

Skin Phototype and Local Trauma in the Onset of Balanitis Xerotica Obliterans (BXO) in Circumcised Patients

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Abstract. *The association between balanitis xerotica obliterans (BXO) and skin disorders is long established, however, the role of skin phototype and local trauma in its onset has never been investigated in detail. Medical records of all Caucasian children circumcised over a 6-year period were reviewed. The excised skin underwent histological examination for BXO. Children with histological diagnosis of BXO were classified as group A, whereas children without histological diagnosis of BXO were classified as group B. The Fitzpatrick phototype (FT) was obtained in all children performing a personal or family interview with regards to their sunburn and suntan experience. According to their FT, both group A and B patients were divided into two subgroups: FT 1-2, with a higher tendency to sunburn due to their low skin melanin content; and FT 3-4 with a higher tendency to tan due to their higher skin melanin content. Maneuvers of mechanical reduction of the foreskin (MRF) performed at least 5-10 times per month during the year preceding circumcision was also considered. Statistical analysis was performed using univariate and multivariate analysis. A total of 297 patients met the inclusion criteria of our study: 78 patients were classified as group A and 219 as group B. The risk of developing BXO was significantly greater in FT 1-2 patients (n=76) (odd ratio=0.232, 95% confidence interval=0.124-0.435, p<0.0001). Furthermore, those undergoing MRF (n=131) had a significantly higher risk of developing BXO (odds ratio= 5.344, 95% confidence interval=2.860-9.987, p<0.0001). Although the foreskin is not directly exposed to*

sunlight, this study emphasizes the role of skin phototype on the onset of BXO in circumcised individuals. Moreover, the data produced suggest should the advantages of repeated MRF be weighed against the increased risk of developing BXO, which in turn may increase complication rate of circumcision surgery.

Balanitis xerotica obliterans (BXO) is a chronic skin disease which mainly affects the genital area, namely the prepuce, gland and urethra, and results in severe phimosis, glanular lesions and meatal stenosis (1). It can also affect other parts such as the vulva or anus, with the generic name of lichen sclerosus (LS). It was first described by Hallopeau in 1887 and its typical histology was defined by Darier in 1892 (2, 3). The male form of BXO was first defined in 1928 by Sthumer (4), who reported it as a post-circumcision phenomenon based on its pathological appearance. Since then, several sporadic case reports have suggested an association between BXO and penile carcinoma (5-7). Two published series highlighted this conspicuous relationship, reporting a 2.6-5.8% incidence of penile carcinomas in patients with BXO (6, 7).

The exact incidence and prevalence of BXO are difficult to estimate. Systematic studies on boys have shown that 10% to 40% of all surgically treated cases of phimosis are due to LS (8-10) and the aetiology remains unknown (11). Several mechanisms have been studied and suggest a multifactorial origin. Wenzel *et al.* and Regauer *et al.* consider LS a lymphocyte-mediated chronic inflammatory disease of the skin with an increasing evidence for an underlying autoimmune mechanism (12, 13). There have been multiple reports of co-occurrence of lichen sclerosus with autoimmune disease, including vitiligo, Hashimoto's thyroiditis, and type 1 diabetes (14). An infective aetiology has also been considered, although initial studies on viruses, spirochetes and acid-fast bacilli were inconclusive or unsubstantiated (15-17). Moreover, Kobner's phenomenon

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Table I. Univariate statistical analysis for the different parameters considered in the two groups of patients (presence or absence of BXO).

	χ^2	P-value	OR	95% CI
FT 1-2/3-4	29.72	<0.0001	0.22	0.13-0.39
MRF	36.01	<0.0001	5.32	2.91-9.44
Skin diseases	18.30	<0.0001	7.78	2.65-22.90
Endocrine disorders	0.078	0.780	1.41	0.13-15.76
Immunological disorders	0.075	0.785	1.21	0.31-4.81
Genetic pathology	2.82	0.093	0.26	0.22-0.32

OR: Odds ratio; CI: confidence interval; FT: Fitzpatrick phototype; MRF: mechanical reduction of the foreskin.

has been considered because it can act as a trigger for the inflammatory process of LS (17). Finally, Carlson *et al.* consider LS as hypopigmentation resulting from reduced melanin production, block in transfer of melanosomes to keratinocytes and melanocyte loss (18).

Although the association between BXO and inflammatory, autoimmune and skin disorders is well established, the role of skin type and local trauma in the onset of such disease has never been investigated in detail. The aim of this study was to evaluate, from charts of all Caucasian children circumcised, the association between Fitzpatrick phototype (FT) (19) and the manoeuvres of mechanical reduction of foreskin (MRF) and BXO.

Materials and Methods

A retrospective study was performed of 297 consecutive Caucasian children undergoing circumcision surgery on medical grounds between January 2005 and January 2010. All underwent surgery for phimosis persisting after application of topical steroids. Patients with immunological and endocrine disorders, genetic pathology and family history of skin disease were included in our study. All patients underwent a complete circumcision and the surgical skin specimen was sent for histological examination. According to the presence or absent of BXO of the glands and foreskin (as assessed by histological study on excised skin), the patients were classified respectively as group A and group B.

The FT was obtained for all children by performing a personal or family interview with regards to their sunburn and suntan experience. According to their FT, both group A and B patients were divided into two subgroups: FT 1-2, with a higher tendency to sunburn due to their low skin melanin content; FT 3-4, with a higher tendency to tan due to their higher melanin content. Brown and black phototypes (FT 4 and 5) were absent from our patient population and so they were not considered in our study. MRF performed at least 5-10 times a month during the year preceding circumcision was considered in all patients.

Statistical analysis. Statistical evaluation with univariate and multivariate analysis was performed with the (backward-stepwise multiple regression) of the selected variables. P-values <0.05 was regarded as statistically significant.

Table II. Multiple logistic regression analysis to calculate the risk of developing BXO with respect to the different skin phototype and to the manoeuvres of MRF.

	B	SE	P-value	OR	95% CI
FT 1-2/3-4	1.46	0.32	<0.0001	0.232	0.124-0.435
MRF	1.68	0.32	<0.0001	5.344	2.860-9.987

B: Coefficient of regression; SE: standard error; OR: Odds ratio; CI: confidence interval; FT: Fitzpatrick phototype; MRF: mechanical reduction of the foreskin.

Results

Seventy-eight patients (26.3%) with histological diagnosis of BXO were included in group A; 219 patients (73.7%) with no signs of BXO were included in group B. At univariate analysis, immunological disorders, endocrine disorders and genetic pathologies were not significant between the two groups. Table I summarizes these data.

According to Fitzpatrick phototype criteria, we considered 76 patients (25.6%) as FT 1-2 and 221 patients (74.4%) as FT 3-4. We then calculated the prevalence of FT 1-2 patients and of FT 3-4 patients in both groups (A and B). It was estimated that the risk of developing BXO was significantly greater in FT 1-2 patients (n=76) (odds ratio=0.232; 95% confidence interval=0.124-0.435). Similarly, taking into account the patients undergoing MRF (n=131) in both groups, it was estimated that the patients undergoing MRF were at significantly higher risk of developing BXO (odds ratio=5.344; 95% confidence interval=2.860-9.99). Table II summarizes these data.

Discussion

BXO is a dermatological condition that commonly occurs on the foreskin and glans penis. It is characterized by the presence of atrophic white patches and hardened ring tissue that may cause phimosis (20). The etiology of BXO remain unknown. Familial cases have been described in identical and non-identical twins, siblings, and with parents and their children (13, 21). But familiarity is a typical aspect of both immune/genetic and environmental/infectious diseases. The probable etiology of BXO is multifactorial and several studies have suggested this (22, 23). In particular, Wenzel *et al.* and Regauer (12, 13) consider LS a lymphocyte-mediated chronic inflammatory disease of the skin, with increasing evidence for an underlying autoimmune mechanism.

Our study aimed to find experimental data that might explain some of the most reliable aetiological hypothesis. The role of local trauma and skin type in the onset of BXO has never been

investigated in detail. We designed our study to evaluate the incidence and the risk of developing BXO in relation to this condition. This study has several limitations: firstly, the interview was based upon non validated questionnaires and some barriers might exist between physicians and families; secondly, FT may represent only one aspect of a multifactorial disease such as BXO; thirdly, this was a retrospective study and many families may fail in recalling MRF or reactions to sunlight in their child. Nevertheless, screening for FT is a quick, non-invasive method of screening individuals for whom circumcision might not be a one-stop procedure, but for whom follow up visits may be recommended.

The concept of skin phototype is a clinical classification system based on an individual's susceptibility to sunlight, sunburn and ability to tan. It is determined by a brief personal interview of the personal sunburn and suntan experience (19). The concept of sun-reactive skin typing was proposed by Fitzpatrick in order to classify persons with white skin in the application of psoralen and UVA (PUVA) therapy (24). Skin types 1 to 4 were determined according to the response of white skin to sun exposures of three minimal erythema doses. Skin types 5 to 6 were subsequently added for brown and black skin respectively (19, 24).

Although the validity and reliability of skin phototype is still controversial due to limitations in accuracy and racial differences in skin response to UV not being fully clarified, the association between phototype and skin disease (25) is well known. Fitzpatrick asserted that racial differences in skin colour arise mainly from differences in the rate at which melanosomes are produced and melanised in melanocytes, and transferred, distributed and degraded in keratinocytes. Carlson *et al.* (18) proposed an explanation for the white appearance of BXO lesions and proposed three responsible mechanisms: reduced melanin production, reduced melanosome transfer to keratinocytes, and melanocyte loss. This theory of individual chromatic tendency is consistent with the prevalence of BXO, which also seems to affect only susceptible individuals (26, 27).

On these findings, we obtained the Fitzpatrick phototype for all children with personal or family interview of sunburn and suntan experience, as previously mentioned. FT was divided into two groups: FT 1-2 and FT 3-4: patients with FT 1-2 have less ability to tan because of reduced melanin content. Risk of BXO was significantly greater in FT 1-2 patients. This suggests the need for a closer postoperative follow-up in children with FT 1-2 since they have a fourfold risk of developing BXO.

In our retrospective study, attention was also directed to MRF performed at least 5 to 10 times a month in the year prior to surgery. In our series, patients undergoing MRF (n=131) had a statistically significant greater risk of developing BXO. This result is in accordance with what was hypothesized by Chernosky *et al.* (28) and by Pock (29) concerning the incidence of LS after a trauma.

In Italy, MRFs are frequently performed as a conservative treatment of phimosis; as such, they are often recommended by the pediatrician. Even though other factors might be involved. In conclusion, the data produced suggest to carefully estimate the advantages of repeated MRF against the increased risk of developing BXO, which in turn may increase complication rate of circumcision surgery.

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