Actinic Granuloma with Focal Segmental Glomerulosclerosis

Ruedee Phasukthaworn  Kumutnart Chanprapaph  Vasanop Vachiramon
Division of Dermatology, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand

Key Words
Annular lesions · Granuloma · Nephropathy · Photosensitivity · Nephrotic syndrome

Abstract
Actinic granuloma is an uncommon granulomatous disease, characterized by annular erythematous plaque with central clearing predominately located on sun-damaged skin. The pathogenesis is not well understood, ultraviolet radiation is recognized as precipitating factor. We report a case of a 52-year-old woman who presented with asymptomatic annular erythematous plaques on the forehead and both cheeks persisting for 2 years. The clinical presentation and histopathologic findings support the diagnosis of actinic granuloma. During that period of time, she also developed focal segmental glomerulosclerosis. The association between actinic granuloma and focal segmental glomerulosclerosis needs to be clarified by further studies.

Case Report
A 52-year-old Thai woman presented with asymptomatic annular erythematous plaques on the forehead and both cheeks that persisted for 2 years. The lesions gradually expanded peripherally. She had no history of previous trauma or foreign material injection. She is a government officer and regularly works indoor. Her underlying diseases were hypertension and dyslipidemia. Current medications include simvastatin 10 mg/day and manidipine 20 mg/day.

Dermatologic examination showed few discrete annular erythematous plaques on her forehead and both cheeks, 1–5 cm in diameter. Some lesions showed central hypopigmentation. There were solar lentigines and telangiectasias on the malar area, nose, and forehead as
shown in fig. 1 and fig. 2. She has no lymphadenopathy or hepatosplenomegaly. Blood pressure was 150/95 mm Hg. Mild pitting edema on both shins was noted. Other physical examinations were unremarkable.

A 4-mm punch biopsy was performed on the lesion of the left cheek. The routine histopathology demonstrated nodular and interstitial inflammatory cell infiltrate of histiocytes intermingled with some lymphocytes in the dermis as shown in fig. 3. Elastic stain showed elastotic material phagocytized by multinucleated cells and marked decrease of elastic tissue in some foci of the affected dermis (fig. 4). According to the clinical and histopathological findings, the dermatologic diagnosis was actinic granuloma (AG).

Complete blood count, liver enzyme, fasting blood glucose, and glycated hemoglobin were within normal range. HIV serology, viral hepatitis profile, and antinuclear antibody were negative. Chest X-ray showed no pulmonary infiltration. Serum albumin was 35.9 g/l (35–50) and globulin was 39.5 g/l (20–39). Urinalysis showed proteinuria and serum creatinine was 1.26 mg/dl (0.55–1.02). Ultrasound of the KUB system showed bilateral parenchymal renal disease. The result of kidney biopsy was compatible with focal segmental glomerulosclerosis.

The patient’s dermatologic condition was treated with prednisolone 15 mg/day for 6 weeks with a good response. However, rapid relapse of the lesions occurred after the treatment was discontinued. Currently, she has been treated with hydroxychloroquine (200 mg/day), topical 0.1% mometasone furoate cream, broad spectrum sunscreen, and sun avoidance with partial improvement.

Discussion

AG was first described by O’Brien in 1975 [1]. It was also termed annular elastolytic giant cell granuloma, atypical necrobiosis lipoidica of the face and scalp, Miescher’s granuloma of the face, and granuloma multiforme [1–4]. The pathogenesis of AG is not well understood. Ultraviolet (UV) radiation, especially UVA, and heat are recognized as causal factors, by changing the antigenicity of elastic fibers. The immune response mediated by helper T cells to degenerated elastic tissue also implicated in the development of granuloma [5].

AG is an uncommon dermatosis. The age of onset is between 40 and 70 years with no gender predilection. The typical cutaneous lesion of AG is an initially smooth, elevated, nonscaly, erythematous papule which centrifugally extends to an annular plaque with central clearing. Atrophies and hypopigmentation are occasionally seen in the center of the lesions. They are usually distributed on chronically sun-exposed areas such as the face, neck, upper back, forearms, and dorsum of the hands. Apart from the skin, conjunctival involvement has been reported in a few cases [6, 7].

There are some reports on the association between AG and internal diseases such as hematologic and solid malignancy, monoclonal gammopathy, temporal arteritis, erythema nodosum, and X-linked dominant protoporphyria [8–11]. Diabetes mellitus has been found in about 37–40% of patient with AG, and may be caused by injury of elastic fiber from hyperglycemic state [12]. As for the renal condition, focal segmental glomerulosclerosis has been described in association with various granulomatous diseases (e.g., sarcoidosis, Wegener’s granulomatosis, Churg-Strauss syndrome, and Kimura’s disease) [13–16]. However, the association of AG and focal segmental glomerulosclerosis has never been reported.

The differential diagnoses of AG are broad. These include granuloma annulare, erythema annulare centrifugum, annular lichen planus, secondary syphilis, necrobiosis lipoidica, tinea corporis, and tuberculoid leprosy. Therefore, histopathology is essential for the diagnosis of
AG. The best method to obtain a precise histopathology is an elliptical biopsy across the annular rim and stained with elastic van Gieson to demonstrate the three zones of elastic tissue change. In the first zone, solar elastosis is identified in the surrounding unaffected skin. In the second zone, a granulomatous reaction consisting of histiocytes and foreign-body type multinucleated cells is seen, with engulfment of elastotic fibers, representing the annular rim. In the third zone, an absence of elastic tissue in the superficial dermis is found in the center of the plaque [17]. Due to aesthetic concern in our case, we decided to perform punch biopsy on her left cheek. The histopathology also showed tuberculoid granuloma with elastophagocytosis, which is compatible with AG.

The treatment of AG is often unsuccessful. Topical corticosteroids, intralesional corticosteroids, systemic calcineurin inhibitors, phototherapy and photochemotherapy (narrowband UVB, PUVA, Re-PUVA) have been used with some benefit [18–20]. Cyclosporine A, dapsone, pentoxifylline, isotretinoin, and acitretin have been reported to be effective in some cases [21–23]. There are a few case reports with positive results from antimalarial therapy (chloroquine and hydroxychloroquine) [24]. To prevent the development of new lesions, patients should be instructed to avoid sun exposure and regularly use sunscreen.

Our patient had good response to a short course of low-dose prednisolone. However, rapid relapse occurred after the treatment was discontinued. Currently, she has been treated with hydroxychloroquine (200 mg/day), topical 0.1% mometasone furoate cream, broad spectrum sunscreen, and sun avoidance with partial improvement.

To the best of our knowledge, AG associated with focal segmental glomerulosclerosis has never been previously reported. The correlation between AG and focal segmental glomerulosclerosis is still unidentified, further investigation is needed to establish the relationship between these two conditions.

**Statement of Ethics**

We state that our patient gave informed consent. The research complies with all ethical guidelines for human studies.

**Disclosure Statement**

The authors declare no conflicts of interest. There was no funding for this work.

**References**

Fig. 2. Annular erythematous plaque with central hypopigmentation on the left cheek.

Fig. 3. Nodular and interstitial inflammatory cell infiltrate of histiocytes intermingled with some lymphocytes in the dermis. Hematoxylin-eosin, original magnification ×100.
Fig. 4. Elastic stain showing elastophagocytosis with marked decrease to absence of elastic tissue (a) and normal elastic tissue (b). Verhoeff-Van Gieson, original magnification ×100.