CASE REPORT

Disseminated Granuloma Annulare: Case report and review of the literature.

Lucy Ortiz Andrade,* Lorena Quiroz, Annette Morán,*** Enrique Loayza******

* First year dermatology resident at Espiritu Santo University
** Dermatologist of the Dermatological Center ¨Dr. Úraga¨
*** Dermatologist of the Centro Dermatológico ¨Dr. Úraga¨
**** Dermatopathologist
***** Dermatologist, Director of the Dermatological Center "Dr. Úraga"

Corresponding author:
lucyortiz_94@hotmail.com
ORCID: https://orcid.org/0000-0002-2687-0309

Key words: granuloma annulare (GA), plaques, disseminated.

Reception date: 6/16/2023
Acceptance date: 9/25/2023

ABSTRACT

Granuloma annulare (GA) is a benign, chronic dermatosis very frequent in childhood and adulthood. It is characterized by annular bordered nodules and plaques affecting more trunk and extremities. The causes are unknown, but certain potential predisposing factors such as trauma, insect bites, vaccinations, sun exposure and certain drugs are reported to predispose to the development of the disease. In addition, GA is related to certain diseases, mainly obesity and dyslipidemias. There are 4 types of GA. A definitive treatment for GA is still unknown, since there are multiple undefined therapeutic reports due to the lack of scientific evidence. We present the case of a 55-year-old patient with papules and annular border plaques on the arm, neck and trunk, with a diagnosis of disseminated granuloma annulare.

INTRODUCTION

Granuloma annulare (GA) is a common condition, which can occur in both childhood and adulthood[1]. It is characterized by erythematous annular-rimmed papules or plaques affecting the most distal part of the extremities[1,2]. They are usually asymptomatic, but in certain cases it is accompanied by pruritus[1]. Many cases remit spontaneously in several months or years. Four types have been described[1,3]. The cause is unknown, but it has been related to potential factors and certain diseases such as diabetes mellitus and dyslipidemias[1,2]. A definitive treatment for this pathology is still unknown, since there are several therapeutic options. The following report describes a clinical case of a 55-year-old patient with a diagnosis of disseminated GA.

CLINICAL CASE

55-year-old male patient with PPP of hypertension (under treatment with Losartan 100mg) and fatty liver, allergic to Ibersartan. He consulted for clinical symptoms of 2 months of evolution characterized by multiple non-pruritic lesions on upper limbs and neck. Physical examination revealed confluent papules forming plaques with annular borders accentuated on a violaceous erythematous base on the arms, trunk and neck (Fig. 1-2). There were no lesions on the hand, feet, nails or mucous membranes. With clinical suspicion of GA vs lichen planus annulare, a biopsy of the lesion on the forearm with a pigmented center was taken and the epidermis was normal. The dermis shows perivascular and interstitial infiltrate of lymphocytes and histiocytes, with the presence of giant cells that phagocytize collagen fibers (Fig. 3). Also mucin deposits in the interstitium confirming the diagnosis of AG (Fig. 4).

DISCUSSION

Granuloma annulare (GA) is a benign, chronic dermatosis, very common in childhood and adulthood, characterized by the presence of nodules or ring-bordered plaques with

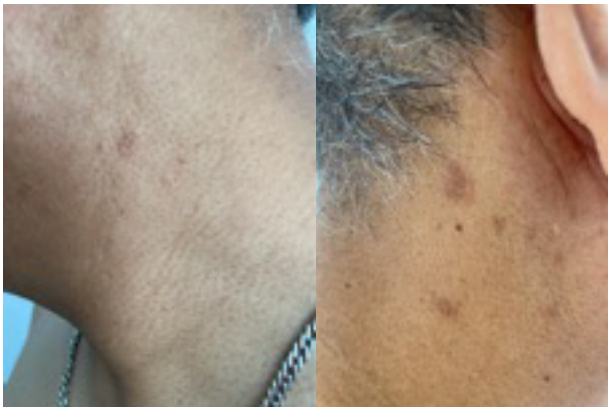

Figure 1. Erythematous papules with annular border on the neck

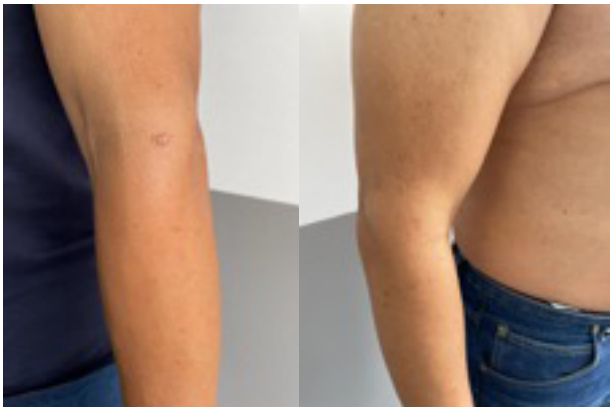

Figure 2. A. Papules converging to form a nodular lesion with central depression on the left arm. B. Papular lesions of 1 to 3 mm on the right arm.

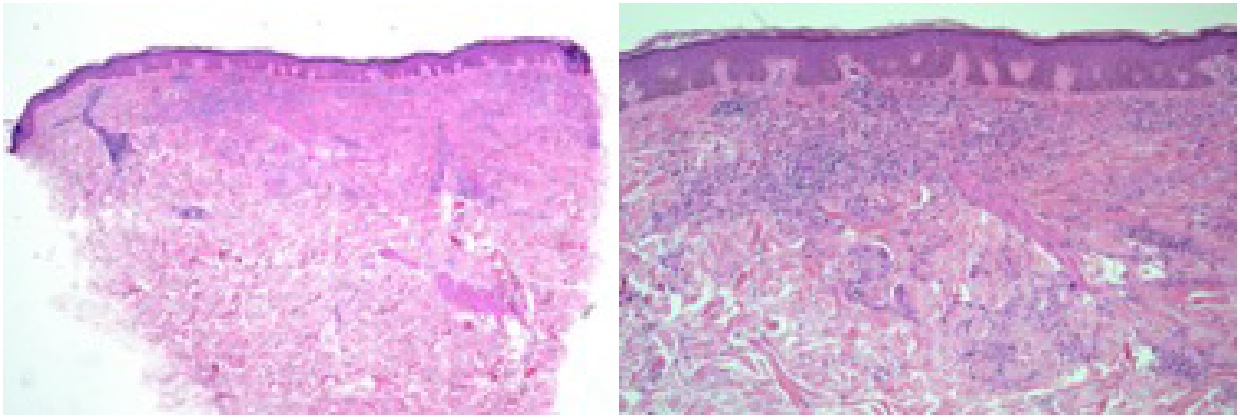

Figura 3. A. Normal appearing epidermis. B. Dermis with perivascular and interstitial infiltrate of lymphocytes and histiocytes.

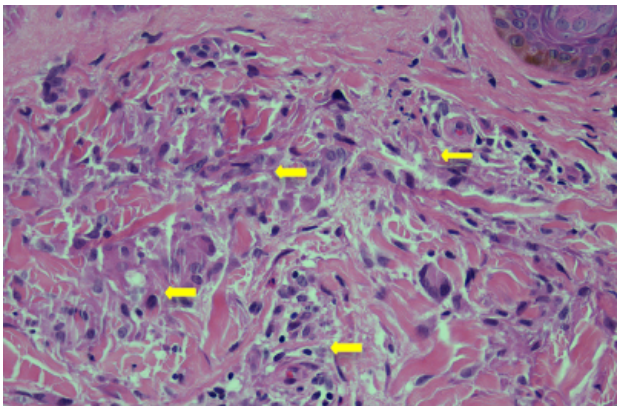

Figura 4. Mucin deposition in the interstitium (yellow arrows).

a symmetrical distribution. It was first described in 1895 by Colcott Fox as "ring-shaped eruptions on fingers" in an 11-year-old girl. The term granuloma annulare was introduced later in 1902 by Radcliffe and Crocker.[4,5,6] Its prevalence is unknown, but it is estimated to affect less than 1% of the population and among GA cases, it occurs more in women than in men in a 2.5:1 ratio.[1]

The causes of this disease are still unknown, but certain potential factors such as trauma, insect bites, vaccinations, sun exposure and certain drugs (allopurinol, diclofenac, amlodipine) have been reported.[1,2,6] Many studies indicate that GA is associated with certain diseases such as diabetes mellitus, hyperlipidemia, autoimmune thyroiditis, rheumatoid arthritis, lymphoproliferative tumors and celiac disease. It may also be associated with certain viruses such as human papilloma virus (HPV) and Epstein Barr virus (EBV).[4,6,7]

It is also unclear whether genetic factors influence the susceptibility to the pathology. It is thought that GA represents a late hypersensitivity reaction involving inflammatory cells composed of Th1 lymphocytes and macrophages.[8,7,9]

Four types of GA have been described: local, disseminated subcutaneous and perforated.[1,2] The most

common form, localized GA, classically presents as an asymptomatic skin-colored or erythematous, annular or arciform plaque with a firm rim and central clearing.[1] Perforating GA is a variety in which damaged collagen from the dermis is extruded to the skin surface. It is seen more in children and is characterized by yellowish umbilicated papules discharging a clear or white fluid.[1] Subcutaneous GA presents as painless, single or multiple, deep dermal or subcutaneous nodules on the scalp or extremities.[1] Disseminated AG is defined as a generalized disease with the presence of more than 10 lesions composed of skin-colored or erythematous papules and plaques that vary from millimeters to a few centimeters in diameter.[4,5] The trunk and extremities are prominent sites of involvement in disseminated AG, while the head, neck, palms, soles and mucous membranes are intact. It may be asymptomatic or accompanied by pruritus.[1] Characteristic histopathologic findings are lymphohistocytic infiltrate, collagen degeneration, and mucin deposits. These findings often present in an interstitial or palisaded pattern.[1]

A definitive treatment for GA is still unknown, as there are multiple undefined therapeutic reports due to lack of scientific evidence. Topical high-potency corticosteroids or intralesional triamcinolone are the most commonly used drugs to treat GA lesions.[4,3] Other treatments also include calcineurin inhibitors, cryosurgery, laser, phototherapy, isotetrinoin, dapsone, hydroxychloroquine, cyclosporines, etarnecept, infliximab or adalimumab.[7,8,2,10]

In the multiple clinical case studies that have been described on therapeutics, they indicate high potency topical corticosteroids (mometasone furoate, clobetazol propionate) as the first line of treatment, followed by UVAI, potassium iodide, PUVA, UVB, intralesional triamcinolone, isotretinoin and plaquenil.[7] In addition, the use of imiquimod 5% cream once daily has reported good therapeutic results.[11] Another alternative is the use of topical dapsone (for its antimicrobial and anti-inflammatory activity) as a safe therapeutic measure, without major adverse effects and accessible, although more studies are needed to evaluate its therapeutic efficacy.[12] Monoclonal antibodies such as adalimumab and dupilumab, which are used in refractory cases, improve symptomatology and induce remission of lesions.[10,13] Also reports on the use of UVB as part of the treatment of disseminated GA, tend to a mild-moderate improvement in lesions.[8]

CONCLUSION

AG is a benign inflammatory disease of unknown origin that remains difficult to treat. Depending on the type of variant, the clinical course and prognosis can vary widely. There are case reports, retrospective and observational studies that provide information to understand more about the pathogenesis and therapeutics of the disease, however, the information is limited. Hopefully, over the years, future studies or therapies will be established to be able to define a definitive treatment for this pathology. In our patient a high potency corticosteroid (mometasone) was used for 7 days. A control was performed after 3 weeks; the use of tacrolimus and topical clobetasol propionate combined with phototherapy sessions was indicated, which have not been performed since the patient discontinued treatment.

REFERENCES

1. Robert T. Brodell, Erick Stratman, Abena O Ofori. Granuloma annulare -UpToDate.pdf [Internet]. UpToDate; 2020. Available from: https://www.uptodate.com/contents/granuloma-annulare-epidemiology-clinical-manifestations-and-diagnosis
2. Kuen Bernardita, Ruiz Diaz Alejandra, Diaz Ysabel M, Lozinsky Liliana del Valle, M. Herrero. Disseminated granuloma annulare (interstitial pattern) in a pediatric patient.pdf. Educandonos. 2019;9(2):17-20.
3. Francisco J. Navarro Triviño, Angela Ayen Rodriguez, Antonio Jose Martin Perez, Ricardo Ruiz Villaverde. Generalized granuloma annulare generalized-paraneoplastic or not.pdf. Skin Form Contin En Dermatol. Mar 2021;36(3):208-10.
4. Jenny Wang, Amor Khachemoune. Granuloma Annulare A Focused Review of Therapeutic Options. pdf. Am J Clin Dermatol. 2018;2018:333-44.
5. E. M. Giménez, B. R. V Gómez, S Molina, V Audi. Disseminated granuloma annulare- apropos of a case.pdf. Argentine journal of dermatology. 2020;101(4):1-10.

6. Dr. Mariela Alonso, Dr. Juliana Martínez del Sel, Dr. Miguel Ángel J. Allevato. Generalized granuloma annulare .pdf. DERMATOLOGIC THERAPEUTIC UPDATES CONTINUING EDUCATION. 2019;42:70-9.
7. Thierry M. Nordmann, Joo-Ri Kim, Reinhard Dummer, Florian Anzengruber. A Monocentric, Retrospective Analysis of 61 Patients with Generalized Granuloma Annulare. Dermatology. May 13, 2020;6.
8. Andrea Dawson, Steven J. Glassman. Generalized Granuloma Annulare Responsive to Narrowband UVB.pdf. june 2019;103(6):2.
9. Myrna del Carmen Rodríguez Acar, Maribet González González, Alfonsina María Decamps Solano, Angélica Adriana Vidal Flores. Diagnostic cases. Annular plaques on trunk and extremities. Revista del Centro Dermatologico Pascua. April 2018;27(1):5.
10. Xiating Song, Zirui Chen, Zuotao Zhao, Aiping Wang. Treatment of generalized granuloma annulare with dupilumab.pdf. Jorunal Dermatol Treat. on Mar 13, 2013;34(1):3.
11. Marcela Nowak, Wioletta Barańska-Rybak, Adrianna Opalska-Tuszyńska. Successful treatment of disseminated granuloma annulare in a 10-year-old patient with 5% imiquimod cream .pdf. Dermatology Review. June 2020;107:4.
12. Gabriela Tapia Tuleda, Carlos Rojas Herrera. Generalized granuloma annulare treated with topical dapsone- An effective, accessible and safe therapeutic alternative.pdf. Skin Continuing education in dermatology. 2021;36(2):130-2.
13. Fatima Moreno-Suarez, Pedro Aceituno-Madera, Carmen Salazar-Nievas, Pablo Bautista- Martinez. Adalimumab-a-therapeutic-option-in-refractory-generalized-granul-2017.pdf. Journal of the American Academy of Dermatology. june 2017;76(6):1.