



Long-term follow-up of Zoon balanitis: a retrospective cohort study

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Dear Editor,

Zoon balanitis (ZB) is an inflammatory disease affecting genital mucosa, particularly the glans and the inside of the foreskin [1]. ZB is deemed a benign condition, nonetheless zoonoid inflammation clinically and histologically frequently complicates other dermatoses, including pre-cancer and cancer [2]. The lesions may be persistent for years prior to diagnosis, long-lasting and treatment resistant. The disease course of ZB and the exact follow-up regime after treatment are unclear [1]. To our knowledge, cohort studies evaluating the course of ZB with a long-term follow-up and the risk of relapse after complete remission are missing. We performed a retrospective observational cohort study on patients attending the Dermatology Unit of the University Hospital of Verona, Italy from 2005 to 2020 to describe the clinical course of ZB in male treated with topical treatments. Inclusion criteria were: (1) male gender, (2) a diagnosis of ZB made on a clinical, dermoscopic, and pathological correlation, (3) and at least two clinical follow-up examinations at 4–6 months. Patients were treated with hydrocortisone 1%, mometasone furoate cream 1%, tacrolimus ointment 0.1%, pimecrolimus cream 1% and/or fusidic acid 2% cream at tailored regimen as needed to achieve complete remission. Patients treated with physical and/or systemic treatments and those with other dermatoses presenting with Zoonoid histology were excluded. Patients were retrospectively reviewed through telephone interview and underwent clinical and anamnestic examination. For

the clinical–pathological correlation, the features reported in European guidelines were considered [3]. The main outcome measures were the improvement of the clinical signs (total vs partial or absent) and the proportion of patients who relapsed after complete resolution. From a total of 198 patients with clinically suspicious ZB, 95 patients were excluded because biopsy was not performed. A total of 103 were included in the study, of which 10 patients were lost at the follow-up (Table 1). The cohort follow-up was 572 person-year. The mean age of the patients at the onset of ZB was 59.6 ± 10.8 years; all were non-circumcised. Complete improvement of clinical signs was reached by 82 out of 93 (88%) patients, while 11 (12%) showed a persistent disease with partial/absent response to topical treatments. Of the patients who underwent clinical remission, 60 out 82 (73%) switched to a second-line topical treatment, in most cases TCI. A total of 25 (31%) experienced at least 1 relapse and 12 (15%) more than 2. The median time to relapse was 21 (IQR 7–45) months. Failure to TCS was associated with higher risk of ZB relapse, independently from age and disease duration; aHR = 4.58 (95% CI 1.83–11.51) (Table 2). None of the patient developed squamous cell carcinoma of the penis. ZB is a neglected nonvenereal dermatosis whose epidemiology is poorly characterized. To date, there are few studies on the clinical course of ZB [4, 5]. In this study, we found that clinical remission of ZB can be achieved with topical treatments, but in one third of the patients, a relapse can occur. Resistance to early topical treatment is associated with higher risk of relapse.

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Table 1 Descriptive characteristic of the patients and disease course

	Zoon balanitis (N=103)
Gender (male), n (%)	103 (100)
Age (years), mean ± DS	59.6 ± 10.8
Non circumcised, n (%)	103 (100)
Disease duration (weeks), median (IQR)*	22 (8–35)
Treatment**	
TCS, n (%)	46 (49)
TCI, n (%)	8 (9)
TCS + TCI, n (%)	33 (35)
Topical antibiotics, n (%)	6 (7)
Disease course*	
Complete remission	82 (88)
Persistence	11 (12)

TCS topical corticosteroids, TCI topical calcineurin inhibitors, IQR interquartile range

*N=82

**N=93

Table 2 Multivariate Cox regression model assessing the risk of relapse

Variable	Univariate analysis		Multivariate analysis	
	HR (95% CI)	p	aHR (95% CI)	p
Age (years)	1.00 (0.99–1.04)	0.943	0.98 (0.94–1.02)	0.328
Disease duration	1.00 (0.99–1.00)	0.789	0.99 (0.99–1.00)	0.501
Failure to TCS	3.71 (1.71–8.03)	<0.001	4.58 (1.83–11.51)	<0.001

N=82

TCS topical corticosteroids

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Data availability The data that support the findings of this study are available on request from the corresponding author (FB).

Declarations

Conflict of interest The authors have no conflict of interest to declare.

Compliance with ethical standards The study was conducted in accordance with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent The ethics committee exempted the study from the informed consent requirement because we only accessed retrospectively a de-identified database for the purpose of data analysis.

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