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Authors

Beutler, Bryce David
Cohen, Philip R

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Peer reviewed

Case presentation

Cryotherapy-induced milia en plaque: case report and literature review

Bryce David Beutler¹, Philip R Cohen²

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¹University of Nevada, Las Vegas

²University of California, San Diego

Correspondence:

Bryce David Beutler
University of Nevada, Las Vegas
brycebeutler@hotmail.com

Philip R. Cohen, MD
Department of Dermatology
University of California San Diego, San Diego, California
mitehead@gmail.com

Abstract

Background: Cryotherapy-induced milia is a rarely described cutaneous reaction that may occur in patients who have received cryotherapy with liquid nitrogen. Cryotherapy-induced milia is characterized by 1-2 millimeter white dermal cysts that develop at the healed cryotherapy site. Milia en plaque, an erythematous plaque containing numerous milia, has not previously been described following treatment of a skin lesion with liquid nitrogen cryotherapy.

Purpose: We describe a man who developed cryotherapy-induced milia en plaque after receiving cryotherapy to his dorsal hand for the treatment of an actinic keratosis. We also summarize the potential complications of cryotherapy, the differential diagnosis of milia en plaque, and therapeutic interventions for this lesion.

Materials and methods: The features of a man with cryotherapy-induced milia en plaque are presented. Using PubMed, the following terms were searched and relevant citations assessed: cryosurgery, cryotherapy, hypothermia, milia and milia en plaque. In addition, the literature on cryotherapy-induced milia and cryotherapy-induced milia en plaque is reviewed.

Results: Our patient developed cryotherapy-induced milia en plaque shortly after his cryotherapy site had healed. Some of the asymptomatic cystic dermal lesions had spontaneously resolved when a lesional biopsy was performed to confirm the diagnosis. The diagnosis, natural course, and potential treatments were discussed with the patient. Subsequent management was to observe the area; at follow-up examination, the remainder of the milia had also spontaneously resolved.

Conclusion: Cryotherapy-induced milia is a benign condition characterized by the development of small white dermal cystic lesions that develop at a healed liquid nitrogen cryotherapy site. The lesions may appear individually or as milia en plaque. Although the mechanism of pathogenesis is unknown, it may represent a variant of traumatic milia. The diagnosis of milia en plaque can usually be established by clinical presentation. If necessary, a biopsy can be performed to provide pathologic confirmation of the suspected diagnosis. Treatment options include manual extraction, topical retinoids, or observation. As was seen in our patient, the milia may resolve spontaneously.

Keywords: cryosurgery, cryotherapy, hypothermia, milia, milia en plaque

Introduction

Cryotherapy has been used to treat many benign and some malignant lesions of the skin [1]. Typically, liquid nitrogen is applied to abnormal tissue in order to lower its temperature below -20°C (or -50°C for malignant lesions) and induce its controlled destruction. Subsequently, the tissue is allowed to gradually thaw at room temperature. Actinic keratoses can usually be effectively treated with a single freeze-thaw cycle, whereas at least two cycles of rapid freezing followed by a slow thaw may be required to completely destroy all abnormal cells of cutaneous neoplasms [2,3]. Potential complications of cryotherapy are listed in Table 1 [4-6].

Table 1. Potential complications of cryotherapy

Bullae
Edema
Hemorrhage
Hyperpigmentation
Hypertrophic scarring
Hypopigmentation
Infection
Milia
Milia en plaque
Nerve damage
Nitrogen gas insufflation
Pain
Pseudocarcinomatous hyperplasia
Retraction
Tissue defects

Milia is a recognized, albeit rarely described, complication of cutaneous liquid nitrogen cryotherapy [4]. However, to the best of our knowledge, cryotherapy-induced milia en plaque has never been reported. We describe a man who developed milia en plaque at the site of cryotherapy after the tissue had healed. We also review the differential diagnosis, postulated pathogenesis, and treatment options of milia en plaque.

Case synopsis

A 66-year-old man, Fitzpatrick type 1, presented with an erythematous plaque with superficial scaling on the dorsal surface of his left hand at the metacarpophalangeal joint of his index finger. He also had several similar appearing lesions on the sun-exposed areas of his scalp, face, and the distal extensor surfaces of his arms. The diagnosis of multiple actinic keratoses was made based upon the correlation of his history of prior sun exposure and the clinical morphology and distribution of the lesions.

Each of the lesions was treated with a single freeze-thaw cycle of liquid nitrogen cryotherapy. The duration of freeze was 5 to 7 seconds and thawing occurred during the subsequent 10 to 15 seconds. The patient then applied mupirocin 2% ointment three times daily; all of the treatment sites healed within three weeks.

The patient returned for evaluation six months later. Cutaneous examination of the cryotherapy site revealed two foci of small (less than 1 millimeter) white cystic papules aggregated on an erythematous base (Figures 1 and 2). The patient requested that a biopsy of the lesions be postponed until his return visit in 3 months.



Figure 1. Cryotherapy-induced milia en plaque on the dorsal surface of the left hand at the metacarpophalangeal joint of the index finger of a 66-year-old man. **Figure 2.** The lesions are more readily observed after the patient makes a fist.

When he returned, some of the lesions were no longer present (Figure 3). A shave biopsy from some of the remaining lesions was performed. Microscopic examination showed cystic spaces - with or without a squamous epithelium lining - containing fragments of keratin (Figure 4).



Figure 3. The left hand at the metacarpophalangeal joint of the index finger shows that some of the milia en plaque lesions have spontaneously resolved.

Based on correlation of the clinical history, lesion morphology, and histopathologic findings, a diagnosis of cryotherapy-induced milia en plaque was established. The patient denied any pain or discomfort and opted to forego treatment. When he returned for clinical follow-up three months later, the residual lesions had spontaneously resolved.

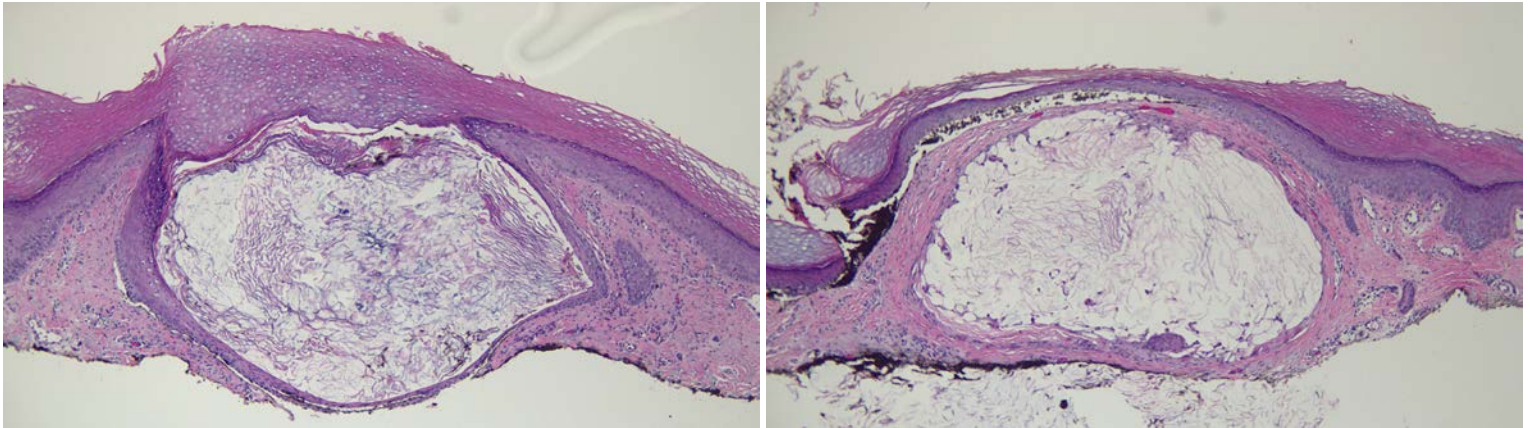


Figure 4 (a and b). Microscopic examination of milia en plaque. One of the lesions shows a small epithelium-lined cystic space containing keratin in the upper dermis (a). A second lesion shows a cystic space without a squamous epithelium lining in the upper dermis (b). (Hematoxylin and eosin; a = x10, b = x10).

Discussion

Milia en plaque was originally described as retroauricular confluent milium by Boulzer and Fouquet in 1903 [7]. In 1978, Hubler et al. identified the condition in two patients and proposed the name milia en plaque [8]. The mechanism of pathogenesis for milia en plaque remains to be determined.

Milia en plaque is typically observed in adults between the ages of 33 and 65 years, with a median age of onset of 44 years [9]. However, the onset of milia en plaque in either childhood [10,11] or old age [12] has also been reported. Women are three times more likely to be affected by the condition than men. There is no known ethnic predilection.

Milia en plaque is most commonly observed in the retroauricular area [9]. However, individuals with milia en plaque located on the nose, lip, eyelid, and supraclavicular area have also been described [13-16]. The lesions initially appear as 1-3 millimeter white cysts aggregated on an erythematous plaque. The lesions may be asymptomatic, as in our patient, or be accompanied by an itching or burning sensation [17]. It is common for the lesions to persist for several months prior to the patient seeking evaluation and the diagnosis being established [9].

The diagnosis of milia en plaque is predominantly based upon the lesion morphology. Pathological evaluation is usually not required but can be performed to confirm the suspected diagnosis. Lesional biopsies reveal keratin-filled cysts; they may be

surrounded by a mild or moderate lymphocytic infiltrate. An associated granulomatous inflammatory infiltrate may also be present if the cysts have ruptured.

The clinical differential diagnosis of milia en plaque is listed in Table 2 [18,19]. It includes not only local conditions, but also systemic disorders with skin lesions that may mimic milia en plaque.

Table 2. Clinical differential diagnosis of milia en plaque

Favre-Racouchot nodular elastosis
Follicular mucinosis
Folliculotropic mycosis fungoides
Lichen planus follicularis tumidus
Nevus comedonicus
Secondary milia
Steatocystoma multiplex
Trichoadenoma
Xanthelasma

The mechanism of pathogenesis for liquid nitrogen-associated milia en plaque and for non-cryotherapy-induced milia en plaque is unknown. However, some epidermal blistering diseases - such as epidermolysis bullosa acquisita and sometimes bullous pemphigoid - can result in milia formation. This occurrence may be related to the healing process.

Cryotherapy-induced milia may be a variant of traumatic milia. Milia can secondarily develop at the site of previous tissue injury [20-23]. Furthermore, milia en plaque has been associated with pseudoxanthoma elasticum [24] and discoid lupus erythematosus [25,26]; in both of these cases, disease-related tissue trauma preceded the development of milia en plaque. Hence, it is reasonable to hypothesize that milia en plaque at the site of prior liquid nitrogen treatment, similar to traumatic milia, occurs in response to cryotherapy-induced tissue damage.

Keohane et al. proposed that cold temperatures could exacerbate milia en plaque. They describe a 50-year-old man who experienced swelling and burning of the ear lobes that worsened in cold weather. Examination revealed indurated violaceous plaques; the lesions resolved following a three month course of oral minocycline [27]. Similar to Keohane et al.'s patient, our patient's lesional site had also been exposed to cold temperature prior to the development of milia en plaque.

Various treatment options exist for milia en plaque. Pharmacological interventions have been used to treat more extensive or recalcitrant examples and have included oral minocycline [28-30] and oral [31] or topical [13] retinoids. Surgical approaches, such as manual extraction [32] and dermabrasion [33], may be effective. However, these modalities present a small risk of post-treatment scarring and/or pigmentary changes [30,34]. Photodynamic therapy also shows some promise as a noninvasive treatment modality [9].

Interestingly, open spray cryotherapy was used to treat a patient with milia en plaque. In 2001, Noto and Dawber successfully treated a 32-year-old woman with bilateral retroauricular milia en plaque using open spray liquid nitrogen cryotherapy [17]. Although this method of treatment was successful in Noto and Dawber's patient, one of the authors had previously highlighted milia as a potential adverse consequence of cryotherapy [5].

If the milia en plaque lesions are asymptomatic, as in our patient, observation is a reasonable management alternative. Indeed, several of our patient's lesions had resolved spontaneously during the three month interval between their initial observation and biopsy. Also, the residual lesions that remained following biopsy had disappeared within the next three months. Indeed, the absence of clinical reports and illustration of the cryotherapy-induced milia in the medical literature may be attributed to spontaneous resolution of the lesions prior to the patient seeking medical attention.

Conclusion

Cryotherapy-induced milia en plaque is a rare complication of cryotherapy and is seldom reported. The pathogenesis of cryotherapy-induced milia en plaque is unknown, but it may be a variant of traumatic milia.

There is no standard treatment for idiopathic or cryotherapy-induced milia en plaque. Similar to our patient, spontaneous resolution of the condition may occur. Therefore, if the lesions are asymptomatic, clinical observation - without additional intervention - may be appropriate.

References

1. Gage AA: History of cryosurgery. *Semin Surg Oncol*. 1998;14(2):99-109. [PMID: 9492880]
2. Jester DA: Cryotherapy of dermal abnormalities. *Prim Care*. 1997;24(2):269-280. [PMID: 9174039]
3. Wetmore SJ: Cryosurgery for common skin lesions. Treatment in family physicians' offices. *Can Fam Physician*. 1999;45:964-974. [PMID: 10216795]
4. Elton RF: Complications of cutaneous cryosurgery. *J Am Acad Dermatol*. 1983;8(4):513-519. [PMID: 6853784]
5. Dawber RP: Cryosurgery: complications and contraindications. *Clin Dermatol*. 1990;8(1):108-114. [PMID: 2203510]
6. Cook DK, Georgouras K: Complications of cutaneous cryotherapy. *Med J Aust*. 1994;161(3):210-213. [PMID: 8035726]
7. Balzer F, Fouquet C: Milium confluent retro-auriculaire bilateral. *Bull Soc Franc Derm Syph*. 1903;14:361-362. (No PMID).
8. Hubler WR, Rudolph AH, Kelleher RM: Milia en plaque. *Cutis*. 1978;22(1):67-70. [PMID: 668413]
9. Stefanidou MP, Panayotides JG, Tosca AD: Milia en plaque: a case report and review of the literature. *Dermatol Surg*. 2002;28(3):291-295. [PMID: 11896786]
10. Bridges AG, Lucky AW, Haney G, Mutasim DF: Milia en plaque of the eyelids in childhood: case report and review of the literature. *Pediatr Dermatol*. 1998;15(4):282-284. [PMID: 9720692]
11. Zhang RZ, Zhu WY: Milia en plaque in a 6-year-old Chinese boy. *Pediatr Dermatol*. 2012;29(4):504-506. [PMID: 21967553]
12. García Sánchez MS, Gómez Centeno P, Sánchez-Aguilar D, Fernández-Redondo V, Toribio J: Milia en plaque in a bilateral submandibular distribution. *Clin Exp Dermatol*. 1998;23(5):227-229. [PMID: 10233607]
13. Nambudiri VE, Habib N, Arndt KA, Kane KS: Milia en plaque of the nose: report of a case and successful treatment with topical tretinoin. *Pediatrics*. 2014. [PMID: 24709934]
14. Gantois C, Cendras J, Guillaudeau A, Bedane C, Bonnetblanc JM: Milia en plaque of the mucous surface of the lip: a complication of piercing. *Ann Dermatol Venereol*. 2010;137(10):667-668. [PMID: 20932454]
15. Wollina U: Bilateral milia en plaque of the eyelids: long eyelashes and unibrow - case report and literature review. *Dermatol Surg*. 2010;36(3):406-408. [PMID: 20100256]
16. Combemale P, Faisant M, Dupin M: Milia en plaque in the supraclavicular area. *Dermatology*. 1995;191(3):262-263. [PMID: 8534951]
17. Noto G, Dawber R: Milia en plaque: treatment with open spray cryosurgery. *Acta Derm Venereol*. 2001;81(5):370-371. [PMID: 11800150]
18. Muñoz-Martínez R, Santamarina-Albertos A, Sanz-Muñoz C, Mirando-Romero A: Milia en plaque. *Actas Dermosifiliogr*. 2013;104(7):638-640. [PMID: 23871459]
19. Ergin S, Basak P, Sari A: Milia en plaque. *J Eur Acad Dermatol Venereol*. 2000;14(1):47-49. [PMID: 10877251]
20. Leong T, Torres A, Macknet KD Jr, Macknet C: Pronounced secondary milia precipitated by a superficial traumatic abrasion in a 4-year-old boy. *J Pediatr*. 2010;156(5):854. [PMID: 20056239]
21. Lee A, Griffiths WA: Multiple milia due to radiotherapy. *J Dermatolog Treat*. 2002;13(3):147-149. [PMID: 12227879]
22. Miller LM, Schwartz JT, Cho S: Milia: a unique reaction to tattoos. *Cutis*. 2011;87(4):195-196. [PMID: 21644494]
23. Peters W: The chemical peel. *Ann Plast Surg*. 1991;26(6):546-471. PMID: 1883165.
24. Cho SH, Cho BK, Kim CW: Milia en plaque associated with pseudoxanthoma elasticum. *J Cutan Pathol*. 1997;24(1):61-63. [PMID: 9027636]
25. Boehm I, Schupp G, Bauer R: Milia en plaque arising in discoid lupus erythematosus. *Br J Dermatol*. 1997;137(4):649-651. [PMID: 9390352]
26. Kouba DJ, Owens NM, Mimouni D, Klein W, Nousari CH: Milia en plaque: a novel manifestation of chronic cutaneous lupus erythematosus. *Br J Dermatol*. 2003;149(2):424-426. [PMID: 12932260]
27. Keohane SG, Beveridge GW, Benton EC, Cox NH: Milia en plaque - a new site and novel treatment. *Clin Exp Dermatol*. 1996;21(1):58-60. [PMID: 8689774]
28. Wong SS, Goh CL: Milia en plaque. *Clin Exp Dermatol*. 1999;24(3):183-185. [PMID: 10354175]
29. Alsaleh QA, Nanda A, Sharaf A, Al-Sabah H: Milia en plaque: a new site. *Int J Dermatol*. 2000;39(8):614-615. [PMID: 10971731]
30. Lo LK, Tsai TF, Hung CM, Chen YF, Ko WC: Milia en plaque - a case report. *Dermatol Sinica*. 2008;26:180-184. (No PMID).
31. Ishiura N, Komine M, Kadono T, Kikuchi K, Tamaki K: A case of milia en plaque successfully treated with oral etretinate. *Br J Dermatol*. 2007;157(6):1287-1289. [PMID: 17927794]
32. Cota C, Sinagra J, Donati P, Amantea A: Milia en plaque: three new pediatric cases. *Pediatr Dermatol*. 2009;26(6):717-720. [PMID: 20199448]
33. van Lynden-van Nes AM, der Kinderen DJ: Milia en plaque successfully treated by dermabrasion. *Dermatol Surg*. 2005;31(10):1359-1362. [PMID: 16188197]
34. Lee DW, Choi SW, Cho BK: Milia en plaque. *J Am Acad Dermatol*. 1994;31(1):107. [PMID: 8021349]