Case 16
Generalized red dermal plaques in a DM patient

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Patient: A 63 year-old woman from Bangkok

Chief complaint:
Erythematous papules on trunk and extremities for 2 months

Present illness:
She presented with generalized erythematous papules on torso, back and all extremities without itching for 2 months. She had no fever and weight loss.

Past history:
- Known case of well controlled DM type 2
- History of erythema nodosum due to pioglitazone
- History of lymphocytosis, without evidence of hematologic malignancy

Skin examination:
- Few erythematous annular plaques on neck
- Multiple crops of erythematous papules on torso, back and all extremities

Histopathology: (S13-031232, back)
- Nodular and interstitial infiltrate of histiocyte, multinucleated giant cell intermingled with perivascular infiltrate of lymphocytes
- Special stains:
  - Toludine blue staining: Negative for mucin
- Verhoeff Van Giemsa: Decrease elastic staining in area of granuloma

**Diagnosis:** Disseminated Granuloma Annulare

**Investigation:**
- Blood sugar 120 mg/dL
- Thyroid function test: Normal
- Hepatitis B and C profiles: Normal
- Anti-HIV: Negative
- Chest radiograph: Unremarkable
- Bone marrow study: No evidence of lymphoma

**Treatment:**
- Advice about the natural history and prognosis of disease
- Acitretin 10 mg daily
- 0.1% Triamcinolone acetonide in 10% urea cream apply lesion twice daily

**Discussion:**
Disseminated GA (DGA) is a variant of granuloma annulare, benign granulomatous skin disease with unknown etiology.\(^1\)\(^,\)\(^2\) DGA can be observed in 15% of GA patients, usually affects children younger than 10 year-old or middle to old-aged adults with female predominance (2.2:1).\(^3\) The clinical feature of DGA is scattered skin-colored to erythematous papules with total lesions more than 10 lesions with chronic relapsing course.\(^4\)\(^,\)\(^5\)

The dermoscopic findings are (1) peripheral, structureless orange-reddish borders, without evident vessels (2) reddish-whitish homogeneous pattern, without evident vessels.\(^6\)

Many drugs were reported causing DGA, including intranasal calcitonin, amlodipine, allopurinol, diclofenac, gold, topiramate, infliximab, adalimumab and BCG vaccine.\(^5\)

Associated systemic diseases (eg. DM, HIV, thyroid disease, RA, DLP, Hepatitis B & C, solid and hematologic malignancy) were reported, so further investigations for associated diseases (e.g. FBS, lipid profile, TFT, anti–HIV, CXR and age-appropriated cancer screening) should be performed in every DGA patients.\(^5\)

In DGA, histopathological findings are the same as other variants. The classical findings are dermal palisading granulomas with central degeneration of collagen, the presence of mucin and lymphohistiocytic infiltration. Mucin deposition is the key feature to distinguish GA from other non-infectious granulomatous diseases. Elastic tissue is reduced or absent within the histiocytic aggregates in approximately 20% of generalized GA.\(^7\)\(^,\)\(^8\)

Although DGA is benign and asymptomatic, patients may ask for treatment due to aesthetic concern. There is no standard therapy in DGA. However, topical corticosteroids and topical calcineurin inhibitor are beneficial options. Systemic therapies are reserved for severe cases.

Many published case reports and cohort studies showed successful treatments with various drugs including isotretinoin, dapsone, doxycycline, methotrexate, cyclosporine, antimalarial agents, nicotinamide, clofazimine, zileuton+oral vitamin E, rifampicin + Ofloxacin + Minocycline, biologic agents
(adalimumab, etanercept and infliximab) and defibrotide intramuscularly. Other options proven by retrospective studies are oral fumaric acid esters and PUVA and NUVB.\textsuperscript{1,5,9,10}

There were 2 reports of successful therapies for generalized GA using PDT with MAL and ALA, respectively.\textsuperscript{11,12} Hence, all of treatments are case reports or cohort studies, the dermatologist should consider risk of adverse effects and benefits in any treatments.

Recently, there was a report of 2 DGA patients successfully treated with topical anthralin. As a local application with few adverse effects were reported, anthralin would be an interesting option for DGA.\textsuperscript{13}

In this patient, DGA with DM was diagnosed. Even though special staining failed to demonstrated mucin deposition, clinical and other histopathological findings were compatible with DGA.

She was prescribed acitretin 10 mg daily along with 0.1% triamcinolone acetonide in 10% urea cream twice daily. Subsequently acitretin was discontinued due to marked xerostomia. However, the lesions improved with topical steroids.

References: