

Localized granuloma annulare and autoimmune thyroiditis in a Saudi patient: Report of a new case

Talal M. Tallab

Department of Medicine,
King Khalid University, P. O. Box 641, Abha, Saudi Arabia.
E-mail: tm151@hotmail.com

Summary

The association of granuloma annulare (GA) and autoimmune thyroiditis has been documented in the literature in 13 previous cases. However, the pathogenesis of GA remains obscure. Possible pathogenetic factors suggested include: humoral and delayed type hypersensitivity, vascular damage, metabolic disorder, or, primary collagen and/or elastin alteration mediated through an immunologic mechanism. We present herein the report of a 37-year old Saudi female who presented with autoimmune thyroiditis associated with GA. The patient was managed with clobetasol propionate, intra-lesional prednisolone and neomercasol. There was complete resolution of the GA lesions and the patient has remained euthyroid after a few weeks. This presentation is a further evidence that GA and autoimmune thyroiditis may be associated.

Keywords: *Granuloma annulare, Autoimmune thyroiditis.*

Résumé

L'association d'un granulome annulaire (GA) et auto-immunité de la thyroïdite a été documenté dans la littérature au cours des 13 cas précédents. Toutefois, la pathogénèse de GA reste obscure. Des facteurs pathogéniques possibles qu'on a suggéré comprend: humoral et type d'hypersensitivité retardée, dégats vasculaire, troubles métabolique, ou bien, collagène primaire et/ou bien changement elastin provoqué par un mécanisme immunologique. Nous présentons dans ce travail, un rapport d'une femme saoudienne qui était atteinte d'une auto-immunité thyroïdite associée au GA. On a soigné le

patient avec propionate clobetasol, prednisolone intra-lesional et néomercasol. Il y avait un résolution complète des lésions GA et le patient était resté euthyroïdie après quelques semaines. A travers cette présentation on peut dire qu'il y a une association entre le GA et l'auto-immunité thyroïdite.

Introduction

Granuloma Annulare (GA) has been considered as cutaneous manifestation of the thyroid disease but the evidence remains limited^{1,2}. We described a new case of GA associated autoimmune thyroiditis. To our knowledge only 14 cases have been documented in the literature, including the case reported herein. Both generalized and localized form of GA has been described with this association.

Case report

A 37-year-old Saudi female presented 4 years ago with protrusion of the eye balls and excessive sweating. Physical examination showed exophthalmos and thyroid gland enlargement affecting mainly the right lobe. Thyroid function tests showed elevated T4 (86.8 pmol/L). Thyroid stimulating hormone (TSH) level was diminished (0.1 IU/ml). Ultrasound scan of the thyroid gland showed diffuse enlargement of the whole gland. Thyroid isotope scan revealed a homogeneous uptake. Anti-Nuclear Antibodies (ANA) and thyroid antibodies peroxidase (TPO) were positive. The patient was started on Carbimazole (Neumercasole) (10 mg/day) and Propranolol (Inderal) (40 mg/day).

The patient's thyroid functions were controlled on the above medications for 2 years at which time she complained of asymptomatic skin lesions affecting the dorsum of hands, palms and knees. The lesions consisted of non-scaly, indurated papules and annulare plaques (Figure 1). The

Table 1 Cases of granuloma annulare and autoimmune thyroiditis reported in the literature

Reference	No of patients	Sex	GA Type	Location
Gross and Shelley ¹⁰	1	F	GGA	Trunk
Willemesmn et al ¹¹	1	F	LGA	Arms, legs
		F	LGA	Elbows, hands, knees, ears
Moran and lamb ¹²	1	F	LGA	Foot
Espinel et al ¹³	1	F	LGA	Elbows, thighs
Velez et al ¹⁴	1	F	LGA	Elbows, wrists
Magro et al ⁷	1	F	LGA	Ankle
Dabski and Winkelman ⁸	3	F	LGA	Trunk
Studer et al ⁹	1	NR	NR	NR
Vazquez-Lopez ²	1	F	LGA	Elbow, foot
Kappler D et al ¹⁵	2	NR	NR	NR
Present case	1	F	LGA	Palms, foot and leg

GA = Granuloma annulare; GGA = Generalised granuloma annulare; LGA = Localised granuloma annulare; NR = Not reported

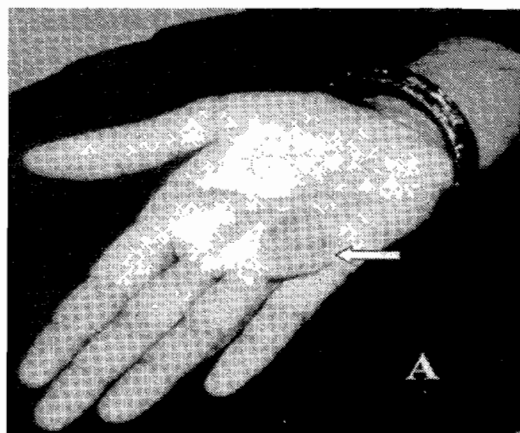


Fig. 1a Granuloma annulare lesions over Palm showing classical non-scaly annulare plaques

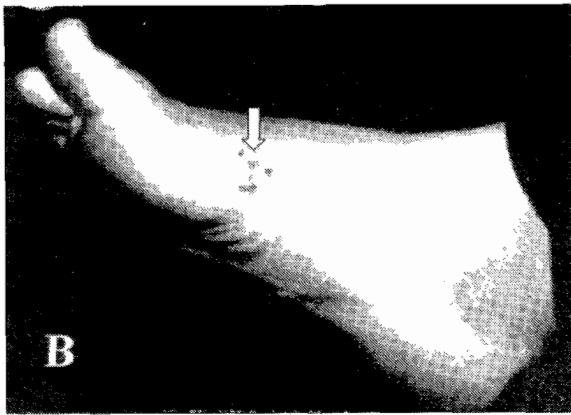


Fig. 1b Granuloma annulare lesions over foot showing classical non-scaly annulare plaques.



Fig. 1c Granuloma annulare lesions over lower Leg showing classical non-scaly annulare plaques.

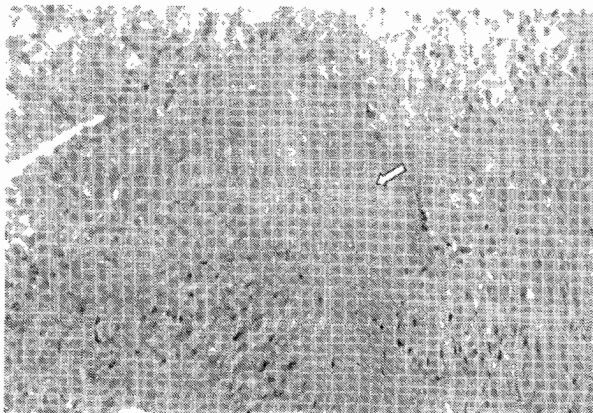


Fig. 2 Photomicrograph of skin biopsy showing an area of necrobiosis (arrow) surrounded by palisading of histiocytes and lymphocytes "arrow".

clinical diagnosis of granuloma annulare was made and subsequent skin biopsy done revealed a dermal infiltrate of histiocytes with interstitial pattern. The lesion contained a few foci of palisading granuloma and sparse perivascular lymphocytic infiltrates (Figure 2).

The patient was treated with clobetasol propionate (0.1% topically) and intralesional methyl prednisolone (10 mg/ml) with complete resolution after a few weeks. The patient continued to be euthyroid on neomercasol and the last T4 and TSH levels were 25pmol/L and 3.1IU/ml respectively.

Discussion

The cause of GA remains obscure. A pathogenetic role has been suggested for the following⁴⁻⁶: (a) hormonal and delayed-type hypersensitivity, (b) vascular damage, (c) metabolic disorder or (d) primary collagen and/or elastin alteration mediated through an immunologic mechanism. The association of GA with thyroid disease has been described in the literature but remains to be clarified¹⁻³. Several studies found 6% to 13% of patients with GA had associated thyroid disease but failed to find a definitive correlation⁷⁻⁹. The association of granuloma annulare with autoimmune thyroiditis had been documented in 13 previous case reports⁷⁻¹⁵ (Table1). The definition of generalized GA is the occurrence of more than 10 lesions on the trunk alone, or the trunk and limbs, while the definition of localized GA is the occurrence of a single lesion or 2 more lesions localized in one or more regions but absent on the trunk. Of the 13 cases documented in the literature, the GA was of the localized type in 11 cases and unspecified in two cases.⁷⁻¹⁵ In the present case, the GA was of the localized type. GA has also been reported to be associated with diabetes mellitus and morphea but this association still remains controversial¹⁶⁻¹⁸. The association of GA with autoimmune thyroiditis might suggest an autoimmune mechanism⁽²⁾. There is no evidence of cross-reaction between thyroid antibodies and dermal antigens⁽²⁾. A cell-mediated apoptosis has also been implicated to be a strong pathogenic factor in both diseases¹⁹.

References

1. Heymann WR. Cutaneous manifestation of thyroid disease. *J Am Acad Dermatol* 1992; 26:885-902.
2. Vazquez-Lopez F, Pereiro Jr, Manjon Haces J.A. Localized Granuloma Annulare and Autoimmune Thyroiditis in Adult Women: A case-control study. *J Am Acad Dermatol* 2003; 48:517-520.
3. Julia Ai, Janie M, Leonhardt. Autoimmune Thyroid Diseases: Etiology, pathogenesis, and dermatologic manifestations. *J Am Acad Dermatol* 2003; 48:641-659.
4. Remero LS, Kantor GR. Eosinophils are not a clue to the pathogenesis of granuloma annulare. *Am J Dermatopathol* 1998; 20:29-34.
5. Smith MD, Downie JB, DiCostanzo D. Granuloma Annulare. *Int J Dermatol* 1997; 36:326-33.
6. Hanna WM, Moreno-Merlo F, Andrighetti L. Granuloma Annulare: An elastic tissue disease? Case report and literature review. *Ultrastruc Pathol* 1992; 2333-8.
7. Margo CM, Croswsen AN, Rregauer S. Granuloma Annulare and Necrobiosis Lipoidica Tissue reaction as manifestation of systemic of disease. *Hum Pathol* 1996; 27:50-6.
8. Dabasky K, Winkelman RK. Generalized Granuloma Annulare: Clinical and laboratory finding in 100 patients. *J Am Acad Dermatol* 1998; 20:39-47.
9. Studer EM, Claza AM, Saurat JH. Precipitating factors and associated diseases in 84 patients with granuloma annulare: A retrospective study. *Dermatology* 1996; 193:364-8.

10. Gross PR, Shelley WB. The association of generalized granuloma annulare with antithyroid antibodies. *Acta Derm Venereol* 197; 51:59-62.
11. Willensem MJ, deConinck AL, Jonckheer MH, Roseeuw DI. Autoimmune thyroiditis and generalized granuloma annulare: Remission of the skin lesion after thyroxine therapy. *Dermatologica* 1987; 175:238-43.
12. Moran J, Lamb J. Localized granuloma annulare and autoimmune thyroid disease, are they associated? *Can Physician* 1995; 41:2143-4.
13. Espinel Vazquez ML, Esteban Chicharro A. Granuloma annulare generalizado y tiroiditis autoimmune. *Acta Dermo-Sif* 1993; 84:105-6.
14. Velez Garcia-Nieto A, de la Mata Garcia M, Valverde Blanco F, Fernandez Roldan JC, Bances Gracia-Roves R. Granuloma Annulare generalizado en una paciente con enfermedad hepatica autoimmune y tiroiditis de Hashimoto. *Acta Dermatol-Sif* 1994; 85:267-9.
15. Kappeler D, Troendle A, Mueller B. Localized granuloma annulare associated with autoimmune thyroid disease in a patient with a positive family history for autoimmune polyglandular syndrome type II. *Eur J Endocrinol* 2001; 145:101-2.
16. Sgonc R, Gruschwitz MS, Dietrich H, Recheis H, Gershwin ME, Wick G. Endothelial cell apoptosis a primary pathogenetic event underlying skin lesion and human scleroderma. *J Clin Invest* 1996; 98:785-92.
17. Ben-Ametai D, Hodak E, Ladipoth M, David M. Coexisting morphea and granuloma annulare – are the condition related? *Clinical Exp Dermatol* 1992; 24:86-9.
18. Benoist C, Mathis D. Cell death mediators in autoimmune diabetes – no shortage of suspects. *Cell* 1997; 89:1-3.
19. Arscott PL, Baker JR. Apoptosis and thyroiditis. *Clin Immunol Immunopathol* 1998; 87:207-17.