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Cutaneous T-cell Lymphomas of the External Genital Organs: Clinical Presentation, Diagnosis, and Treatment

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Abstract

Cutaneous T-cell lymphomas (CTCLs) are a rare group of non-Hodgkin lymphomas that primarily affect the skin. Involvement of the external genital organs is uncommon and remains poorly characterized. This narrative review aimed to summarize the clinical manifestations of CTCL involving the external genital organs in male and female patients and to review the available treatment approaches.

A systematic literature search was conducted in PubMed, the Cochrane Library, and Web of Science using combinations of relevant keywords, including “cutaneous T-cell lymphoma,” “mycosis fungoides,” “Sézary syndrome,” “vulva,” “scrotum,” and “penis.” Following title, abstract, and full-text screening, 22 studies met the inclusion criteria and were included in the review.

The included literature consisted predominantly of case reports and two case series. Twelve studies reported vulvar involvement, three reported scrotal or testicular involvement, and seven described penile T-cell lymphomas. The external genital organs were more commonly involved as a secondary site of disease, and mycosis fungoides was the most frequently reported histopathological subtype. Reported management strategies included surgery, topical therapies, phototherapy, and localized radiotherapy. In advanced disease, systemic treatments included chemotherapy, interferon, bexarotene, methotrexate, brentuximab vedotin, and allogeneic hematopoietic stem cell transplantation.

CTCL involvement of the external genital organs is rare, and the available evidence is largely limited to case reports and small case series. Increased clinical awareness and prompt histopathological evaluation are important for timely diagnosis. Treatment should be individualized according to disease subtype, extent, and stage.

Categories: Urology, Hematology, Dermatology
Keywords: cutaneous t-cell lymphoma, external genitalia, mycosis fungoides, penis, scrotum, sézary syndrome, vulva

Introduction And Background

Cutaneous T-cell lymphomas (CTCLs) comprise a heterogeneous group of rare non-Hodgkin lymphomas characterized by the clonal proliferation of skin-homing T lymphocytes. Mycosis fungoides (MF) is the most common subtype, whereas Sézary syndrome (SS) represents a less common but more aggressive leukemic variant. According to the World Health Organization-European Organisation for Research and Treatment of Cancer (WHO-EORTC) classification, primary CTCLs comprise several distinct clinicopathological entities with heterogeneous biological behavior and prognosis. Accurate classification is essential for appropriate diagnostic evaluation, staging, and therapeutic management [1]. For MF and SS, clinical staging is based on the tumour-node-metastasis-blood (TNMB) classification, which incorporates the extent of skin involvement (T), lymph node involvement (N), visceral involvement (M), and peripheral blood involvement (B) [2].

Despite advances in the therapeutic management of CTCL, treatment is primarily aimed at disease control, symptom relief, and preservation of quality of life, with therapeutic strategies largely determined by disease stage and extent. Patients with early-stage disease generally have a more favorable prognosis and are primarily managed with skin-directed therapies, whereas advanced-stage disease frequently requires systemic treatment [3,4].

Involvement of the external genital organs is an exceptionally rare manifestation of CTCL. Genital lesions may occur as part of established disease (secondary genital involvement) or, less commonly, represent the initial manifestation of CTCL (primary genital presentation). The true frequency of genital involvement remains uncertain, as the available literature consists predominantly of isolated case reports and small case series. Owing to their unusual anatomical location and the broad differential diagnosis of genital dermatoses, these lesions may pose a diagnostic challenge. Furthermore, genital involvement may have a substantial impact on patients' quality of life, including physical discomfort, sexual dysfunction, and psychosocial distress [5].

Given the rarity of genital CTCL, evidence regarding its clinical presentation, diagnostic features, management, and outcomes is largely derived from isolated case reports and small case series. In particular, the clinical differences between primary and secondary genital involvement, the effectiveness of available treatment approaches, and long-term outcomes remain insufficiently characterized. The limited and heterogeneous evidence also makes it difficult to establish site-specific diagnostic and therapeutic recommendations. This narrative literature review, based on a systematic literature search, aimed to summarize the reported manifestations of CTCL involving the external genital organs in male and female patients and to critically review the available diagnostic and therapeutic approaches.

Review

Methodology

A systematic literature search was conducted in August 2025 to identify published reports of CTCLs involving the external genital organs. PubMed, the Cochrane Library, and Web of Science databases were searched, and the study selection process was documented using a PRISMA flow diagram (Figure *1*). The literature search covered all publications indexed in the selected databases from their inception through August 2025, with no restrictions on publication year.

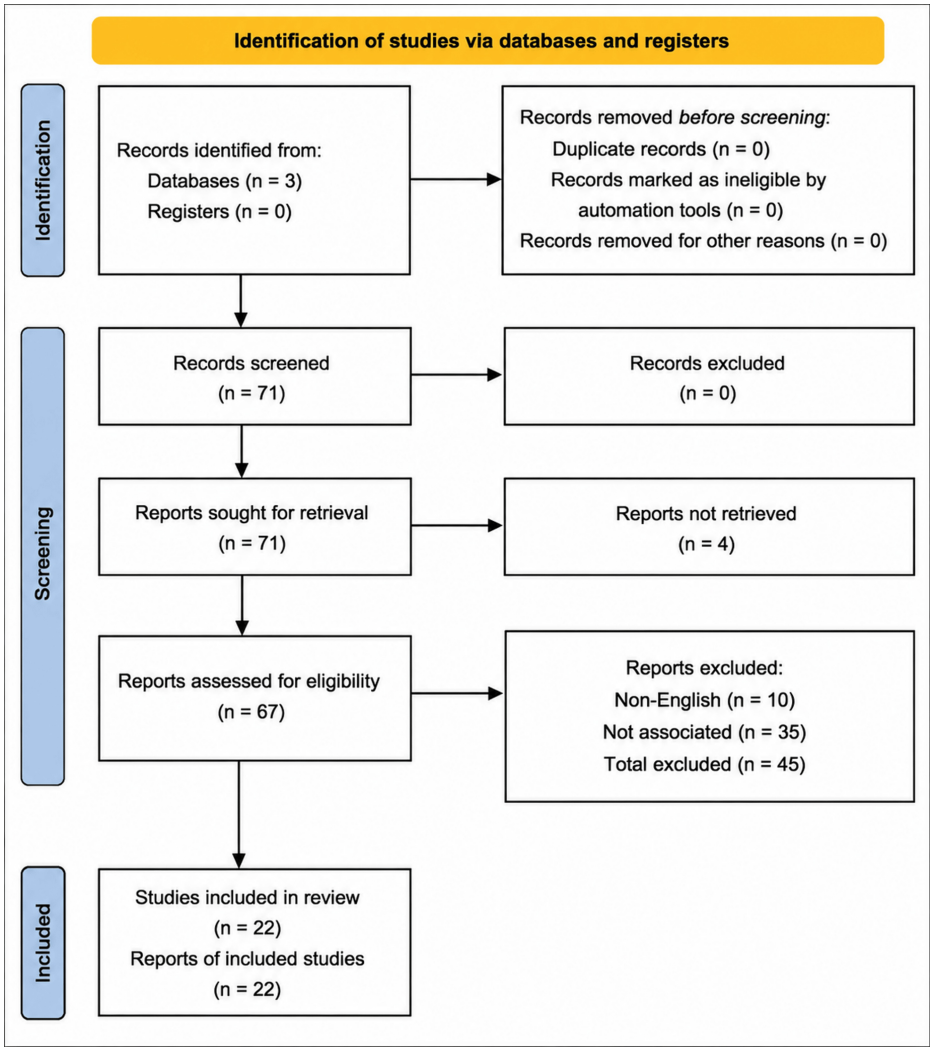


FIGURE 1: PRISMA flow diagram of the study selection process.

The search strategy combined lymphoma-related terms with anatomical terms referring to genital involvement using the Boolean operators AND and OR. The following combination of key search terms was used: ((“cutaneous T-cell lymphoma”) OR (“mycosis fungoides”) OR (“Sézary syndrome”)) AND ((“external genitalia”) OR (“penis”) OR (“penile”) OR (“scrotum”) OR (“scrotal”) OR (“vulva”) OR (“vulvar”) OR (“vagina”) OR (“vaginal”)).

Titles and abstracts were independently screened by two authors (ENK and NK). Non-English-language publications and studies unrelated to CTCL involvement of the external genital organs were excluded. Studies were considered eligible if they met the following inclusion criteria: (1) reported patients with histopathologically confirmed T-cell lymphomas involving the external genital organs; (2) described involvement of the vulva, penis, or scrotum, including cases with associated involvement of adjacent genital structures; (3) provided clinical information regarding disease presentation, histopathological findings, treatment, or outcomes; and (4) were published in English. Both primary genital presentations and secondary genital involvement in patients with previously diagnosed lymphoma were considered eligible. Given the rarity of this condition, case reports and case series were included without restrictions on patient age or sex.

Potentially eligible publications subsequently underwent full-text assessment, and disagreements regarding eligibility were resolved by consensus among the authors.

The initial database search identified 71 records. All records underwent title and abstract screening, and 71 reports were sought for retrieval. Four reports could not be retrieved, leaving 67 reports for full-text eligibility assessment. Of these, 45 were excluded (10 non-English-language publications and 35 reports unrelated to genital CTCL), resulting in 22 studies included in the narrative review (Figure *1*). Disease stage was recorded as reported in the original publications. When staging information was not provided, it was designated as “Not available” below. No retrospective staging was performed.

Given the narrative nature of this review and the predominance of case reports and small case series, findings were synthesized descriptively according to the anatomical site of involvement. No quantitative meta-analysis or formal risk-of-bias assessment of individual studies was performed.

Findings of the literature review

Overview of Included Studies

After screening, we included 22 studies in this narrative review, comprising 25 patients. Twelve studies reported vulvar involvement (15 patients), including one case of MF with oral, cervical, and vulvar involvement, three studies described scrotal or testicular involvement (three patients), and seven reported penile T-cell lymphomas.

The included literature consisted predominantly of case reports, with two case series comprising three and two patients, respectively. In most cases, genital involvement represented a secondary manifestation of CTCL, whereas primary genital presentations were less frequently reported. MF was the most frequently reported histopathological subtype.

Vulvar Involvement

Twelve of the 22 included studies reported vulvar involvement [6-17]. The clinical presentation of vulvar CTCL was heterogeneous. Reported findings included ulcers, erythematous or violaceous plaques, nodules, and vulvar masses, often accompanied by symptoms such as pruritus, swelling, postcoital pain, or dyspareunia [6-17]. In one case, a chronic vulvar fissure was the only presenting finding [10]. Vulvar involvement may also occur in the context of more extensive disease, with concomitant cutaneous or systemic manifestations. For example, lesions involving the trunk, extremities, or inguinal regions and systemic symptoms such as fever were reported in some patients [9,16].

Treatment strategies for vulvar CTCL varied substantially across the reported cases and were influenced by disease subtype, stage, extent of involvement, and previous therapies. Radiotherapy was frequently used for localized vulvar lesions, either alone or as part of a multimodal treatment approach [6,9,11,15,16]. Other reported treatments included surgery [8,12], phototherapy [9,11,13,15], systemic chemotherapy [6-8,13,17], bexarotene [14,15], methotrexate [17], topical clobetasol or chlormethine [14], brentuximab vedotin [11], and hematopoietic stem cell transplantation [7]. Clinical outcomes were heterogeneous, ranging from complete or partial local responses to subsequent relapse, systemic disease progression, and death. Nevertheless, durable responses were reported in individual cases, including long-term survival following treatment [12,13].

Scrotal and Testicular Involvement

Scrotal and testicular involvement by CTCL is exceptionally rare, with only three relevant reports identified in the present review [18-20]. Clinical presentation varied from a progressively enlarging scrotal mass to ulcerated nodular or plaque-like lesions. In one patient with a previous history of MF, testicular involvement occurred in the context of transformed disease [18], whereas the other two reports described primary cutaneous CD30-positive lymphomas involving the scrotal skin [19,20].

Management differed according to the site and extent of disease. Surgical procedures, including excisional biopsy and radical inguinal orchidectomy, were performed for diagnostic and therapeutic purposes [18-20]. Systemic chemotherapy was administered in two of the reported cases [18,19]. Histopathological and immunohistochemical findings also varied according to lymphoma subtype; CD30 expression was reported in the cases of anaplastic large-cell morphology, with BCL2 positivity additionally described in the scrotal cases [19,20]. Favorable short-term responses were reported in two patients [18,19].

Penile Involvement

Seven studies describing penile T-cell lymphomas were identified [21-27]. Clinical manifestations were heterogeneous and included penile pain and swelling, erythematous or ulcerated plaques or masses, dysuria, oliguria, phimosis, and paraphimosis. Lesions involved the glans, foreskin, or deeper penile structures.

Management was similarly heterogeneous and depended on the extent and subtype of disease. Surgical procedures, including circumcision, local or excisional biopsy, and penile reconstruction, were performed in several cases [22,24-27]. Radiotherapy was used either as a local treatment or as part of multimodal management in patients with more extensive disease [24,27], while systemic therapies were administered according to the underlying CTCL subtype and disease extent. These included methotrexate, chemotherapy, and brentuximab vedotin [24,26].

Reported outcomes varied considerably. Some patients achieved local disease control or remission, whereas others experienced subsequent progression or required additional treatment. Notably, systemic brentuximab

vedotin resulted in complete response of the penile lesions in one patient with MF; however, the patient subsequently developed refractory disease and died four months after restarting chemotherapy [26].

The characteristics and outcomes of the included studies are presented in Table *1*.

Reference	Age (years)	Clinical presentation	P/S	Stage	Histologic subtype	Treatment	Outcome/Follow-up
Vulvar							
Vang, 2000 [13]	43	Vulvar pruritus and dyspareunia; no mass	S	IV	MF	Chemotherapy; phototherapy	Initial CR followed by relapse; alive with disease four years after vulvar involvement
Koh, 2009 [6]	35	Vulvar ulcer	P	NA	PC-ALCL	Chemotherapy; RT	CR at 15 months
Reichman, 2010 [10]	55	Postcoital vulvar pain, infrequent bleeding, and chronic vulvar fissure; no mass	S	IA	MF	NA	NA
Pan, 2010 [8]	42	No vulvar mass; vaginal obliteration	S	NA	CTCL	Chemotherapy; surgery	Initial CR followed by relapse; died
Buras, 2015 [12]	50	Labial swelling, occasional pruritus, and redundant labia	P	NA	MF	Surgery	CR; alive 13 years after surgery
Bakar, 2015 [9]	33	Cutaneous patches on trunk, arms, and inguinal regions; solitary vulvar tumor	S	NA	MF	RT; phototherapy; IFN	CR of vulvar lesion
Geller, 2018 [11]	30	Pink-to-violaceous plaques involving the extremities, buttocks, and vulva; 2-cm right labia majora tumor	S	IIB	MF	Brentuximab vedotin; electron-beam RT; TSEB	Partial response followed by CR
Geller, 2018 [11]	85	Rapidly growing labial mass	S	IIB	MF	Photon RT	Near-CR; died of pneumonia
Geller, 2018 [11]	52	Painful right labia majora tumor with widespread cutaneous patches and plaques	S	IIB	MF	Electron-beam RT; clinical trial	Significant local improvement; subsequent progression of generalized skin disease without genital progression
El Alami, 2019 [14]	81	Violaceous plaques of the inguinal folds and vulva with oral mucosal lesions	S	IA	MF	Bexarotene; topical clobetasol	CR after three months
El Alami, 2019 [14]	82	Erythematous plaques of the right labia majora and left groin	S	IIB	MF	Topical clobetasol; topical chlormethine	Partial improvement
Dashraath, 2020 [16]	86	Fever and painful vulvar swelling; necrotic enlargement of the left vulva and medial-thigh plaques	P	NA	γδ CTCL	Palliative RT	Disease progression; died of disease
Morse, 2021 [15]	64	Left buttock nodule involving perineal skin	P	NA	PC-AECyTCL	Bexarotene; PUVA; RT	Initial partial response followed by disease progression; subsequently CR at six months
Tjalma, 2021 [7]	58	Pruritus; painless 3-cm right labium majus nodule with adjacent hypopigmented/white patch	S	NA	MF	Chemotherapy; TSEB; haploidentical HSCT	GVHD, neutropenic fever, and hemodynamic instability; died 13 months after diagnosis of vulvar MF
Feletti, 2024 [17]	62	Facial lesions with cervical and vulvar tumor involvement; subsequent oral involvement	S	NA	MF	Methotrexate; local RT; subsequently CHOP	NA
Scrotal/testicular							
Borgmann, 2014 [18]	38	Growing scrotal mass; previous MF; ulcerated skin tumors and left testicular tumor	S	IVA	Transformed MF	Radical inguinal orchidectomy; pegylated liposomal doxorubicin	Tumor regression and good response at six months

Mehdi, 2011 [19]	59	Progressive ulceration of the right scrotal skin with ulcerative nodular lesion and lymphadenopathy	P	IIB	PC-ALCL	Excisional biopsy; systemic CVP-R chemotherapy	Tumor regression
Modi, 2009 [20]	63	Slowly growing 3-cm red scrotal nodule; no systemic symptoms	P	IIB	Primary cutaneous CD30+ large-cell lymphoma	Skin biopsy	NA
Penile							
Thorns, 2003 [25]	59	Dysuria, oliguria, recurrent balanitis, ulcerated foreskin lesion, and severe phimosis	P	IA	Woringer-Kolopp-like MF with CD30+ large-cell transformation	Circumcision; local resection	NA
Chiam, 2007 [21]	32	Chronic painful, enlarging psoriasiform plaque of the glans penis	P	IA	MF	Topical clobetasol; topical imiquimod	No response to clobetasol; CR after imiquimod
McNab, 2011 [22]	90	Painful penile swelling and discharge with bleeding, edema, indurated foreskin, and paraphimosis	P	IA	PC-ALCL	Circumcision	Died of natural causes three months after diagnosis
Terada, 2012 [23]	55	Painless penile tumor	NA	NA	CD30+ T-cell lymphoma/ATLL	NA	NA
O'Brien, 2017 [24]	64	Progressive phimosis and painful ulcer at the penile meatus	S	IIB	MF with large-cell transformation	Excision and glans reconstruction; methotrexate; external-beam RT; mini-CHOP	Widespread cutaneous relapse followed by remission; continued palliative management
Schaufler, 2021 [26]	71	Erythematous plaques of the glans and shaft, decreased urinary stream, phimotic foreskin, and preputial lesion	S	IB	MF	Biopsy; urethral dilation; circumcision; topical imiquimod; brentuximab vedotin; chemotherapy	CR of penile lesions followed by systemic progression; died of refractory disease four months after restarting chemotherapy
Kodama, 2023 [27]	63	Pain with erections and enlarging circumferential penile mass	S	IIB	MF	Excisional biopsy; diagnostic cystourethroscopy; perioperative RT	Significant reduction in penile mass; erectile dysfunction

TABLE 1: Characteristics and outcomes of the included studies.

P: primary; S: secondary; MF: mycosis fungoides; CTCL: cutaneous T-cell lymphoma; PC-ALCL: primary cutaneous anaplastic large-cell lymphoma; PC-AECyTCL: primary cutaneous CD8+ aggressive epidermotropic cytotoxic T-cell lymphoma; ATLL: adult T-cell leukemia/lymphoma; CR: complete response; RT: radiotherapy; IFN: interferon; TSEB: total skin electron beam therapy; HSCT: hematopoietic stem cell transplantation; GVHD: graft-versus-host disease; CHOP: cyclophosphamide, doxorubicin, vincristine, and prednisone; CVP-R: cyclophosphamide, vincristine, prednisone, and rituximab; PUVA: psoralen plus ultraviolet A; NA: not available

Discussion

The present narrative review highlights the considerable clinical and therapeutic heterogeneity of CTCLs involving the external genital organs. Although the available literature provides valuable insights into the manifestations and management of these rare presentations, the evidence is predominantly derived from isolated case reports and small case series. Consequently, the reported findings should be interpreted cautiously, particularly when considering diagnostic approaches, treatment efficacy, and long-term prognosis.

Clinical Features and Diagnostic Considerations

The diversity of clinical presentations identified in this review, together with the nonspecific nature of genital manifestations, underscores the potential for diagnostic uncertainty and delayed recognition.

The differential diagnosis is broad and depends on the anatomical site and clinical morphology. Vulvar lesions may resemble inflammatory dermatoses, including lichen sclerosus, lichen planus, eczema, and

psoriasis, as well as infectious conditions and vulvar intraepithelial or invasive neoplasia. Penile involvement may mimic balanitis, inflammatory dermatoses, sexually transmitted infections, penile intraepithelial neoplasia, or squamous cell carcinoma. Scrotal lesions may similarly resemble inflammatory or infectious disorders, epidermal cysts, or other cutaneous neoplasms [28].

Persistent, progressive, atypical, or treatment-resistant genital lesions should prompt histopathological examination, particularly in patients with a previous diagnosis of CTCL. Histopathological findings should be interpreted in conjunction with clinical presentation, immunohistochemical characterization, and, when appropriate, molecular studies. Distinguishing between MF, primary cutaneous CD30-positive lymphoproliferative disorders, and other aggressive T-cell lymphoma subtypes is essential because these entities differ in clinical behavior, prognosis, and therapeutic management [1].

Furthermore, comprehensive clinical evaluation is necessary to distinguish primary genital presentations from secondary involvement in patients with established CTCL. Disease staging and assessment for extracutaneous involvement should be guided by the underlying lymphoma subtype and clinical findings [2]. However, the limited number of reported cases does not allow the establishment of genital-specific diagnostic criteria or prognostic markers.

Therapeutic Considerations and Interpretation of Reported Outcomes

The management of genital CTCL represents a particular challenge because therapeutic decisions must account for both the underlying lymphoma and the functional sensitivity of the affected anatomical region. The heterogeneity of treatment approaches identified in this review reflects differences in lymphoma subtype, disease extent, previous therapies, and anatomical considerations.

Localized radiotherapy was associated with favorable local responses in several patients with vulvar or penile involvement [9,11,24,27]. These findings suggest that radiotherapy may provide effective local disease control in selected cases. However, the small number of treated patients, differences in radiation techniques and doses, and inconsistent follow-up prevent conclusions regarding optimal treatment protocols or long-term effectiveness.

Surgical management requires careful consideration of the balance between local disease control and preservation of genital anatomy and function. Although favorable outcomes were described in individual cases, the available evidence does not establish the comparative effectiveness of surgery versus other local treatment modalities.

An important consideration emerging from the reviewed cases is the distinction between local response and overall lymphoma control. In some cases, complete or substantial local responses were followed by progression at extracutaneous or other cutaneous sites [11,25]. This distinction emphasizes the importance of evaluating both local treatment response and overall lymphoma activity when assessing therapeutic outcomes.

The considerable variability in lymphoma subtype, disease stage, previous treatments, and follow-up duration makes direct comparisons between therapeutic strategies inappropriate. Therefore, the available evidence does not support a genital site-specific treatment algorithm. Instead, management should be individualized according to established CTCL treatment principles, while considering the anatomical location, extent of disease, symptoms, and potential treatment-related morbidity [3,4].

The anatomical characteristics of the external genital organs introduce additional considerations when selecting local treatment modalities. The sensitivity of genital skin and mucosal surfaces, the proximity of urinary and reproductive structures, and the potential consequences for sexual function require careful evaluation of treatment-related morbidity. These considerations may influence the selection and feasibility of local treatment approaches, particularly when balancing therapeutic benefit against potential functional impairment. The application of topical therapies and phototherapy may also be influenced by anatomical accessibility, local tolerability, and the extent of disease. Nevertheless, evidence regarding genital-specific treatment toxicity, functional outcomes, and optimal therapeutic protocols remains insufficient.

Multidisciplinary Management

Multidisciplinary collaboration is particularly relevant when genital involvement presents diagnostic uncertainty or requires complex therapeutic decisions. Dermatologists and hematologists contribute to disease characterization, staging, and systemic treatment planning, while dermatopathologists play a central role in histopathological classification. Gynecologists and urologists may assist in evaluating anatomical extension, managing urinary or genital complications, and determining the feasibility of surgical interventions. Radiation oncologists are essential when localized radiotherapy is considered. In addition, attention to sexual health, psychological well-being, and quality of life should form part of comprehensive patient care, particularly when treatment may affect genital function or body image.

The potential impact of genital involvement extends beyond local disease control. Pain, pruritus, ulceration, urinary symptoms, and sexual dysfunction may substantially affect patients' quality of life. Although the broader burden of CTCL on health-related quality of life has been documented [5], genital-specific patient-reported outcomes remain insufficiently characterized. Incorporating functional and psychosocial considerations into treatment planning may therefore be particularly relevant in this population.

Limitations of the Available Evidence and Future Directions

Several limitations should be considered when interpreting the findings of this review. First, the available evidence consists predominantly of case reports and small case series, which are inherently susceptible to publication and selection bias. Unusual presentations and favorable therapeutic responses may be more likely to be published, potentially limiting the representativeness of the reported cases.

Second, substantial heterogeneity exists in histopathological subtypes, disease stage, anatomical involvement, treatment modalities, and follow-up duration. These differences preclude meaningful comparisons of treatment efficacy and prevent reliable estimation of recurrence rates, survival outcomes, or the prognostic significance of genital involvement.

Third, outcome reporting was inconsistent across the included studies. Although complete and partial responses were frequently described, standardized response assessments and long-term follow-up were not uniformly available. Moreover, genital-specific functional outcomes, sexual health, and patient-reported quality-of-life measures were rarely documented.

Although standardized response criteria have been established for MF and SS, their application was not consistently documented in the reviewed reports. This limits the comparability of treatment outcomes and highlights the need for more uniform reporting of therapeutic responses in future studies [29].

Finally, the available literature does not adequately establish whether genital involvement independently influences prognosis or primarily reflects the underlying biological behavior and stage of CTCL. Distinguishing these possibilities remains an important area of uncertainty.

Given the rarity of genital CTCL, large prospective studies may be difficult to conduct. Nevertheless, multicenter collaborations, standardized reporting of clinical and histopathological findings, and systematic documentation of treatment responses and long-term outcomes could substantially improve the available evidence. Particular attention should be directed toward diagnostic delays, optimal local treatment strategies, functional outcomes, and the role of multidisciplinary management.

Conclusions

CTCL may involve the external genital organs, most commonly as a secondary manifestation of disease, although primary genital presentations have also been reported. Given its rarity and heterogeneous clinical presentation, genital CTCL may represent a diagnostic and therapeutic challenge. Increased clinical awareness and histopathological evaluation of persistent or atypical genital lesions are important for timely diagnosis. Management should be individualized according to lymphoma subtype, disease stage, extent of involvement, and previous treatment, while further evidence is needed to better define optimal therapeutic strategies and long-term outcomes.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

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