REVIEW ARTICLE

Zoon's Balanitis - Update of Clinical Spectrum and Management

Vineet Relhan, Abhinav Kumar, Aneet Kaur

From the Department of Dermatology, Maulana Azad Medical College, New Delhi, India

Address for correspondence:
Dr. Aneet Kaur,
Department of Dermatology,
Maulana Azad Medical College,
New Delhi, India.
E-mail: kaur_aneet@ymail.com

Abstract

Zoon's balanitis or balanitis plasmacellularis circumscripta is a chronic inflammatory disorder of the genital mucosa that can affect both males and females (Zoon's vulvitis). It is not a sexually transmitted disease but can still cause anxiety to the patients because of its chronic nature. Hence, proper diagnosis and early management are necessary. It is a clinical mimicker of other commoner genital dermatoses and is mostly a diagnosis of exclusion when other diseases have been ruled out. It is characterised by a well-demarcated shiny erythematous patch or plaque over the genital mucosa. Histopathological examination becomes necessary when we are unable to differentiate it from premalignant lesions. It reveals lozenge-shaped keratinocytes with siderophages, haemorrhages and variable plasma cell infiltrate in the dermis. Dermoscopy shows spermatozoa-like, convoluted vessels with structureless red orange areas. Response to topical therapy alone is not always satisfactory. However, lasers and surgical management can provide long-term remission.

Key Words: *Diagnosis, recent updates, treatment, zoon's balanitis*

Introduction

Zoon's balanitis was first described by Dr. Zoon in 1952 as a chronic inflammatory disorder of the genital mucosa persisting for months to years.[1] It mimics various premalignant conditions and can also cause great distress to the patient for the fear of being a sexually transmitted disease. Pathogenesis still remains to be established, although it is most commonly thought to be due to chronic irritation of genital mucosa owing to various factors like trauma, friction, heat, poor hygiene, etc., Histopathology is typical, showing plasma cell predominant inflammatory infiltrate in the dermis with variable number of lymphocytes and eosinophils. Dilated capillaries and hemosiderosis can also be seen.[2] In this review, we will discuss the pathogenesis, clinical features, differential diagnosis, investigations, recent treatment modalities and prognosis of Zoon's balanitis.

Materials and Methods

The present review was conducted by extensive search of the literature on popular databases like Science Direct, PubMed, Scielo, Medline, the National Institutes of Health, the US National Library of Medicine and the online database of clinical trials (ClinicalTrials.gov) for scientific articles published by 2022. The keywords employed included Zoon's balanitis, *balanoposthite chronique circonscrite bénigne á plasmocytes* or balanitis chronica circumscripta plasmacellularis in the title or abstract. Articles reporting irrelevant information were excluded. For recent advances on the treatment of this condition, 24 articles published from January 2000 to August 2022 focussing on the management of Zoon's balanitis were selected.

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Discussion

History

Zoon first identified this distinct entity in eight patients of chronic balanitis, which had been previously diagnosed as Erythroplasia of Queyrat, and labelled it as "*balanoposthite chronique circonscrite bénigne á plasmocytes*" or "balanitis chronica circumscripta plasmacellularis." Biopsy of these patients showed benign changes as characteristic signs of erythroplasia or cytological atypia were absent.[1] A similar clinical condition has been described in women and named vulvitis circumscripta plasmacellularis by Garnier in 1954.[3] Similar extragenital lesions occurring in the oral mucosa and conjunctiva were identified by Nikolowski[4] and Kortnig,[5] respectively.

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Aetiological factors

Zoon's balanitis is most commonly believed to be a non-specific reaction pattern occurring either alone or in combination with other diseases affecting glans and prepuce like lichen sclerosus et atrophicus and Erythroplasia of Queyrat.[6] Traditionally thought to be a benign condition, a few cases of co-occurrence of penile malignancies with Zoon's balanitis have been reported, which highlights the importance of this disease. Few factors that are thought to provoke this disease are irritation, trauma, friction, heat, dribbling of urine and poor hygiene.[7] Hence, it is most commonly seen in uncircumcised men. Chronic infection with mycobacterium smegmatis and human papilloma virus is also implicated. There has been no evidence of bacterial infection and polymerase chain reaction failed to detect DNA of HPV; hence, definitive evidence is lacking.[8] Immediate hypersensitivity response to an unknown exogenous antigen leading to the production of IgE antibodies has also been implicated in its pathogenesis by Nishimura *et al*.[9] Due to the presence of marked haemorrhage along with lichenoid infiltrate, it has also been linked to lichen aureus.[10] Hyman and Leider speculated that due to the presence of plasmacytic infiltration in such areas, it could be an expression of occult myeloma.[11] Since the infiltrate is polyclonal in nature, the above said theory has been negated.

Age group

Uncircumcised middle-aged and elderly men are most frequently affected by this condition.

Known to be a disease of males over 30 years of age, it has also been reported in paediatric patients as young as 7 months of age.[12] It is under-reported in children and should be included in differential diagnosis. However, clinical features and treatment do not differ in adult and paediatric patients. Plasma cell vulvitis seen in females between fifth and eight decade of life is a chronic itchy mucosal condition affecting the vulva.[13]

Clinical presentation

Classical morphology of plasma cell balanitis is described as an erythematous shiny well-demarcated patch [Figures 1 and 2] over the mucosal surface of the penis (the glans, prepuce or frenulum). Solitary lesions are most common but mirror lesions or kissing lesions have also been reported to occur over the adjacent mucosa. Surface might show some red stippling due to microhaemorrhages, which are known as cayenne pepper spots.[14] Lesions might erode to leave behind a rusty stain. Morphology usually remains unchanged over a long span of time. Care should be taken to look for other co-existing conditions like lichen sclerosus et atrophicus, lichen planus or penile intraepithelial neoplasia over the adjacent mucosa. Erosive variant that presents with bleeding and an atypical vegetative variant is rarely reported.[15] It can also occur in uncircumcised HIV-positive patients.[16]

Figure 1: Shiny erythematous plaque over the glans in a middle-aged male

Clinical criteria for diagnosis given by Kumar *et al*.[14] are as follows:

1. Shiny erythematous patches over glans/prepuce
2. Persistent for >3 months
3. Absence of lesions suggestive of LP, psoriasis elsewhere
4. Poor response of minimum 4 weeks of topical therapies
5. Absence of concurrent infections (negative Tzanck, Gram stain, KOH and VDRL).

Plasma cell vulvitis- In females, an analogous form, Zoon's vulvitis, is known to present as a shiny red-brown flat to slightly elevated plaque with "lacquer paint" appearance, which might have overlying tiny haemorrhages. Lesions maybe asymptomatic or patient may complain of local pain, intractable pruritis, stinging, burning, dysuria, dyspareunia, vulvodynia or bloody discharge. Tumorous variant (plasmoacanthoma) has also been described in the literature.[13]

Zoon-like lesions at other sites- Zoon's lesions having histopathological features similar to plasma cell balanitis have also been described in the oral mucosa and conjunctiva, near eyelid, nose, lips, oral cavity, epiglottis and larynx where the term "idiopathic lymphoplasmacellular mucositis–dermatitis" or plasmacytosis mucosae was coined by Brix.[17] It is a diagnosis of exclusion where other causes of plasma cell infiltration (syphilis, spirochete mediated, plasmacytoma, lichen planus, etc) have been ruled out. In contrast to genital lesions, these lesions are not strictly mucosal and have an intensely erythematous appearance with overlying papillomatosis, cobblestoning, nodularity or velvety surface changes.[17]

Differential diagnosis

Clinically, the lesions of zoon's balanitis can mimic other dermatoses like lichen planus (annular violaceous plaque presents over the glans), genital psoriasis (erythematous plaque over glans that can show scaling in circumcised men), Erythroplasia of Queyrat (well-demarcated, velvety, shiny, bright red, plaque-like appearance, which may have occasional bleeding), allergic and irritant contact dermatitis (ill-defined erythema), circinate balanitis (erythematous annular or serpiginous plaques on glans penis that might be hyperkeratotic in circumcised males), candidiasis (fragile papulopustules with superficial erythematous erosions having collarette of scale), syphilis (acute onset painless indurated ulcer with clean base), herpes (multiple painful erosions coalescing to form single erosion with polycyclic margins), pemphigus vulgaris (coalescent widespread erosions of glans and corona) and fixed drug eruption (history of recurrent sharply demarcated livid red macules that evolve into plaque bullae and erosions after every intake of offending drug).[18]

Relation to malignancy

It is generally considered to be a benign condition, and its association with malignancies has been rarely reported (only three case reports so far). In 1999, Joshi *et al*. described a case of penile carcinoma arising in Zoon's balanitis.[19] The presence of Zoonoid changes in histopathology of lichen sclerosus, lichen planus, Bowenoid papulosis and penile cancer could also suggest that Zoon's balanitis is a premalignant condition.[20] A case of Erythroplasia of Queyrat of the glans on a background of Zoon's plasma cell balanitis has also been described. Another case report described the occurrence of carcinoma in a long-standing case of Zoon's balanitis affecting the same area. A possible association between Zoon's balanitis and penile cancer could be that of chronic inflammation. This highlights the importance of long-term follow-up and adequate treatment of Zoon's balanitis.[21]

Figure 2: Well-demarcated erythematous patch over glans in an elderly male

Diagnosis

Histopathology remains the gold standard for diagnosis despite emerging diagnostic modalities like reflectance confocal microscopy (RCM) and dermoscopy.

Histopathology [Figure 3a and 3b] depends on the stage of lesion biopsied and is described in the Table 1.[2]

Shah M *et al*.[22] conducted a retrospective study in 23 patients clinically and histopathologically diagnosed as Zoon's balanitis. The most common histological feature observed was vascular proliferation (87%) in the dermis followed by dense plasma cell infiltrate (83%). Lozenge-shaped keratinocytes were the next most common feature seen in 78% of cases. Other common features seen were vertical orientation of dermal vessels (69%), spongiosis (56%), acanthosis (48%), lichenoid

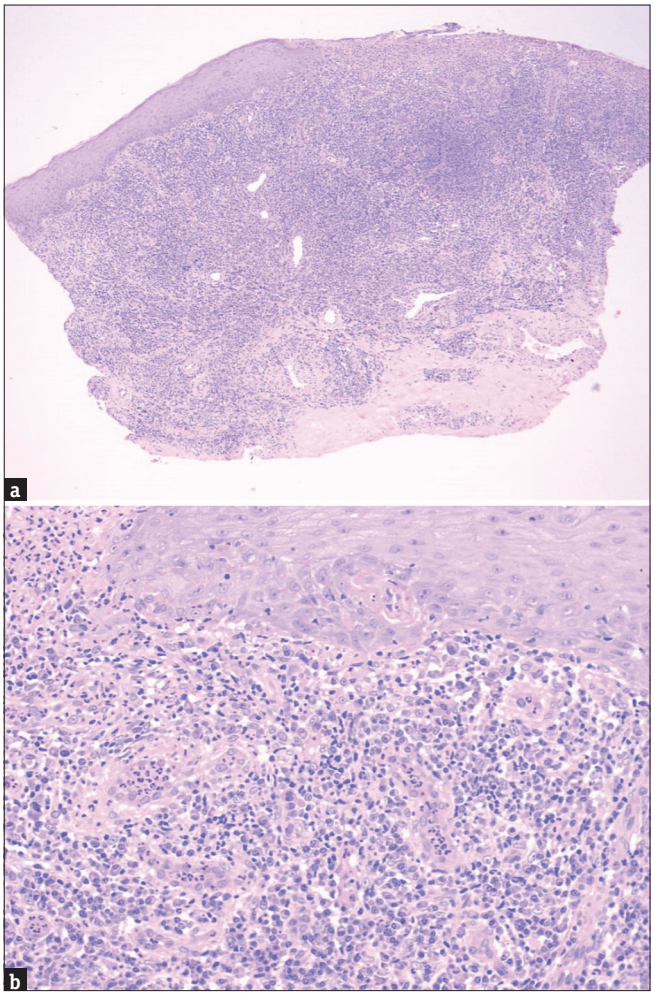

Figure 3: (a) Biopsy from the lesion showing superficial full thickness epithelial ulceration with few neutrophils and spongiosis. Dense diffuse sheet like inflammatory infiltrate predominantly composed of plasma cells admixed with lymphocytes present in most of the dermis. (b) Predominant plasma cell infiltrate in the dermis with few lymphocytes

Table 1: Histopathological changes in Zoon's balanitis

Stage	Epidermal changes	Dermal changes
Early	Normal to thickened. Parakeratosis may be seen.	Patchy lichenoid infiltrate with occasional plasma cells (polyclonal)
Advanced	Superficial erosions with few neutrophils in upper epidermis. Effacement of rete ridges with mild spongiosis.	Dense infiltrate of many plasma cells. Tortuous blood vessels with plump endothelium. Extravasated RBCs
Late stage	Epidermal atrophy and subepidermal clefts. Lozenge-shaped keratinocytes – diamond-shaped keratinocytes with horizontal axis exceeding vertical	Plasma cell infiltrate with fibrosis. Hemosiderosis presents.

infiltrate of lymphocytes and basal cell hydropic degeneration (43%), superficial erosions (30%), neutrophilic infiltrate and atrophy (26%), hemosiderin deposition (17%), erythrocyte extravasation (13%), parakeratosis (9%) and fibrosis (4%). Homogenisation of collagen and atypical cells were not observed. Because of variable histological features in these cases, they concluded that Zoon's balanitis should be considered a non-specific inflammatory disorder, which can mask features of the underlying disease rather than a distinct entity.

Similarly, Weyers W *et al.*[2] found that the common findings observed during the histopathological examination of 45 cases of Zoon's balanitis were neutrophils in the epidermis and dermis, prominent blood vessels and fibrosis in the dermis followed by plasma cells and red blood cell extravasation.

It has been frequently observed that plasma cells can be the predominant cells in the inflammatory response at mucocutaneous junctions in a variety of benign and malignant processes. Thus, the term *circumorificial plasmacytosis* was introduced for benign plasma cell infiltrates on the glans penis, vulva and lips. However, the combination of histologic and clinical features seen in balanitis circumscripta plasmacellularis and probably also in vulvitis circumscripta plasmacellularis is unique and deserves recognition as a separate entity.[2]

Dermoscopic features of plasma cell balanitis are as follows:[23]

1. Vascular- Serpentine or spermatozoa like vessels, convoluted, curved and chalice shaped vessels. Linear irregular blurry vessels, arborising, looped vessels and dotted vessels can be seen. Epidermal atrophy seen in Zoon's balanitis makes the underlying vasculature more prominent. In Erythroplasia of Queyrat, vessels will be scattered and glomerular, which is an important differentiating point, and hence, we can avoid biopsy of delicate areas. After treatment, the vascular pattern tends to disappear.
2. Others- Diffuse or focal orange brown/rust-coloured structureless areas [Figure 4], spatter-like pattern may be seen. These structureless areas can be attributed to the combination of vascular dilation, red blood cell extravasation and hemosiderin deposition in dermis. Chauhan *et al.*[24] observed yellow-white areas in patients of Zoon's balanitis having disease duration of more than 6 months which they attributed to underlying dermal fibrosis. Red blotches were also seen in two out of seven patients, that could be due to erosions, haemorrhage and red blood cell extravasation.

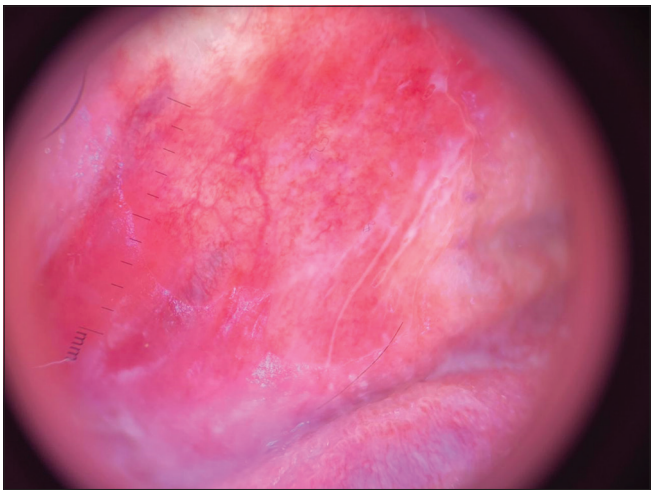

Figure 4: Dermoscopy of Zoon's balanitis showing structureless orange red areas with dotted, short linear and arborising vessels

Reflectance Confocal microscopy- On RCM, the normal honeycomb pattern in the epidermis, suggesting that the absence of any cellular atypia with tortuous vessels running parallel to the surface (vermicular vessels) in the upper dermis can be visualised. Diffusely scattered small bright cells representing the inflammatory infiltrate are seen in the upper dermis.[25]

Treatment

It is important to teach the patients about adequate hygiene measures since trauma, friction, poor hygiene and smegma have been postulated as the possible triggers of this disease. Many medical and surgical therapies have been used for the management of Zoon's balanitis with variable responses.

An extensive literature search for the treatment of Zoon's balanitis was conducted by searching keywords

like zoon's balanitis, *balanoposthite chronique circonscrite bénigne á plasmocytes* or balanitis chronica circumscripta plasmacellularis in title or abstract of papers published from January 2000 until August 2022. The summary of the final 24 articles focussing on the management of Zoon's balanitis selected for review is highlighted in Table 2.

Among topical therapies, calcineurin inhibitors, especially tacrolimus, were the most commonly used treatment modality. Studies denote that use of 0.03-0.1% topical tacrolimus twice a day can lead to significant resolution of lesions as early as 2 weeks.[26-28] However, intermittent use of tacrolimus might have to be advised to prevent recurrence. Similarly, pimecrolimus cream 1% has favourable outcome.[29,30] Many other authors have used topical calcineurin inhibitors for treatment with variable results.[31,32] Topical cyclosporine is the newest therapeutic option as observed by Giorgio CMR *et al*.[36] who used galenical cream with cyclosporine 5% twice a day to cure an erythematous plaque on glans in a 46-year-old male, non-responsive to antibiotics and antifungals. Improvement was observed in a span of 4 weeks. To prevent relapses, the therapy was continued for another month. Follow-up visit at 3 and 6 months showed no recurrences. Studies have shown that cyclosporine can induce endothelial apoptosis and inhibit angiogenesis, hence thought to be more effective in the management of Zoon's balanitis. However, long-term use of calcineurin inhibitors has been linked to carcinogenesis.[52]

Mupirocin, a topical antibacterial, has also been used in Zoon's balanitis with good results.[37,38] Few case reports have highlighted the used of imiquimod, an immune response modifier.[39,40] As compared to topical calcineurin inhibitors and mupirocin, the effect is achieved late. Local irritation is the main side effect.

Ten males, aged 29 to 62 years, were prescribed Trimovate cream containing clobetasone 17-butyrate 0.05% w/w, oxytetracycline 3.0% w/w as calcium oxytetracycline and nystatin 100,000 units per gram, out of which three patients had recurrences within 3 months after cessation of therapy and responded to a second course of Trimovate cream.[41] Fourth patient had 3 recurrences within 12 months and each responded within a few days. A 43-year old HIV-positive man with itchy erosion on glans present for one year responded well to 4 weeks of 3% oxytetracycline ointment application.[42]

Systemic drugs have not been widely used for the management of Zoon's balanitis. On extensive literature search, thalidomide art a dose of 100 mg/day was the only drug, which was found to be used effectively for the management of Zoon's balanitis in a 32-year-old HIV patient.[43] Other procedures like cryotherapy, electrodessication, griseofulvin, topical antifungals have been used with little response.

Apart from drugs, Lasers including Erbium Yag and CO_2 Laser have also been commonly used for the treatment of Zoon's balanitis. Complete clearance, defined as complete absence of erythematous, smooth-faced, "wet"-looking patches or erosions and re-epithelialisation was achieved within a span of 2-3 weeks of use of Erbium Yag Laser.[44] Other studies also mention good response to this treatment modality.[45,46] Retamar RA *et al*.[47] treated five patients of Zoon's balanitis using CO_2 Laser. A "silk touch technique" was used in which tissue damage is minimised as a scanner spins the laser beam rapidly in a spiral pattern so that the time taken to absorb Laser energy is shorter time than the tissue's thermal relaxation time. Downtime is minimal as re-epithelialisation is achieved in 1–2 weeks without any postsurgical complication. Thus, CO_2 Laser proves to be a less traumatic alternative than surgical therapy (circumcision) for treatment of Zoon's balanitis. Laser-treated patients relapsed 1 and 3 years later, respectively. One patient treated with a CO_2 laser in the glans penis area developed lichen sclerosus et atrophicus of the prepuce 3 years later. Patients treated with topical therapy and cryosurgery showed different degrees of improvement. Another case report showed good improvement and no recurrence after treatment of Zoon's balanitis with CO_2 Laser at an irradiance of 200 W/cm^2.[48]

Photodynamic therapy (PDT) using topical porphyrin precursors, 5-aminolaevulinic acid (ALA) or methyl aminolevulinate (MAL), has also been considered a moderately effective and safe option for Zoon's balanitis. Activated T-lymphocytes are sensitive to PDT, leading to immunosuppression with subsequent inhibition of cytokines attracting the plasma cells, thus inhibiting the colonisation of plasma cells in the dermis. Main side effects noticed with its use are mild pain, erythema and oedema. However, a relapse-free period as long as 6 months has been observed with the use of PDT.[49]

Surgical modalities, although definitive treatment option, are not always preferred by the patients due to their invasive nature. Circumcision has been used as a definitive treatment modality with complete healing.[50,51]

Prognosis

Relapses following stoppage of topical therapy (topical antibiotics, steroids and calcineurin inhibitors) are common, while laser treatment (Erbium-Yag and CO_2) and photodynamic therapy provide longer period of

Table 2a: Treatment modalities used for Zoon's balanitis

Topical Treatment Modalities				
Study	**Patient characteristics**	**Modality used**	**Response**	**Recurrence/follow-up**
		Calcineurin inhibitors		
Zoon's balanitis treated with topical tacrolimus.[26]	A 28-year-old married, uncircumcised male with 1 month history of a reddish patch over inner preputial mucosa.	Tacrolimus 0.1% was advised for twice daily application for 6 weeks.	Complete resolution of lesion was achieved	There was no recurrence of lesion in the preceding 6 months.
Treatment of balanitis of Zoon's with tacrolimus 0.03% ointment.[27]	A 70-year-old, uncircumcised male, with erythematous plaque present over the glans penis since past 2 years.	0.03% tacrolimus ointment twice daily.	Great improvement of the lesion was observed after two weeks of treatment. The treatment was continued for four more weeks and then tapered over the next two weeks.	No side effects were observed. No recurrence at six-month follow-up.
Successful treatment of Zoon's balanitis with topical tacrolimus.[28]	A 43 y old male with lesion over glans of more than 20 year duration, non-responsive to various steroids and antifungals	0.03% topical tacrolimus ointment	Good response within 4 weeks. By 8 weeks both the patient's symptoms and the clinical signs further improved	Intermittent use of topical tacrolimus has since been required to prevent recurrence
Zoon's plasma cell balanitis: a report of two cases treated with pimecrolimus.[29]	Two male patients (37y & 62y) diagnosed with Zoon's plasma cell balanitis, confirmed by biopsy.	Daily treatment with topical pimecrolimus1%.	Significant improvement was noted in patient 1 after 6 weeks and after 8 weeks in patient 2.	No recurrence at 3 months follow-up period
Two cases of Zoon's balanitis treated with pimecrolimus 1% cream.[30]	Two 66 and 71 year old males with disease duration of 3 years and 2 years respectively	Pimecrolimus 1% cream, twice daily.	Complete regression after 2 months of treatment	No recurrence after 10 month follow up.
Topical tacrolimus: An effective therapy for Zoon balanitis.[31]	Three patients aged 58,74 and 66 years with disease duration of 10,6 and 10 years respectively.	0.1% topical tacrolimus twice daily application	No signs of inflammation after 3 weeks. Disease controlled after 4-5 months	Not mentioned
Plasma cell balanitis of zoon treated with topical tacrolimus 0.1%: Report of three cases.[32]	Three patients aged 74,81 and 82 years with disease duration of 3,5 and 4 years respectively.	0.1% topical tacrolimus twice daily application	Complete remission of signs and symptoms after 3-4 weeks.	No relapse after 7,9 and 11 months in these patients respectively
Plasma cell balanitis treated with tacrolimus 0.1%.[33]	Two patients aged 69 and 72 years with disease duration of 7 years and 2 years respectively	0.1% topical tacrolimus twice daily application	Disease improved after 1 month and 21 days respectively	No recurrence in follow up period of 1 year
Plasma cell balanitis of Zoon treated successfully with topical tacrolimus.[34]	A 63 year old male. Asymptomatic lesion over glans since 2 years.	0.03% topical tacrolimus daily	Response in 2 months	Not mentioned
Discordant results with pimecrolimus 1% cream in the treatment of plasma cell balanitis.[35]	Two patients	Pimecrolimus cream 1% twice daily	Improvement after 6 weeks and 8 weeks respectively	Not mentioned
Topical cyclosporine 5% cream in Zoon's balanitis resistant to other therapies: A case report.[36]	A 46-year-old man with burning sensation and erythematous plaque on glans, non-responsive to antibiotics and antifungals	Galenical cream containing cyclosporine 5% bid.	Marked improvement at the end of 4 weeks	To prevent relapses, the therapy was continued for another month. Follow up visit at 3 and 6 months showed no recurrences.

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Table 2a: Contd...

MUPIROCIN				
Successful Management of Zoon's Balanitis with Topical Mupirocin Ointment: A Case Report and Literature Review of Mupirocin-Responsive Balanitis Circumscripta Plasmacelluaris.[37]	Asymptomatic red lesions on foreskin and glans since 2 years in a 51y old healthy male. Unresponsive to topical clotrimazole.	Topical mupirocin ointment thrice a day.	Lesion clearance within 6 weeks of use.	Recurrence was seen on discontinuation of treatment. Three months later, a focal residual erythematous plaque remained which resolved within a month once treatment with mupirocin 2% ointment was reinitiated.
Zoon Balanitis Revisited: Report of Balanitis Circumscripta Plasmacellularis Resolving With Topical Mupirocin Ointment Monotherapy.[38]	A 62-year-old healthy, heterosexual, uncircumcised male with asymptomatic red lesion on foreskin and glans	The patient had been given mupirocin ointment to apply to the biopsy site three times daily initially and then two times a day.	Complete resolution was noted after three months of therapy	No recurrence two months after mupirocin was discontinued.
IMIQUIMOD				
Treatment of Zoon's balanitis with imiquimod 5% cream.[39]	A 43-year-old uncircumcised Caucasian, diabetic man with a 4-year history of Zoon's balanitis unresponsive to topical steroids	Imiquimod 5% cream applied 3 times a week.	Clinical but not histological resolution of lesions was obtained after 4 months. However due to irritation, several days of rest period during which no treatment was given, were advised.	No relapses were seen at an 18-month follow-up.
Zoon's balanitis treated with imiquimod 5% cream.[40]	A 59-year-old man suffering from Zoon's balanitis for three years	Imiquimod 5% cream, 3 times a week.	After 12 weeks the patient showed a complete response.	Not specified
STEROIDS/ANTIBIOTIC COMBINATION				
Plasma cell balanitis of Zoon: response to Trimovate cream.[41]	Ten cases, age ranging from 29-62y, duration of lesions- 2 to 24 months	Trimovate cream containing clobetasone 17-butyrate 0.05% w/w, oxytetracycline 3.0% w/w as calcium oxytetracycline and nystatin 100,000 units per gram applied over the lesions	Treatment continued till complete resolution i.e., 2 to 12 months	Three patients had recurrences within 3 months after cessation of therapy and responded to a second course of Trimovate cream. A fourth patient had 3 recurrences within 12 months and each responded within a few days to same treatment.
OXYTETRACYCLINE				
Balanite de Zoon chez un homme circoncis et infecté par le VIH, à Cotonou (Bénin) [Zoon's balanitis in circumcised and HIV infected man, at Cotonou (Benin)].[42]	A 43-year old HIV+man with itchy erosion on glans for one year.	4 weeks of 3% oxytetracycline ointment application	Good outcome	Not mentioned

remission (around 2 years)[45-50] with only a single study[47] showing no recurrence even after a follow-up period of as long as 6 years after using CO_2 laser ablation in a patient. Circumcision is the definitive treatment option. In general, it is advisable to follow up patient for a long term since few case reports highlight the association of Zoon's balanitis with malignancy, although more studies are needed.

Conclusion

Zoon's balanitis continues to be an underdiagnosed entity with varied clinical presentation. It can mimic

Table 2b: Treatment modalities used for Zoon's balanitis

SYSTEMIC DRUG TREATMENT				
THALIDOMIDE				
Thalidomide in plasma cell balanitis refractory to conventional topical treatment.[43]	A 32-year-old HIV positive patient complained of a painless lesion on the glans penis over a period of four months refractory to tacrolimus.	Thalidomide (100mg/day) was prescribed for six weeks.	Remission of the disease achieved after 6 weeks.	No relapse in eight months of follow-up

Table 2c: Treatment modalities used for Zoon's balanitis

LASERS/PHOTODYNAMIC THERAPY				
ERBIUM YAG LASER				
Ablative Erbium: YAG Laser treatment of idiopathic chronic inflammatory non-cicatricial balanoposthitis (Zoon's disease)--a series of 20 patients with long-term outcome.[44]	Twenty Caucasian male patients (mean age 64.8 years) who presented with chronic inflammatory non-cicatricial balanitis or balanoposthitis. The patients received multiple topical treatments. The disease duration ranged from 1 to more than 7 years. Diagnosis was confirmed by histology.	The settings used for Erbium: YAG laser ablation were as follows- focus 1.6-5 mm; frequency 8 Hz; impulse energy mostly 800 mJ; fluence between 11.3 and 20 J/cm2. The pulses were partly overlapping. The pain sensation was recorded by visual analogue scale.	Complete clearance, defined as complete absence of erythematous, smooth-faced, 'wet'-looking patches or erosions and re-epithelialization was achieved within a span of 2-3 weeks.	A regular follow up once a year was ensured. A complete clearance of lesions was observed between 3 months and 30 months (mean 12.1 +/- 7.2 months), in all the patients. No severe adverse effects were seen. In a 67 year old male, 3-6 overlapping passes of Erbium Yag Laser with 3mm spot size, 5Hz frequency and power of 0.5J/cm2 were given. At the follow up period of 4 months, perimeatal erythema was seen, hence 2 sittings were given again. Remission period as long as 2 year was achieved using this treatment modality.
Zoon's balanitis treated with Erbium: YAG Laser ablation.[45]	Zoon's balanitis in a 67 year old male	3-6 overlapping passes, 3mm spot size, 5HZ, 0.5J/cm2. 4mo- perimeatal erythema was seen, hence 2 sittings were given again	Good response	No recurrence after more than 2y follow up
The Role of Erbium: Yag Laser in the Management of Zoon's Balanitis - A Case Report with Mini Review.[46]	A 58 y old male with asymptomatic lesion on glans for 10 years.	Fractional Erbium: YAG Laser ablation was done with 15 J/cm^2 fluence, 5 mm spot size, 8 Hz frequency with 50% overlapping. Topical mupirocin was applied for the next 5 days. The session was repeated twice at monthly intervals.	Good response with appearance of normal mucosa was seen.	There was no recurrence in the next 6 months' follow-up.

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Table 2c: Contd...

CO_2 LASER				
Zoon's balanitis: presentation of 15 patients, five treated with a carbon dioxide Laser.[47]	Fifteen patients, ages ranged from 36 to 69 years (average, 50.8 years). The average time of development to consultation was 10.2 months (range, 1–24 months). One of these five cases had received fusidic acid, two cryosurgery, and two no previous treatment.	Five patients were treated with a CO_2 Laser. a continuous wave CO_2 Laser with scanner ("silk touch") (intensity, 1–2 W; two to four passes) was performed. Postoperative mupirocin, twice daily, was used. Of the remaining patients, six were given fusidic acid cream, one gentamicin cream, two cryosurgery, and one fusidic acid and cryosurgery.	Patients treated with topical therapy and cryosurgery showed different degrees of improvement. Good improvement in patients treated with Laser.	Two of the five Laser-treated patients relapsed 1 and 3 years later, respectively. The remaining three have been followed up for 2, 5, and 6 years, respectively, without relapse. One patient treated with a CO2 Laser in the glans penis area developed lichen sclerosus et atrophicus of the prepuce 3 years later.
Treatment of Zoon's Balanitis with the Carbon Dioxide Laser.[48]	57y old male, single 2X3 cm lesion on glans penis.	Treated with CO_2 Laser with irradiance 200W/cm^2	Free of lesions in 3 months.	No recurrence even after 2y
ALA PHOTODYNAMIC THERAPY				
Zoon's balanitis successfully treated with photodynamic therapy: Case report and literature review.[49]	A 35y old male with 2 y old history of itching and red shiny plaque over glans and prepuce. Had relapsed after treatment with steroids and tacrolimus.	Polyethylene glycol ointment containing 10% ALA was applied under occlusion for 3 hours and then irradiated with diode red light at 630 nm wavelength (S630, AlphaStrumenti, Milan, Italy). The light source was positioned 50 mm from the skin surface, giving an irradiance of about 160 mW/cm^2. The light exposure period was 8 min. Patient was treated every 2 weeks for a total of 3 treatments.	Only side effects observed after first exposure were mild pain , erythema and edema. On subsequent exposures, minimal discomfort was noted. After the end of treatment period, lesions partially resolved with improvement in erythema and pruritis.	Lesions almost completely cleared at 3 months follow-up. One month later, erythema recurred, a single session of ALA-PDT was performed. A prompt relief of symptoms and improvement in lesions was seen. At six months follow-up, a lasting remission with favourable cosmetic results was observed.

Table 2d: Treatment modalities used for Zoon's balanitis

SURGICAL TREATMENT MODALITIES				
Simultaneous Occurrence of Balanoposthitis Circumscripta Plasmacellularis Zoon, Phimosis and in Situ Carcinoma of the Penis: Case Report with An Unusual Ulcerated Polypoid Variant of Zoon's Disease and a Carcinoma in Situ of Reserve Cell Type.[50]	A 68-year-old male patient presented with an asymptomatic reddish papular lesion of the foreskin with phimosis with two shiny reddish ulcerated lesions of the glans penis.	Surgical excision in combination with circumcision to correct phimosis was performed	Complete clearance of lesions	Follow up not mentioned
Circumcision as treatment for Zoon's balanitis in an HIV-positive teenage patient.[51]	An 11y old HIV + teenage male with painful erythematous patches over glans since 2y.	Circumcision was done.	At one-week follow-up, the glans lesions were healed, with significant improvement in pain sensation.	One month postoperatively, there was a complete healing of all lesions and the patient had no symptoms of pain or itch.

various venereal and non-venereal genital dermatoses. Since there have been reports of association of this condition with malignancy, prompt diagnosis and long-term follow-up are advised. The management is still a challenge for the dermatologist. Relapse with topical immunomodulators and antibiotics is almost always universal. Systemic drugs have a limited role in treatment. However, Erbium-Yag Laser is an upcoming promising treatment that can lead to long-term remission. Apart from this, circumcision and surgical excision are the definitive treatment modalities, which can be offered in recalcitrant cases.

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Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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