Adult colloid milium is clinically distinguishable from its histopathologic mimic cutaneous amyloidosis

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Abstract

Colloid milium, also known as colloid degeneration of the skin or dermal hyalinosis, is a cutaneous deposition disease that presents as three subtypes: juvenile, nodular, and adult. Adult colloid milium is characterized by amyloid-like depositions in the dermis, mimicking cutaneous amyloidosis histologically. A 70-year-old man presented with lesions on the sun-exposed skin of the face, dorsal hands, and dorsal forearms resembling adult colloid milium. A punch biopsy was performed on the left zygoma and histopathological features were consistent with this diagnosis, though cutaneous amyloidosis was considered. A case of adult colloid milium is presented to emphasize the clinical and histopathologic differentiation from cutaneous amyloidosis.

Keywords: colloid milium, lichen amyloidosis, nodular amyloidosis, primary localized cutaneous amyloidosis

Introduction

Colloid milium, also known as colloid degeneration of the skin or dermal hyalinosis, is a rare cutaneous deposition disease first reported by Wagner in 1866 [1,2]. There are three subtypes: juvenile, nodular, and adult (**Table 1**), [1,2]. Adult colloid milium is the most common and appears between age 30-50 in individuals with light complexions. It affects males more than females in a ratio of 4:1[3]. Adult colloid milium resembles primary localized cutaneous amyloidosis histologically, but clinically these conditions are quite different.

Case Synopsis

A 70-year-old man with a history of non-melanoma skin cancer presented with papules and plaques on the face, dorsal hands, and dorsal forearms. The eruption slowly worsened over 20 years and was occasionally associated with burning. Treatment with topical corticosteroids and tretinoin cream over several years led to no improvement. There was no family history of a similar condition. Physical examination revealed symmetric pink-to-orange smooth, translucent papules coalescing into plaques over the zygoma and lateral forehead, with less pronounced papules on the dorsal hands and forearms (**Figure 1**). A punch biopsy was performed on the left cheek. Histopathology demonstrated homogenous, pale-pink, fissured masses in the superficial and mid-dermis with adjacent solar elastosis consistent with colloid milium (**Figure 2**). In this case, the patient sought no further treatment, other than utilizing protective measures to minimize further ultraviolet damage.

Case Discussion

Adult colloid milium is a rare cutaneous condition which can be differentiated from lichenoid, macular, and nodular forms of primary localized cutaneous amyloidosis and systemic amyloidosis based on clinical findings more effectively than utilizing histopathology. Adult colloid milium presents as translucent, asymptomatic, dome-shaped amber, pink, or yellow papules varying in diameter from 0.5-5mm and can form confluent plaques. Lesions develop over a period of years and are limited to severely sun-damaged skin on the dorsum of the

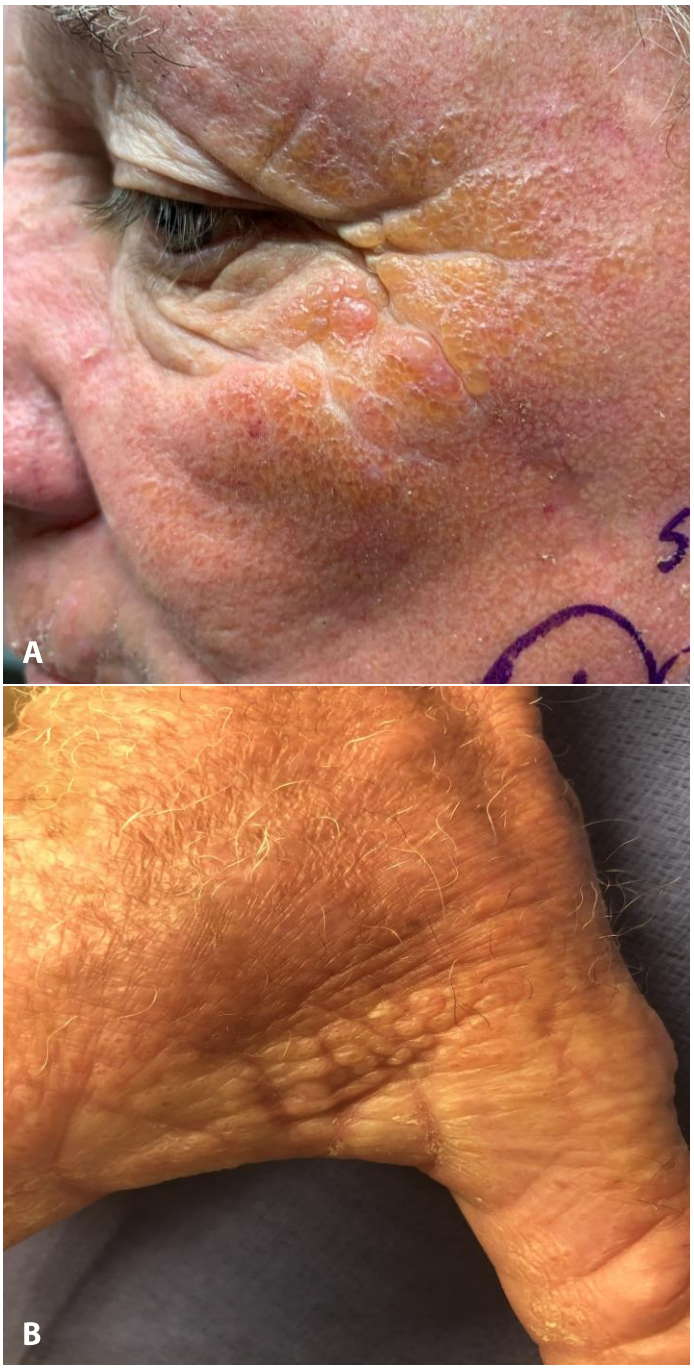

Figure 1. *Clinical findings of patient.* ***A)*** *Tan-yellow smooth, translucent papules coalesce into plaques on the left zygoma and lateral forehead.* ***B)*** *Similar tan-yellow papules on the dorsal right hand at the web between the index and thumb.*

hands, web between the thumb and index fingers, knuckles, forearms, malar regions, nose, ears, sides and back of neck, and temporal areas [1,3,4]. With the addition of considerable pressure, a clear to yellow mucoid substance can sometimes be expressed from these firm papules [1]. Development of adult colloid milium may be potentiated by hydroquinone, petroleum derivatives, phenols, and gas oils, all known to augment cutaneous effects of UV light [2,4].

Lichen amyloidosis and macular amyloidosis result from chronic rubbing and scratching and an amyloid keratin protein is believed to be the amyloid fibril precursor. Erythema and scaling are present most commonly on the anterior lower legs [5].

Nodular amyloidosis, though classified as a form of primary cutaneous amyloidosis, is not a form of amyloid keratin disease. This amyloid derives from light chain precursor produced at the site by adjacent plasma cells and produces nodules on the face, trunk, extremities, and genitalia [6]. These patients may later develop systemic amyloidosis and therefore, regular follow-up office visits are required [7].

Systemic amyloidosis is caused by amyloid light-chain deposits and usually associated with monoclonal light chain protein that can be identified in blood or urine [6]. Papules and plaques are frequently associated with purpura (pinch purpura) related to amyloid in blood vessels. Waxy papules forming confluent plaques frequently occur on eyelids and the central face. The clinical differential diagnosis is highlighted in **Figure 3**.

The presence of amyloid-like deposits in the skin is the hallmark of all these conditions. Hematoxylin and eosin staining of adult colloid milium reveals large,

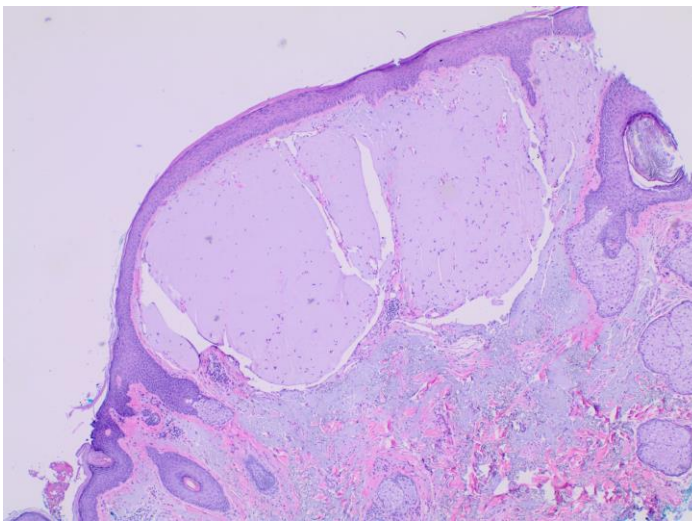

Figure 2. *Biopsy specimen. Homogenous pale-pink, fissured deposits are present in the superficial and mid-dermis, typical of the appearance of colloid milium or cutaneous amyloidosis. H&E, 40×.*

clefted colloid nodules located within the papillary dermis and separated from the epidermis by a grenz zone [1,4]. Solar elastosis is present at the periphery of the colloid deposits [4,5,8]. The epidermis is thinned with loss of the normal pattern between epidermal rete ridges and dermal papillae [5]. Nodular amyloidosis and systemic amyloidosis can demonstrate very similar large dermal amyloid deposits [7]. Lichen and macular amyloidosis show smaller, globular, eosinophilic amyloid deposits lacking clefts and associated with angioplasia; solar elastosis is usually not seen [5].

Special histochemical stains, such as Van Geison stain, pagoda red, methyl violet, and crystal violet, produce distinctive findings in cases of amyloidosis and adult colloid milium. Differentiation of lichen and macular amyloidosis from adult colloid milium can be accomplished with staining against amyloid-K. However, Congo red, periodic acid-Schiff, antiserum against amyloid-P, and thioflavin T staining all yield positive results in amyloidosis and adult colloid milium; thus they cannot be used to differentiate between these conditions [9], (**Table 2**).

Electron microscopy of adult colloid milium shows short, wavy, branching filaments with diameter of 1.5-10nm, whereas 6-10nm thick straight, nonbranching filaments are observed in amyloidosis [4]. In many cases, clinical findings may preclude the need for an extensive workup with special stains and electron microscopy.

An effective treatment for adult colloid milium has yet to be determined. Various strategies, including dermabrasion, curettage, cryotherapy, erbium laser resurfacing, and retinoic acid have yielded variable results [3].

Conclusion

A 70-year-old man is presented with lesions on the left zygoma and dorsa of the hands. Sections of the zygoma punch biopsy showed eosinophilic fissured masses located in the upper dermis and separated from the overlying epidermis by a narrow zone of collagen, a grenz zone. Severe solar elastosis was noted in the adjacent dermis. Upon initial

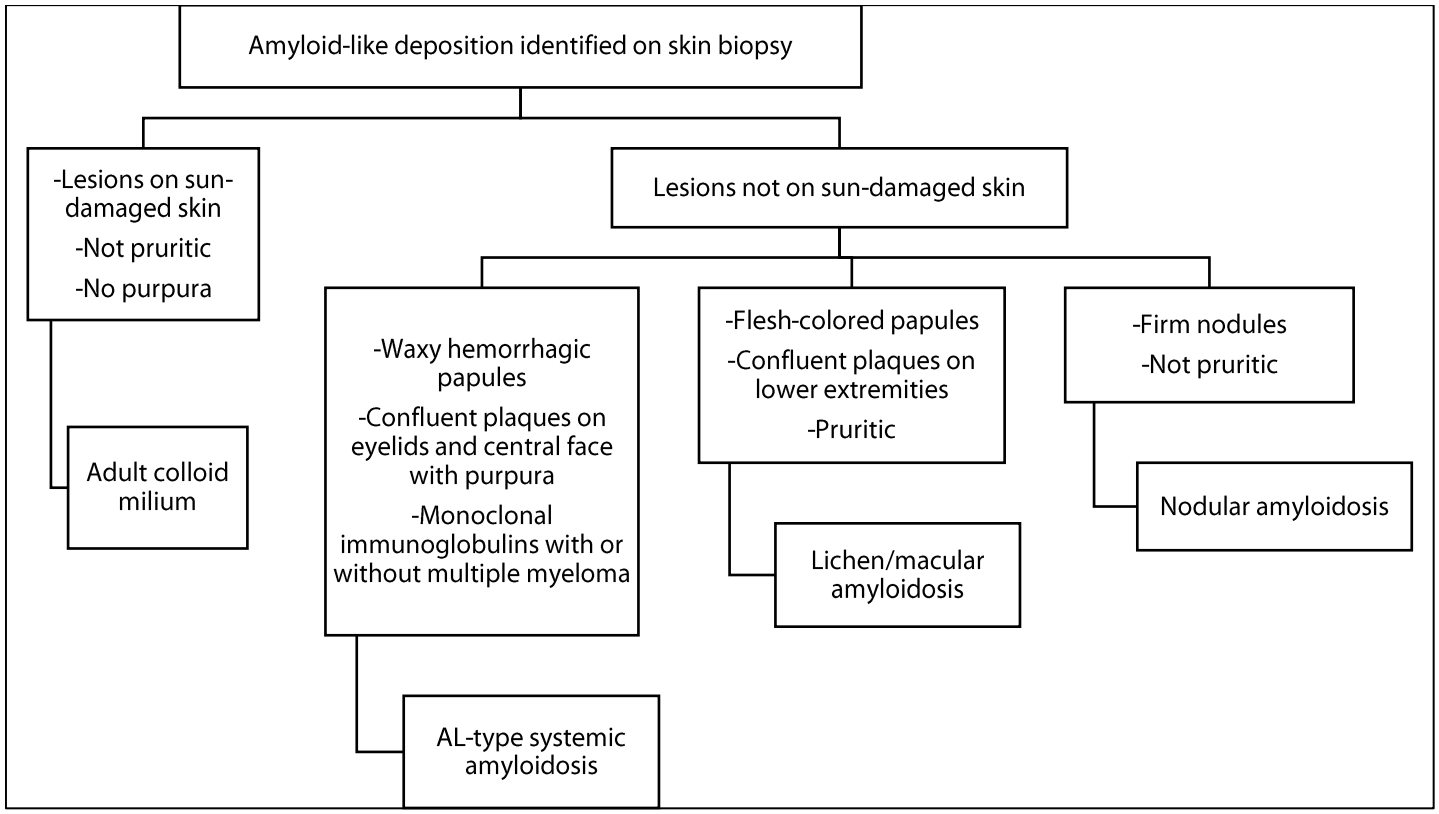

Figure 3. *Clinical differential diagnosis of adult colloid milium and cutaneous amyloidosis [3,4,6].*

Table 2. *Histopathologic differential diagnosis of adult colloid milium and cutaneous amyloidosis [1,4,5,7,9].*

	Lichen/macular amyloidosis	Nodular amyloidosis	Systemic amyloidosis	Adult colloid milium
Epidermis	Papillated epidermal hyperplasia with hyperkeratosis overlies amyloid	Epidermis may or may not be separated from subcutaneous tissues by narrow zone of collagen	No change to epidermis	Thinned, flattened epidermis with loss of normal pattern between epidermal rete ridges and dermal papillae Presence of grenz zone
Depositions	Small globular amyloid deposits without clefts in upper portion of dermis, sparing blood vessels	Large, fissured masses of amyloid in dermis, extending into subcutaneous fat	Large amyloid deposits in both dermis (deeper in dermis than PLCA) and vessel walls	Large clefted colloid deposits within upper half of dermis, sparing blood vessels
Presence of Solar Elastosis	Usually not seen	Usually not seen	Usually not seen	Always present at periphery of colloid masses
Amyloid fiber type	AK	AL	AL	---
Antiserum against amyloid-P	+	+	+	+
Congo red	+	+	+	+/-
PAS-D	+	+	+	+
Thioflavin T	+	+	+	+
Antiserum against amyloid-K	+	-	-	-
Methyl violet/crystal violet	Pink/red	Pink/red	Pink	Purple/red
Pagoda red/cotton dyes	+	+	+	-
Van Geison	Pink amyloid	Pink amyloid	Pink amyloid	Yellow colloid

consideration, the material resembled amyloid. However, the clinical and histopathologic findings clearly support the diagnosis of adult colloid milium.

Potential conflicts of interest

The authors declare no conflicts of interest

References

1. Graham JH, Marques AS. Colloid Milium: A Histochemical Study. *J Invest Dermatol*. 1967;49:497-507. [PMID: 6065120].
2. Rahman S, Bari A, Mumtaz N. Colloid milium: A rare cutaneous deposition disease. *J Pak Med Assoc*. 2008;58:207-9. [PMID: 18655433].
3. Zamora AB, Simón MP, Tirado A, Olivera RM. Adult colloid milium. An underdiagnosed and difficult to treat entity. *Revista Médica Del Hospital General De México*. 2015;79. [DOI: 10.1016/j.hgmx.2015.10.002].
4. Muscardin LM, Bellocci M, Balus L. Papuloverrucous colloid milium: an occupational variant. *Br J Dermatol*. 2000;143:884-7. [PMID: 11069478].
5. Ackerman AB, Niven J, Grant-Kels JM. Differential Diagnosis in Dermatopathology: Lea & Febiger; 1982. p. 174-175.
6. Blancas-Mejía LM, Ramirez-Alvarado M. Systemic amyloidoses. *Ann Rev of Biochem*. 2013;82:745-74. [PMID: 23451869]. [PMID: 23451869].
7. Li W-M. Histopathology of primary cutaneous amyloidoses and systemic amyloidosis. *Clin Dermatol*. 1990;8:30-5. [PMID: 2224734].
8. Goldblum JR, Beals TF, Weiss SW. Neuroblastoma-like neurilemoma. *Am J Surg Pathol*. 1994;18:266-73. [PMID: 8116794].
9. Desai AM, Pielop JA, Smith-Zagone MJ, Hsu S. Colloid Milium: A Histopathologic Mimicker of Nodular Amyloidosis. *Arch Dermatol*. 2006;142:781-98. [PMID: 16785390].

Table 1. *Comparison of juvenile, adult, and nodular colloid milium [1,2].*

	Juvenile colloid milium	Adult colloid milium	Nodular colloid milium
Age	Before puberty Usually resolves in adulthood	30-50 years	Any age
Risk factors	Can be familial (autosomal dominant) Sun exposure	Sun exposure, hydroquinone, petroleum, and chemical fertilizers	Sun exposure
Lesion Location	Face Lesions develop symmetrically in irregular groups in areas exposed to sunlight	Sun exposed areas, especially on face, neck, dorsa of hands, and pinnae of ears Lesions develop symmetrically in irregular groups in areas exposed to sunlight	Face, trunk, scalp
Clinical Features	Small dermal papules 1-2mm in diameter, yellowish brown and sometimes translucent	Small dermal papules 1-2mm in diameter, yellowish brown and sometimes translucent	Isolated nodules, approximately 5cm in diameter
Histology	Fissured eosinophilic colloid masses in papillary dermis Solar elastosis Grenz zone separating the lesion from the rest of the epidermis	Fissured eosinophilic colloid masses in papillary dermis Solar elastosis Grenz zone separating the lesion from the rest of the epidermis	Flat epidermis with subepidermal colloid masses
Other			Considered a variant of amyloidosis Associated with multiple myeloma