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Cutaneous mucinosis of infancy: report of a rare case and review of the literature.

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Abstract

Cutaneous mucinosis of infancy (CMI) is a rare dermatologic condition, first reported in 1980 and currently classified within the complex group of papular mucinoses. We report a case of CMI and review the prior 13 cases in the literature. The patient was a 5-year-old girl who presented with asymptomatic dermal papules and plaques on her leg and back with no overlying color change. These lesions were first noticed during infancy and had become slightly more evident over time. The patient had a history of birthmarks and eczema. Her family history included eczema, allergies, photosensitivity, and Graves disease. Pre-biopsy clinical differential diagnosis included connective tissue nevus, granuloma annulare, myofibroma, lipofibroma, and lymphangioma. Biopsies revealed significant increase in interstitial mucin within the reticular and mid dermis, without significant sclerosis or fibroblastic proliferation. The relatively quiescent pattern of interstitial mucinosis with slight fibrocyte hyperplasia presenting as dermal papules-plaques on the trunk and extremities was most consistent with a diagnosis of CMI. We report another case of CMI in an otherwise healthy patient. Our patient is unique as she is the first CMI patient with a family history of Graves disease, although our patient appeared euthyroid. We also review the literature on this rare entity.

Keywords: mucinosis, papular mucinosis, cutaneous mucinosis of infancy

Introduction

Cutaneous mucinosis comprises a heterogeneous group of disorders with diverse clinical and histological manifestations. Idiopathic primary cutaneous mucinosis includes three major clinicopathological subsets: generalized papular and sclerodermoid, localized papular, and an intermediate or atypical form. All of these entities share in common mucin deposition within the dermis. Localized papular mucinosis is further divided into 5 subtypes: discrete papular mucinosis involving any site, acral persistent papular mucinosis, self-healing papular mucinosis (juvenile and adult forms), papular mucinosis of infancy (cutaneous mucinosis of infancy), and nodular mucinosis [1, 2]. Cutaneous mucinosis of infancy (CMI) is the rare pediatric variant of the localized papular mucinosis form with at least 13 reported cases in the literature [2-14]. Herein, we present a 5-year-old girl and review the literature on this rare entity.

Case Synopsis

Clinical presentation

Patient was a 5-year-old girl who was referred to the outpatient dermatology clinic of an academic medical center with several skin lesions, including a 5.0×4.0 cm ill-defined, firm, slightly rippled, dermal plaque on the right anterior thigh with subtle overlying mottled hypopigmentation (**Figure 1A**), a

2.5×2 cm ill-defined papule on the right posterior calf (**Figure 1B**), and similar smooth papules on the right lateral back. There was no overlying hypertrichosis. Per parents' report, the papules had been present since infancy and were believed to become more apparent with sun exposure over time. They were neither painful nor pruritic. The patient was well-appearing and appropriately developed with an otherwise unremarkable review of systems. The past medical history included birthmarks and eczema. The family history included eczema, seasonal allergies, photosensitivity, and Graves disease. The patient did not report any medications or allergies to medications. Clinically, the differential diagnoses of connective tissue nevus, granuloma annulare, myofibroma, and lipofibroma were considered.

After obtaining informed consent from the parents, two 4mm punch biopsies were performed from papules on the right posterior calf and right lower back. Hematoxylin and eosin sections were prepared and immunohistochemical studies were conducted.

Light microscopic and immunophenotypic findings

Both biopsies showed similar findings of significant increase in interstitial mucin primarily within the reticular and middle portion of the dermis with some extension to the dermal-subcuticular interface, highlighted by Alcian blue preparation, pH 2.5 (**Figures 2, 3**). There was a relative sparing of the subcutaneous fat. Significant fibroblastic proliferation was not seen. The elastic tissue stain did not reveal significant disruption in the elastic fibers. The CD68 preparation was minimally positive, suggesting no significant increase in interstitial histiocytes. Although there was a mild interstitial hypercellularity with focal disorganization of collagen bundles, the main abnormality was interstitial mucinosis. The overall degree of collagen alteration and fibrocyte hyperplasia was not considered diagnostic of a scleromyxedematous process, in light of the lack of a greater degree of sclerosis and fibroblastic proliferation. The smooth muscle actin and CD34 preparations did not reveal a scleroderma phenotype.

The relatively quiescent pattern of interstitial mucinosis with slight fibrocyte hyperplasia, presenting initially during infancy as isolated papule-plaques with truncal and extremity distribution, strongly suggested a diagnosis of CMI. For thoroughness, thyroid function tests were also performed and revealed normal results.

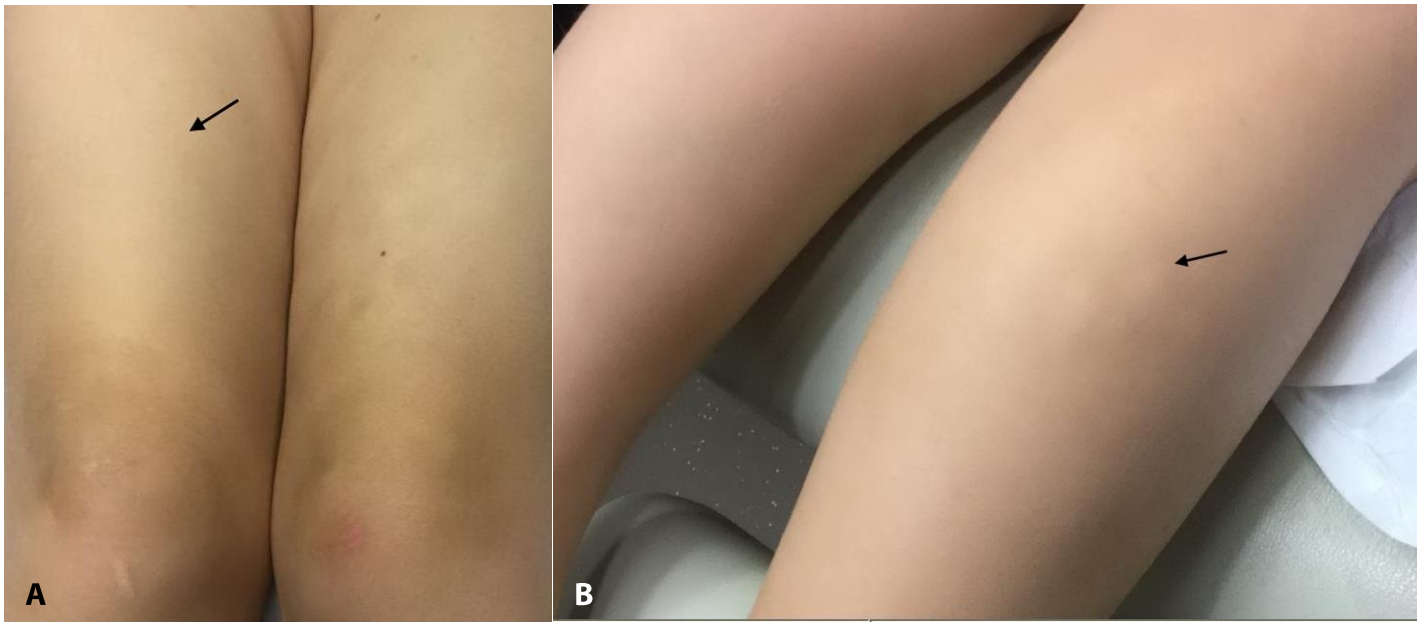

Figure 1. ***A)*** *The patient presented with multiple skin lesions including a 5.0×4.0 cm ill-defined, firm, slightly rippled, dermal plaque on the right anterior thigh with a subtle overlying mottled hypopigmentation although without hypertrichosis.* ***B)*** *2.5×2 cm ill-defined papules on the right posterior calf.*

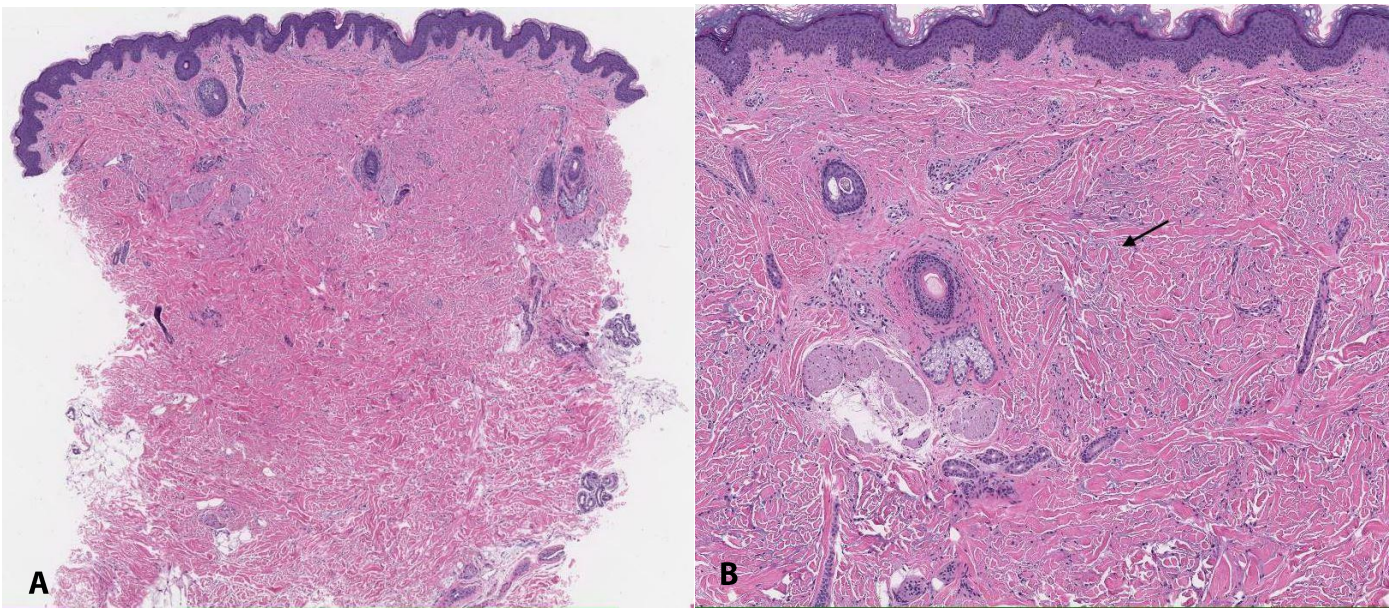

Figure 2. *Both biopsies show similar findings of significant increase in interstitial mucin primarily within the reticular and middle portion of the dermis with some extension to the dermal-subcuticular interface (**A**, 40×; **B**, 200×).*

Case Discussion

CMI was first described in 1980 [3]. A subtype of localized papular mucinosis, CMI is considered to be a very rare disorder of mucin deposition, with at least 13 reported cases in the literature [2-14]. A summary of those cases is provided in **Table 1**.

Clinically, CMI manifests as asymptomatic (nonpainful, nontender, and nonpruritic) and variably sized, colored, and distributed dermal papules and/or plaques. The lesions can be scattered, grouped, or coalesced. Widths have ranged from a 0.5mm papule [7] to papules coalescing into a 20cm plaque [10]. Colors have been mostly described as white, fair, or skin-like. Common locations are the trunk/torso followed by proximal limbs (upper arms and thighs), as in our patient; less commonly reported areas are the neck, hands, fingers, and toes. The plaques may become larger and more numerous, or may self-resolve [2, 5, 6, 11]. Our patient's lesions became more noticeable with sun exposure, in contrast to the case reported by Velho et al. in 1998, whereby there was improvement with sun exposure [12]. CMI is generally not associated with rheumatologic or thyroid disease or monoclonal gammopathy [1, 2, 15]. A pre-biopsy clinical differential diagnosis could include connective tissue nevus, granuloma annulare, myofibroma, lipofibroma, and lymphangioma.

Histologically, CMI presents as abnormal interstitial mucin deposition confined to the dermis without fibroblastic proliferation. The main consideration in the differential diagnosis for this cutaneous mucinosis is lichen myxedematosus (LM), which consists of typical scleromyxedema (generalized LM), localized papular LM, self-healing juvenile cutaneous mucinosis (SHJCM), and atypical presentations [1, 15]. In scleromyxedema, there is a greater extent of collagen bundle alteration, fibrocytic and fibroblastic proliferation, and fibrohistiocytic sclerosis. It is associated with

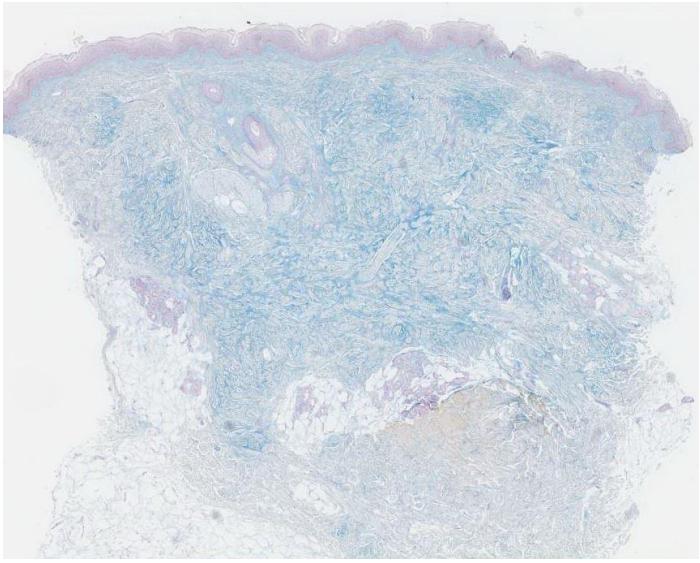

Figure 3. *Alcian blue preparation highlights dermal mucin (40×).*

Table 1. *Summary of cases of cutaneous mucinosis of infancy.*

Reported Cases	Age at diagnosis	Age 1st noticed	Sex	Clinical presentation	Follow up	PMH	FH	Rx
Lum [3]	16 months	4 months	F	Firm white symmetrical papules, <2 mm, elbows, upper arm and dorsal hands	Increased in number over 12 months	Miliaria, thrush, diaper rash, viral infections	None	NA
McGrae et al. [7]	26 months	Birth	F	White round papules, 0.5-1 mm, some isolated and other linear/contiguous, dorsal surface of fingers	Increased in number over 9 months	Congenital extra digits of each 5th finger	DLE in maternal great grandmother	2 months of topical steroid and 2 months of topical tretinoin with no improvement
Carapeto et al. [8]	2 years	Birth	NA	Tan and slightly erythematous Papules, grouped but not confluent, asymptomatic, lumbar area	Increased in number over 2 years	None	None	NA
Redondo Bellón [13]	16 years	Birth	NA	Irregular, brown plaque, 6-7 cm consisting of 2-3 mm firm individual and coalescent papules, interscapular region	Increase in size without change in appearance over 3 years	None	None	None
Stokes et al. [9]	16 months		F	NA	NA	Developmental delay, congenital cataracts, bilateral inguinal hernias, accessory tragus	NA	NA
Calza et al. [10]	6 years	3 months	M	Flesh-colored, smooth, papules, 10-20 cm, asymptomatic, lower back, lateral thorax and hips, abdomen, and posterior thighs	Increase in size and number	Viral infections	Father with similar lesions on the legs in childhood that disappeared by age 20 years	None
González-Enseñat et al. [11]	2 years	3 months	M	Slightly erythematous papules and subcutaneous nodules, asymptomatic, trunk and neck	Resolved by 15 years	None	Similar lesion in brother	NA

Table 1, continued. *Summary of cases of cutaneous mucinosis of infancy.*

González-Enseñat et al. [11]	18 months	3 months	M	Slightly erythematous papules and subcutaneous nodules, asymptomatic, trunk	Increasing in number and size over 1 year	None	Similar lesion in brother	NA
Velho et al. [12]	15 years	Birth	F	Pink-brown papules w/ slightly wrinkled surface, 1-2 mm Symmetrical, isolated or linear Trunk, arms and thighs	Increase in size slowly over years, improvement with sun exposure	None	None	NA
Podda et al. [5]	9 years	9 months	F	Tan slightly hyperpigmented papules, 0.2-1 cm, chest, upper limbs, scalp, back and a 2-3 cm groin nodule	Some increase in size and number, some remained unchanged, some resolved	None	Father with similar lesions as kid, which disappeared during adolescence	NA
Chen et al. [2]	7 months	Birth	M	Soft papule, <5 mm, fingers, and toe	Resolved after 5 years of follow up	None	None	None
Mir-Bonafe et al. [6]	4 months	Birth	M	Yellow and erythematous papules, asymptomatic, 2-4 mm, trunk, neck, back, and proximal extremities Mostly dispersed, but also coalesced into 3-4 cm plaques on thigh, back, and thorax	Increase in size over 2 years, several resolved, and a few new scattered developed	None	None	None
Reddy et al. [4]	4 years	2 years	F	Flesh-colored, cobblestoned plaque, 7.5 x 6.5 cm, asymptomatic, lateral left thigh	Increase in size over 2 years	None	None	None

PMH: Past Medical History, FH: Family History, Rx: Treatment, F: Female, NA: Not Available, M: Male.

monoclonal gammopathy. In SHJCM, there is reactive fibroblastic proliferation and mucinosis involving both the dermis and subcutis. It mostly presents in children older than 7 years of age as skin lesions with characteristic facial and joint distribution [16, 17]. It is usually associated with arthralgias, myositis, and lymphocytosis. There is insufficient data to establish whether or not CMI is a disease independent of papular LM [1, 5, 6, 15].

Mucin is produced and secreted by fibroblasts. Its functions include regulating fluid balance and being a component of the extracellular matrix. The aforementioned diseases have, for unknown reasons, abnormal mucin deposition that presents as cutaneous lesions. Abnormal extracellular deposition of mucin or mucin variants can also be related to a secondary disease process, such as exophthalmos and pretibial myxedema in Graves

disease. Intriguingly, our patient's family history included Graves disease and photosensitivity, although she appeared euthyroid with normal thyroid function test results. Most reported CMI cases have been idiopathic, except in one patient whose maternal great grandmother had chronic discoid lupus erythematosus [7], two patients whose fathers had CMI-like lesions that disappeared by age 20 [5, 10], and 2 brothers who may have both had CMI [11]. Proposed pathogeneses of cutaneous mucinoses include fibroblast overstimulation, hypersensitivity reactions, viral infections, and neoplastic changes [18, 19]. There has been insufficient data to propose a pathophysiologic model for CMI.

Conclusion

We report a rare case of CMI in an otherwise healthy 5-year-old patient. Our patient is unique as she is the first CMI patient with a family history of Graves disease, which is associated with secondary extracellular deposition of mucin, although our patient appeared euthyroid with normal thyroid function test results; the clinical significance of the family history remains unclear. The clinical presentation, histologic characteristics, proposed pathogeneses, differential diagnosis, and existing literature on this rare entity were reviewed.

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