

## Perforating Granuloma Annulare and HIV

Sir,

Perforating granuloma annulare (PGA) is a relatively rare variety of granuloma annulare (GA) (1). PGA has been reported infrequently in patients with human immunodeficiency virus (HIV) infection (2).

A 37-year-old HIV-positive woman reported a 7-month history of pruritic cutaneous lesions on her legs and arms. Her medical history disclosed recurrent herpes zoster, HIV retinopathy, visceral leishmaniasis controlled with antimonials, *Pneumocystis carinii* pneumonia and sulphona-related hepatitis and hemolytic anemia. No association with diabetes was found. Physical examination revealed 8 raised erythematous patches, 1–3 cm in diameter, with a central ulceration covered by a black crust affecting arms and legs. Complete blood cell count values revealed  $3.1 \times 10^9/\text{mm}^3$  leukocytes and 120,000 thrombocytes. T-lymphocyte subsets revealed 220 CD4 lymphocytes/ $\text{mm}^3$ . Biopsy specimens of two cutaneous lesions both showed a hyperkeratotic crust overlying an epidermal perforation containing extruded necrobiotic collagen. This was contiguous with a large necrobiotic focus that filled the corresponding papillary dermis and extended to the midreticular dermis, all surrounded by a palisade of histiocytes and lymphocytes. Polaroscopic examination did not reveal doubly refractile birefringent material. Special stains for fungal and acid-fast organisms were negative. Immunohistologic markers revealed that the dermal inflammatory infiltrate consisted almost entirely of CD8-lymphocytes. The histopathologic diagnosis was PGA. No response was observed after a 6-week topical steroid regimen. At this time the patient started treatment with didanosine (ddI) 200 mg bid. Four weeks later, concomitant with the improvement of immunologic parameters (290 CD4 lymphocytes/ $\text{mm}^3$ ), the skin lesions began to disappear and resolved completely in 3 months.

GA is a lymphocytic process of unknown cause, characterized by necrobiotic dermal papules. There are several clinical variants, including disseminated, subcutaneous, erythematous and perforating types (1). PGA was first described by Owens & Freeman in 1971 (3). Shimizu divided PGA into two types (4). One type is characterized by multiple umbilicated papular lesions, 7–8 mm in diameter (P-type). The other type appears less frequently, consisting in umbilicated ulcerations, 1–4 cm in diameter, covered by crusts (U-type). There is some evidence suggesting a delayed hypersensitivity reaction and a vascular injury in the pathogenesis of PGA (5, 6). The lymphocyte population in GA lesions in non-HIV patients has a preponderance of T helper/inducer cells to T cytotoxic/suppressor cells, supporting the cell-mediated immunity as the type of immune response involved (7). Lesions of GA occurring in HIV patients have been previously described, including PGA in one case (2, 8–10). The inflammatory infiltrate in PGA lesions in an HIV patient was predominantly of T-cell components, consisting almost exclusively of cytotoxic/suppressor T-cells paralleling with the ratio helper/inducer cells to cytotoxic/suppressor T cells in the patient's peripheral blood (2). Remission of generalized GA with oral zidovudine in an HIV patient has also been

reported (11). It is well known that zidovudine can improve certain skin diseases in HIV-positive patients. DdI has been approved for the treatment of HIV infection in patients who are unable to tolerate zidovudine, but no reports about the effects of ddI in cutaneous diseases have been communicated (12). In our patient, PGA lesions disappeared after 3 months' treatment with ddI. However, spontaneous resolution does occur in some patients, but the average time for resolution is 3 to 4 years. These findings question the role of cell-mediated immunity in the pathogenesis of GA. If lymphocytes do mediate in the apparition of GA, then it is of interest that patients with a severe depression of cell-mediated immunity would develop PGA lesions.

Further investigations are required to elucidate if the T-lymphocyte profile observed in the skin lesions of PGA in HIV-positive patients depends on the specific type of GA or is due to HIV infection.

## REFERENCES

1. Samlaska CP, Sandberg GD, Maggio KL, Sakas EL. Generalized perforating granuloma annulare. *J Am Acad Dermatol* 1992; 27: 319–322.
2. Huerter CJ, Bass J, Bergfeld WF, Tubbs RR. Perforating granuloma annulare in a patient with acquired immunodeficiency syndrome. *Arch Dermatol* 1987; 123: 1217–1220.
3. Owens DW, Freeman RG. Perforating granuloma annulare. *Arch Dermatol* 1971; 103: 64–67.
4. Shimizu H, Harada T, Baba E, Kuramochi M. Perforating granuloma annulare. *Int J Dermatol* 1985; 24: 581–583.
5. Umbert P, Winkelmann RK. Histologic, ultrastructural, and histochemical studies of granuloma annulare. *Arch Dermatol* 1977; 113: 1681–1686.
6. Dahl MV, Ullman S, Goltz R. Vasculitis in granuloma annulare: histopathology and direct immunofluorescence. *Arch Dermatol* 1977; 113: 463–467.
7. Buechner SA, Winkelmann RK, Banks PM. Identification of T-cell subpopulations in granuloma annulare. *Arch Dermatol* 1983; 119: 125–128.
8. Bakos L, Hampe S, da Rocha JL, Pires AS, Weissbluth M, Zampese M. Generalized granuloma annulare in a patient with acquired immunodeficiency syndrome (AIDS). *J Am Acad Dermatol* 1987; 17: 844–845.
9. Ghadially R, Sibbald RG, Walter JB, Haberman HF. Granuloma annulare in patients with human immunodeficiency virus infection. *J Am Acad Dermatol* 1989; 20: 232–235.
10. Cohen PR, Grossman ME, Silvers DN, De Leo VA. Human immunodeficiency virus-associated granuloma annulare. *Int J STD AIDS* 1991; 2: 168–171.
11. Leenutaphong V, Hölzle E, Erckenbrecht J, Zuleger S, Plewig G. Remission of human immunodeficiency virus-associated generalized granuloma annulare under zidovudine therapy. *J Am Acad Dermatol* 1988; 19: 1126–1127.
12. Shelton MJ, O'Donnell AM, Morse GD. Didanosine. *Ann Pharmacother* 1992; 26: 660–670.

Accepted February 10, 1995.

María Núñez, Enrique S. Miralles, Natalia del Olmo and Antonio Ledo, Department of Dermatology, Hospital Ramón y Cajal, Universidad de Alcalá, Madrid, Spain.