 9 months after the onset of symptoms of the disease (Table II). The average time elapsed between the onset of the first symptoms of the disease and clinical diagnosis was 6.00 ± 1.26 months.

Comorbidities. In terms of sexual behavior prior to the onset of the disease, 120 (73%) of the patients reported undergoing extramarital and/or occasional sexual intercourse prior to BXO. Regarding comorbidities, it was found that 81 (49.3%) of the studied patients were found with the comorbidity of diabetes mellitus and 91 (55.4%) patients were either obese or overweight (Table III). Specifically, of the 81 (49.3%) patients with diabetes, 70 (86.4%) were found with confirmed type 2 diabetes and 11 (13.6%) patients were found with type 1 diabetes (Table III). Based on anamnesis, only 70 patients were confirmed with diabetes at the moment of presentation (11 with type 1 diabetes; 59 with type 2 diabetes), whereas 11 were diagnosed with diabetes type 2 by screening (Table III). In terms of BMI, 91 patients (55.4%) exhibited a higher BMI compared with normal. Amongst this group, 75 (82.4%) patients were considered overweight with a mean BMI of 26.1 ± 0.6 , whereas 16 (17.6%) patients were considered obese with a mean BMI of 31.20 ± 0.42 (Table III).

Clinical data. When analyzing the severity of the disease, based on the criteria set in the present study, it was found that

Table I. Clinical results and comorbidities sorted by age group.

Age group	≤20 years (%)	21-30 years (%)	31-40 years (%)	41-50 years (%)	51-60 years (%)	61-70 years (%)	≥70 years (%)
Total number of cases, N/%	1 (0.6)	10 (6.1)	18 (10.9)	60 (36.6)	70 (42.8)	4 (2.4)	1 (0.6)
Stage I, N	1 (0.6)	3 (1.8)	4 (2.4)	-	-	-	-
Stage II, N	-	7 (4.3)	14 (8.5)	4 (2.4)	2 (1.3)	4 (2.4)	1 (0.6)
Stage III, N	-	-	-	56 (34.2)	68 (41.5)	-	-
Diabetes, N	-	-	-	40 (49.3)	41 (50.7)	-	-
High BMI (>25 kg/m ²), N (/%)	-	2 (2.2)	4 (4.4)	40 (44)	41 (45)	4 (4.4)	-

Table II. Delay of diagnosis.

Delay of diagnosis	3 months (%)	4 months (%)	5 months (%)	6 months (%)	7 months (%)	8 months (%)	9 months (%)
Number of cases	3 (1.8)	15 (9.1)	44 (26.8)	51 (31.2)	33 (20.2)	13 (7.9)	5 (3)

Table III. Clinical results and comorbidities.

Parameter	N (%)
Area of penis	
Balano-foreskin area	146 (89)
Meatus area	12.0 (7.4)
Trunk of the penis	6 (3.5)
Severity of balanitis xerotica obliterans	
Stage I	8 (4.9)
Stage II	32 (19.5)
Stage III	124 (75.6)
Diabetes (n=81)	
Confirmed	70 (86.4)
New detected	11 (13.6)
BMI	
High >25.0	91 (55.4)
Overweight (25.0-29.9)	75 (82.4)
Obese (≥30.0)	16 (17.6)

124 (75.6%) of the patients were at stage III of the disease, whereas 32 (19.5%) were at stage II and only 8 (4.9%) of the patients were at stage I. Dermatological lesions were found, in 146 (89%) cases located in the balano-foreskin area, in 12 (7.4%) cases at the urinary meatus area, and in 6 (3.5%) cases on the trunk of the penis (Table III). All patients were treated with potent local corticosteroids (mostly cream with betamethasone and clobetasol) with favorable outcome (lesion healing). During the follow-up period, 24 cases of relapse were reported, all of which were from patients with diabetes at stage III of disease, who belonged to the 41-50 (15 patients) and 51-60 years (9 patients) age group. Only 9 (5.48%) of the cases required surgical treatment, namely circumcision. No cases of malignancy as a result of BXO were detected during the follow-up period.

Discussion

BXO is an acquired, non-infectious chronic inflammatory skin disease with a controversial etiology (2). It is such a rare disease that its true accurate incidence remains unknown. Boksh and Patwardhan (8) have previously estimated the prevalence rate of lichen sclerosus to between 0.1 and 0.3%. However, concerning the prevalence of BXO, epidemiological data remain scarce (8). In terms of the age distribution of the disease, Kyriakis *et al* (16) performed a clinical study on 51 cases of BXO, where among 20909 male patients, it was found that the majority of cases fell in the 51-60 years old age groups. This is consistent with the findings of the present study, where 70 (42.8%) patients belonged to this age group and >79% of the cases are in the 40-60 years old age group. The reason could be that at that age, men are more prone to hormonal dysregulations, such that the risk of auto/immunological disorders is correspondingly increased (17). In addition, the present study found that, the period of time between disease onset and when the patients present to medical consultation varied from 3 to 9 months with an average value of 6 months. Several explanations can be proposed for this delay in diagnosis. These patients are less likely to seek medical assistance because the early stages of the disease are almost entirely asymptomatic with only mild symptoms (such as itching) and no visible or painful lesions. They will typically only present to a medical consultation either if sexual intercourse is affected by the disease or after important local lesions have appeared, which are clearly visible and painful. These appear to correspond well with the results in the present study regarding the severity of this disease. The data showed that 124 (75.6%) cases of the 164 in total seek medical consultation when they were already in a stage III of the disease. This stage was characterized by ulcerations and phimosis with visible and painful sclerotic plaques, which severely aggravated their sexual dynamic disorders. Another cause of this delayed diagnosis could be the absence of a precise diagnosis protocol for physicians, due to the lack of knowledge and early diagnostic indications

of this disease. Nair (16) previously stated that due to the asymptomatic nature of lichen sclerosus at the early stages of the disease and the lack of awareness by patients and doctors, the diagnosis is frequently delayed. Furthermore, a cause may also be the initial presentation of the patients to physicians from a wide array of specialty backgrounds, since BXO lies on the borderline of different medical disciplines (18). BXO can also cause psychological problems, including embarrassment, shame and emotional stress, which will prevent patients from seeking medical assistance. Virgili *et al* (19) previously performed a multicenter Italian study on 729 cases of lichen sclerosus, which observed a mean diagnostic delay of 3.5 years for men in the case of BXO. This previous study continued to state that because BXO is commonly located on the genitals, patients tend to feel more ashamed to visit a medical office (19). Another cause of this delay is the anamnesis data on sexual behavior, namely extramarital sexual intercourse, prior to the onset of BXO, which was present in 120 (73%) of all patients included in the present study. The majority of patients considered that the cause of this disease was the acquisition of infection due to the extramarital sexual act. Relevant reasons for these could be that men tend to have sexual intercourse without protection, with different individuals, increasing the risk of possible bacterial and viral infections, such as Epstein-Barr or Human Papilloma Virus, which can also serve an etiological role in the manifestation of BXO (20). Since other relevant studies corresponding to these findings are not openly available for comparison, further clear and pertinent data are required (20,21).

The most frequent comorbidities in the studied group in the present study were diabetes and obesity. It was found that 81 (49.3%) of the studied patients presented with diabetes mellitus, where 91 (55.4%) of the patients were either obese or overweight. The presence of these comorbidities would suggest a sedentary lifestyle, which is causing overweight/obesity, in turn promoting general metabolic diseases, such as diabetes mellitus or hypertension. These may serve to be important etio-pathological factors in the development of BXO, in addition to the genetic or autoimmune disposition. Hofer *et al* (15) previously found a significant association between the BMI and lichen sclerosus, in addition to between diabetes mellitus and penile lichen sclerosus. In addition, the majority of the patients are presenting whilst they were already at advanced stages of lichen sclerosus. Following analysis of the data regarding the age of the patients and the stage of the disease, all the patients at stage III of the disease belonged to the age groups of 41-50 and 51-60 years. Correspondingly, all patients with diabetes and higher BMI were at stage III of the disease. All patients were treated with potent local corticosteroids (mainly cream with betamethasone and clobetasol), the first-line treatment option for this disease (22). The majority of patients exhibited favorable outcomes. Furthermore, potent steroid treatment has yielded favorable results in cases of multiple relapse following other types of treatment. Only 9 (5.48%) of the cases required surgical treatment, namely circumcision. Kirtschig *et al* (22) previously revealed that clobetasol propionate and pimecrolimus are both effective treatment strategies for the case of BXO, but clobetasol propionate should be used as the first-line treatment. Other treatment options can also be used, specifically testosterone

ointment, ciclosporin, retinoids, UVA light, laser, stanazolol, which reported different outcomes (23-29). Malignant transformation, especially to squamous cell carcinoma, can occur in 3-6% of females and 2-8% of males after 5 years (30-32). No cases of malignancy following BXO were detected during the follow-up period in the present study. The majority of the patients are presenting already at advanced stages, exhibiting clinical symptoms and severe sexual dynamic problems. This delay in diagnosis can have a number of causes, such as the lack of diagnosis, psychological issues, and sexual behavior. Diabetes mellitus and overweight/obesity were found to be important comorbidities for BXO, since a substantial proportion of the patients were affected. These comorbidities may have important etiological implications. The first-line treatment option is local potent steroids, which conferred beneficial effects. Due to the risk of malignant transformation as a result of BXO, these patients should be followed up for a longer period of time.

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Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Authors' contributions

GLF was responsible for the clinical management of the cases, the design of the study, the evaluation, and the analysis of data. LF and DB made substantial contributions to the conception and design of the study and the preparation of the manuscript. DSK, IB and LF were responsible for the analysis and interpretation of data and revision of the manuscript. GLF and FL are responsible for confirming the authenticity of all the raw data. All authors have read and approved the final manuscript.

Ethics approval and consent to participate

Ethics approval was obtained from the Ethics Committee for Research of the CMI DERMAMED private medical office (approval no. 27/2021). Written informed consent from the patients was obtained. One patient aged <18 years was included in the present study. Informed consent signed by both parents was obtained for this patient.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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