Int. j. adv. multidisc. res. stud. 2026; 6(4):1598-1601

Received: 04-07-2026
Accepted: 14-08-2026

International Journal of Advanced Multidisciplinary Research and Studies

ISSN: 2583-049X

Successful Management of Multiple Trichoepitheliomas in Identical Twins Using Combined Cryotherapy and Topical Tretinoin: A Four-Year Follow-up Case Report

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Abstract
Background: Trichoepithelioma is a rare benign adnexal tumor of hair follicle origin. When multiple papules affect cosmetically sensitive areas, treatment is challenging. Literature reports show both surgical/ablative and pharmacologic options (topical tretinoin, imiquimod) used with varied success.
Case: A 15-year-old Omani female with a three-year history of multiple slow-growing whitish papules over the nasal bridge and perinasal area. Her identical twin sister had similar lesions. Examination and biopsy confirmed multiple trichoepitheliomas.
Management: Treated with cryotherapy (liquid nitrogen, 20 seconds per lesion, two sessions) plus topical tretinoin cream (0.025–0.05%) applied daily.
Outcome: Marked cosmetic improvement, with an estimated 90% reduction in lesion count and no new lesions, by the latest follow-up at approximately four years. Mild transient erythema and dryness reported, managed with emollients. No scarring or recurrence observed.
Conclusion: Combined cryotherapy and topical tretinoin may represent a practical, safe, and effective treatment for multiple trichoepitheliomas, particularly in young patients with lesions in cosmetically important facial regions.

Keywords: Trichoepithelioma, Cryotherapy, Tretinoin, Case Report, Dermatology

Introduction

Trichoepithelioma is a benign adnexal tumor derived from the hair follicle, classified among the trichoblastic neoplasms together with trichoblastoma, trichoadenoma, and the desmoplastic variant [4]. It may present as a solitary, non-familial lesion or as part of multiple familial trichoepithelioma (MFT), an autosomal dominant disorder with reduced penetrance in males, or within syndromic forms such as Brooke-Spiegler syndrome and Rombo syndrome [4]. Onset typically occurs in childhood or around puberty, with lesions progressively increasing in size and number over time [4].

Multiple familial trichoepithelioma and Brooke-Spiegler syndrome share a common genetic basis: heterozygous germline mutations in the CYLD tumor-suppressor gene at chromosome 16q12–13, which normally encodes a deubiquitinase that restrains nuclear factor-kappa B signaling [5, 6]. Loss of CYLD function is thought to permit unchecked proliferation of follicular germinative cells, and the same gene defect can underlie a phenotypic spectrum ranging from isolated trichoepitheliomas to coexistent cylindromas and spiradenomas, depending on the specific mutation and as-yet poorly understood modifying factors [5, 6]. Many patients with multiple trichoepitheliomas, however, have no identifiable family history, and sporadic cases are well documented [4].

Clinically, firm, whitish or skin-colored papules are most commonly located on the central face — particularly the nasolabial folds, nasal bridge, and perinasal areas — though the eyebrows, cheeks, scalp, and trunk may also be involved [7]. Disease severity ranges widely, from a handful of inconspicuous papules to hundreds of confluent nodules causing marked facial disfigurement, and for reasons that remain unclear, females tend to be more severely affected than males [7]. Because lesions are typically visible and centered on the face, multiple trichoepitheliomas carry a well-recognized psychosocial burden: affected individuals — particularly adolescents, for whom onset frequently coincides with a developmentally sensitive period for body image — commonly report embarrassment, social avoidance, and impaired quality of life [7, 12].

Histologically, trichoepithelioma is characterized by branching nests of basaloid cells, keratin-filled horn cysts, and a surrounding fibrous stroma that recapitulates normal follicular architecture. Distinguishing trichoepithelioma from basal cell carcinoma (BCC) can be challenging, since both share basaloid cells and peripheral palisading; immunohistochemical panels — including CD34 (stromal positivity favoring trichoepithelioma), CD10, and androgen receptor (typically negative in trichoepithelioma but positive in BCC) — can help resolve equivocal cases, although no single marker is fully reliable in isolation [9, 10, 11]. Dermoscopy is a useful, non-invasive adjunct, classically demonstrating in-focus arborizing vessels, milia-like (keratin) cysts, and a whitish or pinkish background, occasionally with rosettes — findings also present in this case (Fig 1) [8].

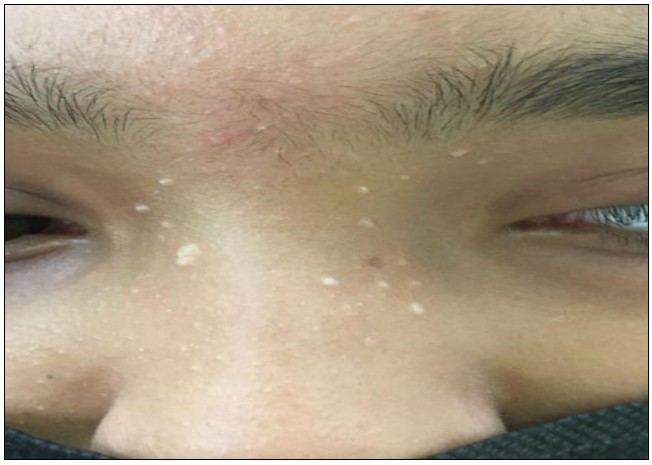

Fig 1: Lesion under dermoscopy showing white clods and fine arborizing vessels consistent with trichoepithelioma

Fig 2: Clinical image before treatment showing firm whitish papules over the nasal bridge and paranasal areas

Fig 3: Clinical image after combination therapy showing complete cosmetic improvement with no residual papules or scarring

The differential diagnosis of multiple facial papules includes basal cell carcinoma, Rombo syndrome, and Brooke-Spiegler syndrome, among other adnexal tumors. Rare malignant transformation of trichoepithelioma into basal cell carcinoma or trichoblastic carcinoma has been described, which underscores the value of histological confirmation, as performed in this case, together with continued clinical surveillance, particularly for lesions that grow rapidly [4].

Case Presentation

A 15-year-old female presented with a 3-year history of slowly progressive whitish papules over the nasal bridge and paranasal area. Her twin sister had similar lesions. Examination revealed firm whitish papules. Dermoscopy demonstrated white clods and fine arborizing vessels consistent with trichoepithelioma.

Management

Cryotherapy: Liquid nitrogen was applied to selected lesions (20 seconds per lesion) in two sessions. Topical Therapy: Daily tretinoin cream 0.025–0.05% at night. Emollients used to relieve dryness. Counseling: Patient and family were informed about the benign nature, hereditary background, and need for genetic counseling.

Outcome

14/10/2021 (Initial treatment): Patient started management with cryotherapy (liquid nitrogen, 20 seconds per lesion). 15/03/2023 (Adjunct therapy): Topical tretinoin cream (0.025–0.05%) was added as a daily application to enhance epidermal turnover and reduce papular prominence. 09/09/2025 (Latest follow-up): The patient showed complete cosmetic improvement, with no new lesions or recurrences. No additional cryotherapy was required at this stage.

Discussion

The combination of cryotherapy and topical tretinoin used in this patient targets two complementary mechanisms. Cryotherapy with liquid nitrogen destroys targeted tissue through direct freeze–thaw injury, intracellular ice-crystal formation, vascular stasis/microthrombosis, and a secondary inflammatory response; rapid freezing followed by slow thawing maximizes cell death and underlies its long-standing use for benign and premalignant skin lesions [13, 14]. Topical tretinoin, a first-generation retinoid, binds nuclear retinoic acid receptors and increases epidermal turnover and desquamation, an effect originally exploited in acne but proposed by Urquhart and Weston to also reduce the prominence of trichoepithelioma papules by thinning the overlying epidermis and accelerating clearance of keratinous debris [1, 15].

Urquhart and Weston (2005) reported that imiquimod combined with tretinoin led to approximately 80% lesion clearance over three years [1]. Pharmacologic therapies used alone, including topical imiquimod, generally yield partial rather than complete responses and may relapse after discontinuation [3, 19].

Surgical and ablative methods — excision, dermabrasion, electrosurgery, and laser ablation (CO_2 or erbium:YAG) — can achieve good short-term cosmetic results, particularly for solitary lesions, but become impractical when dozens to hundreds of facial papules are present [16, 17]. Importantly, lesions treated by dermabrasion or laser have been reported

to regrow into elevated papules or nodules, sometimes within months and sometimes only after several years, and all ablative techniques carry a risk of scarring, hypopigmentation, or further disfigurement — an outcome of particular concern in young patients facing lifelong disease [3, 16, 17]. Radiotherapy has also been described but is rarely used today, given the long-term carcinogenic risk relative to the benign nature of the tumor [18].

More recently, targeted pharmacologic approaches have emerged from the recognition that CYLD loss dysregulates downstream pathways, including mechanistic target of rapamycin (mTOR) and hypoxia signaling, in trichoepithelioma [22]. Topical sirolimus (rapamycin), an mTOR inhibitor, has produced sustained reduction in lesion number and size in small case series of multiple familial trichoepithelioma, used either alone or in combination with CO_2 laser [20, 21]. Other reported approaches include anti–tumor necrosis factor-alpha therapy [23] and, in cases with concomitant basal cell carcinoma, the hedgehog-pathway inhibitor vismodegib [24]. These agents are promising but remain largely off-label, costly, and supported only by small case series rather than controlled trials [3].

Within this landscape, cryotherapy combined with topical tretinoin compares favorably as a low-cost, widely accessible, and technically simple regimen that does not require specialized equipment such as a laser or biologic agents — an important consideration in resource-limited settings such as ours. In the present case, the extended follow-up period without recurrence, scarring, or need for repeat cryotherapy after the initial two sessions compares favorably with the regrowth rates reported for ablative monotherapies [3, 16, 17], suggesting that pairing tissue destruction with a topical agent that suppresses keratinocyte/follicular proliferation may help sustain remission. Tolerability was also favorable; the mild, transient erythema and dryness observed are consistent with the well-described irritant profile of tretinoin, which typically improves with continued use and adjunctive emollients [1, 15].

Beyond the cosmetic outcome, addressing multiple trichoepitheliomas in adolescence carries meaningful value for psychosocial wellbeing, given the documented burden of facial disfigurement on self-esteem and social functioning in this population [7, 12]. The family history identified in this patient — an affected twin sister — is consistent with the autosomal dominant inheritance typical of MFT and Brooke-Spiegler syndrome, and reinforces the rationale for genetic counseling, even though formal CYLD mutation testing was not performed in this case [5, 6].

This report carries the limitations inherent to a single-patient design: outcome was assessed clinically rather than with a validated quality-of-life or photographic scoring instrument, the underlying CYLD mutation status was not confirmed, and the durability of response beyond the most recent follow-up remains to be established. Nonetheless, the absence of recurrence over an extended observation period, combined with the simplicity, safety, and low cost of the regimen, supports cryotherapy plus topical tretinoin as a reasonable first-line option before more invasive or expensive therapies are considered, particularly in adolescent patients with cosmetically sensitive disease.

Conclusion

Cryotherapy combined with topical tretinoin may be considered a minimally invasive, effective therapy for multiple trichoepitheliomas, particularly in adolescents and young adults. It offers favorable cosmetic outcomes and avoids aggressive surgical interventions.

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