CASE REPORT

# Papular Granuloma Annulare: Rare Variant of a Common Disease Entity

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**Abstract:** Granuloma annulare is a rare cutaneous granulomatous disease of uncertain etiology, often characterized by ringed or annular papules or plaques. Here, we present a case of a 9-year-old Filipino girl with asymptomatic bilateral skin-colored papules on her elbows. The patient's mother had attempted self-medication with cashew-based cream, which yielded no improvement. Physical examination revealed well-defined papules, and laboratory tests showed neutrophilia, lymphopenia, and normal metabolic profile. A skin biopsy confirmed the diagnosis of papular granuloma annulare, characterized by granuloma formation with increased mucin deposition. Treatment with topical clobetasol propionate resulted in remarkable improvement. However, the patient was subsequently lost to follow-up. This case underscores the atypical presentation of granuloma annulare in a pediatric Asian patient and highlights the importance of considering this diagnosis in unusual cases.

Keywords: Granuloma annulare, Papular variant, Case report, Dermatopathology

## Introduction

The epidemiologic data available for granuloma annulare is sparse and limited, it has been said that the prevalence is between 0.1 to 0.4%. Granuloma annulare is described as a cutaneous granulomatous disease with an unknown etiology. It has been proposed that association was seen in infection, metabolic diseases, and trauma [1]. Granuloma annulare is usually benign and thought of as self-limited when not associated with serious conditions such as malignancy or HIV [2]. Granuloma annulare as the name suggests commonly presents clinically as a ringed or annular papule or plaque with a granulomatous inflammation seen in histology. Over the decades, there have been atypical and rare variants described in the literature but the lack of large-scale case studies and confusing classification has made it difficult for proper classification [3].

## Case Presentation

A 9-year-old female Filipino child presented to the clinic with a history of 1 year of asymptomatic bilateral skin-colored papules on the elbows. The patient's mother claims she was not seen by any other physician and has self-medicated with cashew-based cream, for which the said lesions were unresponsive to. The patient was otherwise normal and healthy with unremarkable past medical history. Physical examination revealed multiple well -defined skin-colored papules and plaques measuring 1 to 2 cm localized on bilateral

elbows **(Figure 1A, Figure 1B)**. The rest of the physical examinations were unremarkable with no affectation of the hair, nail, and mucosa. A complete blood count revealed neutrophilia (56.25%), lymphopenia (30.59%), and eosinophilia (3.42%). The metabolic panel was unremarkable except for a slightly elevated HbA1C (5.8%), patient was subsequently referred to pediatric services for further evaluation and management. A slit skin smear with an acid-fast smear was done with one of the lesions which revealed negative results. A 4 mm skin punch biopsy with a lesion on the right elbow stained with Hematoxylin and Eosin (H&E) was done and revealed a normal epidermis with a granuloma formation **(Figure 2A)**. On low power magnification (10x) of the H&E slide showed infiltrates surrounding degenerated collagen **(Figure 2B)** on high magnification (40x) confirms palisading lymphohistiocytic infiltrates **(Figure 2C)**. Special staining with alcian blue showed positive highlighting in the granuloma indicating increased mucin deposition **(Figure 2D)**.

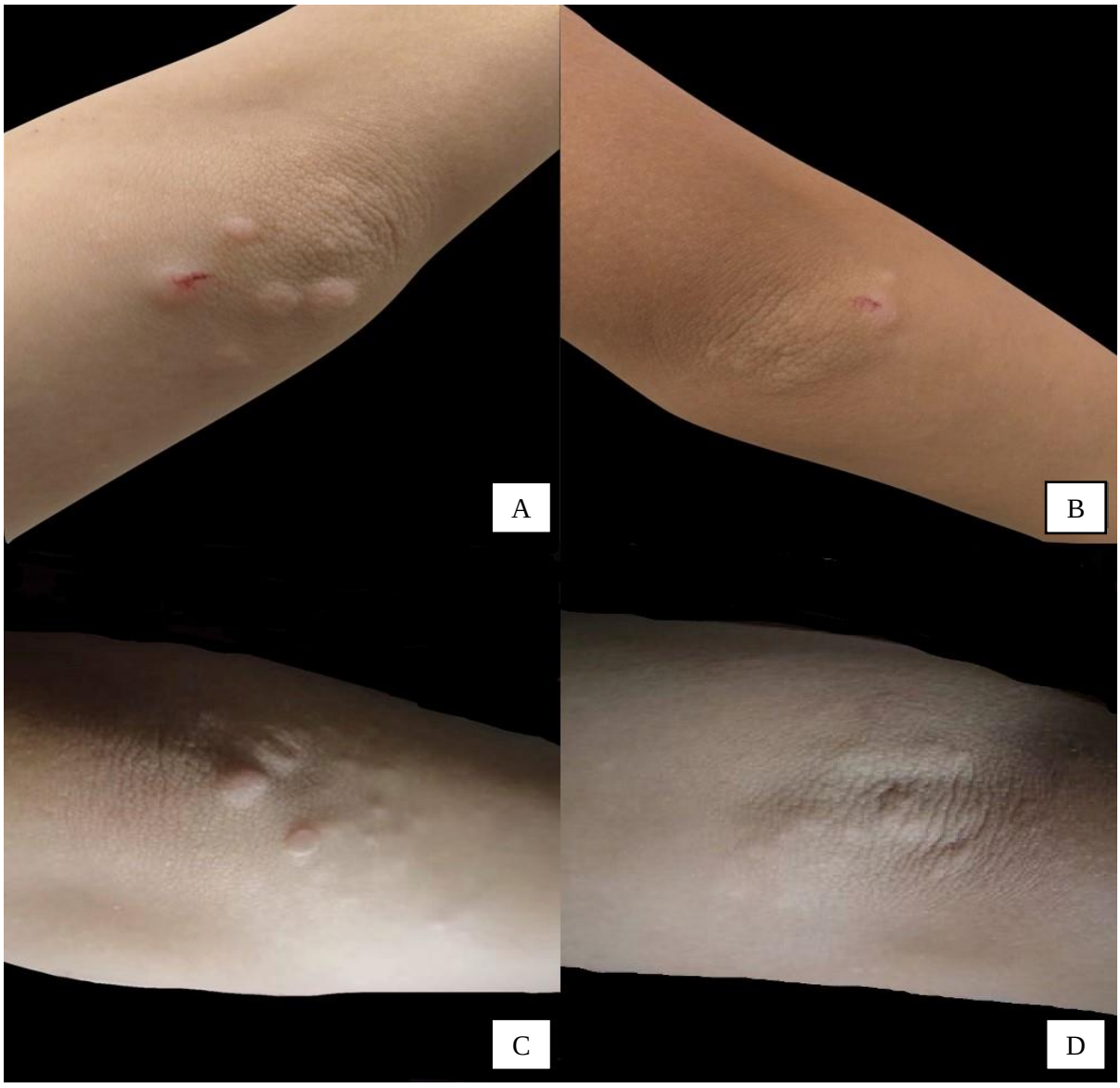


**Figure 1 A**; Left elbow **B**; Right elbow (Both showing multiple asymptomatic well-defined skin-colored papules and plaques measuring 1-2 cm). **C**; Left elbow **D**; Right elbow (Both showed improvement after 2 weeks of clobetasol propionate 0.05% ointment application). *Linear excoriation due to slit skin smear procedure done on the patient.

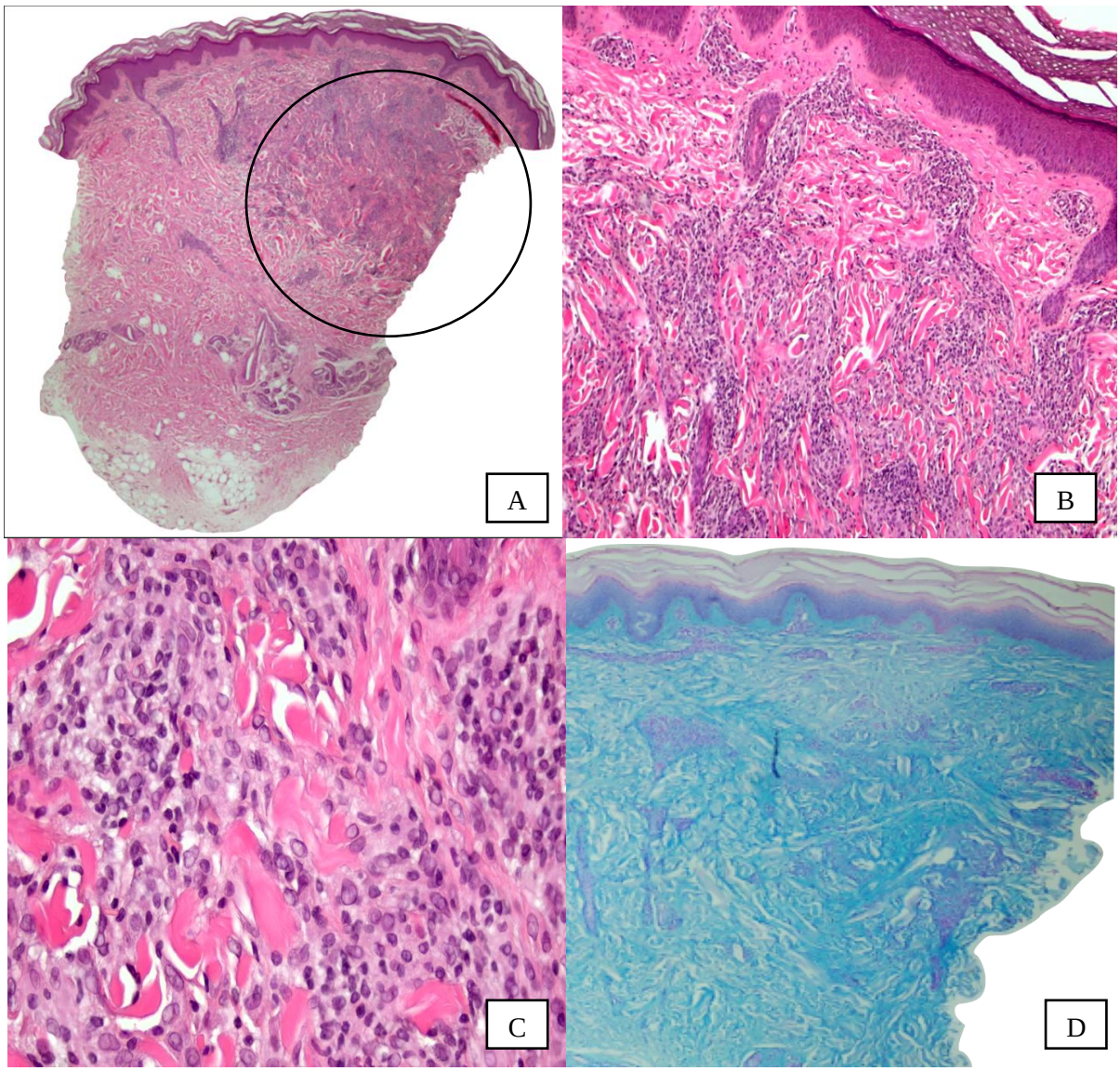


**Figure 2 A**; Scanning view(4x) of lesion stained with H&E showing granuloma formation highlighted by a black circle. **B**; Low power magnification (10x) of the H&E slide showing infiltrates surrounded by degenerated collagen. **C**; High power magnification of the H&E slide confirming predominance of lymphohistiocytic infiltrates. **D**; Scanning view(4x) of the same slide stained with alcian blue indicative of increased mucin content.

**Management and Outcome**

The patient was subsequently diagnosed as papular granuloma annulare and was started on topical clobetasol propionate 0.05% ointment for 2 weeks since the presentation of the lesions was localized. Upon follow-up 2 weeks later, the patient noted almost complete resolution of her cutaneous symptoms with only hypertrophic scarring of the previous biopsy site with no dyspigmentation **(Figure 1C, Figure 1D)**. The patient was advised to shift to tacrolimus 0.1% ointment for 2 more weeks but was subsequently lost to follow-up.

**Discussion**

Granuloma annulare is a relatively common disorder that presents more in white females in the third to fifth decade of life, although it could be noted that it is a rare finding in Black, Hispanic, and Asian individuals [4] which is an exception as our patient is an Asian child. Granuloma annulare has a prototypic classic variant of ringed or

arcuate erythematous plaques clinically. The presentation in this case is papules which have been previously reported by Smith [5] but has not been truly validated in large case series if truly a different distinct morphology of the disease This presentation appears more commonly as localized forms but can also present as generalized or disseminated if presenting with 10 or more widespread annular plaques. Based on morphology, there have been different reports of subcutaneous nodules, patches, umbilicated papules, and even pustules. Histologically, granuloma annulare presents with focal necrosis surrounded by a palisade of histiocytes. The hallmark of granuloma annulare is the finding of increased mucin deposition. Additional findings of multinucleated giant cells, eosinophils, lymphocytes, and neutrophils all have been reported. The important triad of degraded collagen, histiocytic infiltrate, and the presence of mucin have been indicative findings in all granuloma annulare subtypes [6].

There are a few differential diagnoses that should be considered in lesions presenting as asymptomatic skin-colored papules on the elbows. We list down some of which we considered for this case:

a) Papular sarcoidosis: Papular sarcoidosis is an idiopathic multisystem granulomatous illness, sarcoidosis typically affects the skin, lymph nodes, lungs, and eyes. Approximately two-thirds of patients are female, and the condition often manifests at age 40. There are different morphological presentations including: papules, micropapules, plaques, subcutaneous nodules, scar sarcoidosis, lupus pernio, erythema nodosum, ulceration [7]. Upon biopsy, histopathologic findings will include characteristic granulomatous inflammation is a well-defined chronic inflammatory process where the primary cell is an activated macrophage that resembles an epithelial cell, hence the term "epithelioid cell." A granuloma is a well-defined, well-organized region of granulomatous inflammation made up of lymphocytes, leukocytes, epithelioid cells, and occasionally plasma cells [8]. Papules tend to develop on the face (often around the eyes) or neck. These papules can be reddish brown, violet, tan, brown, or the same color as skin which makes it different from our patient's case.

b) Papular acrodermatitis of childhood: A benign rash known as papular acrodermatitis of childhood (Gianotti-Crosti syndrome) can develop in children as a result of certain viral infections and vaccines. Childhood papular acrodermatitis presents as an acral papular rash with accompanying systemic symptoms. Acute eruptions of monomorphic skin-colored to pink-red papules on the cheeks, buttocks, and extensor surfaces of the extremities are the hallmark lesions, which makes it different from our patient's case. Papular acrodermatitis of childhood has a non-specific histology. Para-keratosis and localized epidermal spongiosis are possible findings. In the papillary dermis, there might also be a perivascular, lymphocytic infiltration [9].

c) Tuberous xanthomas: Are benign plaques, papules, or nodules that form in the subcutaneous and cutis and are defined by a build-up of lipid-laden macrophages. Tuberous xanthomas typically measure no more than 2 cm and are observed in a number of lipidoses. Typically, they are suggestive of a disruption in lipoprotein metabolism, specifically familial hyper-cholesterolemia. Histopathological analysis typically reveals areas of fibrosis and cholesterol clefts, together with clusters of foam cells and lipid-laden macrophages [10].

d) Histoid leprosy: A rare kind of multibacillary leprosy known as histoid leprosy is characterized by the development of papules, plaques, or nodules that have an erythematous, skin-colored, or keloid-like appearance. The predominant histological characteristic is fusiform cells. Clinicians and pathologists face a diagnostic problem because it can mimic other dermatological lesions, such as dermatofibroma and neurofibroma. Histopathology is character-ized by an infiltrate that is primarily made up of fusiform histiocytes, which resemble fibroblasts and can occasionally resemble a fibrohistiocytic

tumor. It is also associated with a large number of acid-fast bacilli and a small number of foamy macrophages [11].

In literature, it has been mentioned that patients presenting with granuloma annulare have a significant increase in associated autoimmune, diabetes mellitus, hyperlipidemia, hypothyroidism, and ischemic heart disease [12]. In our patient it was noted that she is otherwise normal for her age in terms of thyroid function and lipid levels, it was noted however that there is a slight elevation of her HbA1C but with normal fasting blood sugar levels [13]. Recently, according to the study of Emre et al [14], viral infections such as Epstein-Barr virus, human immunodeficiency virus, varicella-zoster virus, and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) have been described to cause granuloma annulare as well.

Granuloma annulare is benign and often self-limited. Numerous treatment regimens have been reported in treating this disease entity, which include topical and systemic steroids, psoralen UV-A, isotretinoin, dapsone, pentoxifylline, hydroxychloroquine, cyclosporine, interferon-gamma, chlorambucil, potassium iodide, nicotinamide, niacinamide, salicylic acid, chlorpropamide, thyroxine, dipyridamole, methyl aminolevulinate photodynamic therapy, fumaric esters, etanercept, infliximab, adalimumab, and efalizumab [15]. In our patient, it was decided that it would be optimal to start on topical corticosteroid since the patient presented with a localized form of granuloma annulare for which the patient responded positively with noted improvement in terms of regression of size of previously seen lesions and was planned to shift to a topical calcineurin inhibitor, however patient was lost to follow up.

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