

環狀肉芽腫繼發於帶狀疱疹感染 — 病例報告 —

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Granuloma Annulare Occurring in Herpes Zoster Scar — A Case Report —

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One case of granuloma annulare in herpes zoster scar, was first described by Guill and Goette in 1978. Here, we report a similar case. A 61-year-old man suffered from herpes zoster over the right lower back 5 months ago. About one month after vesicular lesions resolved, many erythematous papules appeared at the site of the scar relating to herpes zoster with itching and painful sensation. Microscopically, there are necrobiosis with the accumulation of lymphocytes, histiocytes, and fibroblasts in a palisading fashion. Giant cells and nuclear dusts were also seen in the palisading granuloma. Alcian blue stain was mildly positive. The clinical picture and histopathological feature suggest that this is a case of granuloma annulare in herpes zoster scar. True etiology is unknown. Treatment methods include topical or intralesional steroid. (*Dermatol Sinica* 15 : 280-284,1997)

KEY WORDS: HERPES ZOSTER, NECROBIOSIS, PALISADING GRANULOMA, GRANULOMA ANNULARE

帶狀疱疹感染之後引發的環狀肉芽腫在1978年首先由Guill等人發表。在此,我們提出一個類似的病例。一位61歲的男性病人在5個月前右背長出帶狀疱疹。在水疱好了一個多月後,病人發現有許多新的紅丘疹長在原來帶狀疱疹的疤痕上,並有癢感及刺痛感。病理上可見真皮內有局限性中心凝固壞死病灶,由柵狀排列的淋巴球,組織球,結締組織細胞等圍繞而無纖維化的變化,膠原纖維則呈現斷裂,壞死,排列亂,且可見殘餘細胞核及巨大細胞。Alcian blue 染色為弱陽性。為典型之環狀肉芽腫。至於其成因至今仍未明。治療為局部塗抹或注射類固醇。(中華皮誌 15 : 280-284,1997)

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Accepted for publication : April 29, 1997

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Granuloma annulare is a chronic benign inflammatory dermatosis that presents clinically as dermal papules, plaques, or nodules with an annular configuration. Granuloma annulare has been reported at sites of healing tuberculin skin tests^{1,2} and at the site of previously documented herpes zoster infection.³⁻¹⁰ Preceding trauma,¹¹ sunlight,¹¹ insect bite,^{12,13} varicella infection,¹⁴ and verruca vulgaris¹⁵ have also been associated with the development of granuloma annulare.

CASE REPORT

A 61-year-old man had grouped vesicles with erythematous base over right lower back (T10-T11 dermatomes) 5 months ago. He visited a

dermatologist then and received treatment under the impression of herpes zoster.

About one month after vesicular lesions resolved, zosteriform eruptions at the site of the scar relating to herpes zoster appeared. The size of new lesions increased in recent 2 months with itching and painful sensation. Therefore, the patient visited our OPD for help.

Physical examination revealed that many pea-sized erythematous papules on an oval-shaped, palm-sized plaque present over right lower back (Fig. 1). No diabetes, hypertension or malignancy history was noted. Laboratory examinations including VDRL, tissue culture for fungus, bacteria, and mycobacteria are all negative. Chest X-ray revealed old pulmonary



Fig.1. Many pea-sized erythematous papules on an oval-shaped, palm-sized plaque present over right lower back.

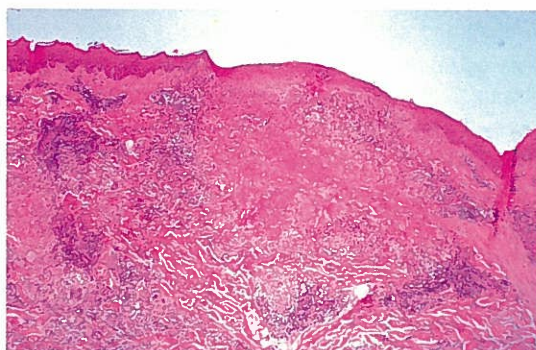


Fig.2. Necrobiosis with an accumulation of lymphocytes, histiocytes, and fibroblasts in a palisading fashion. (HE stain X 40)

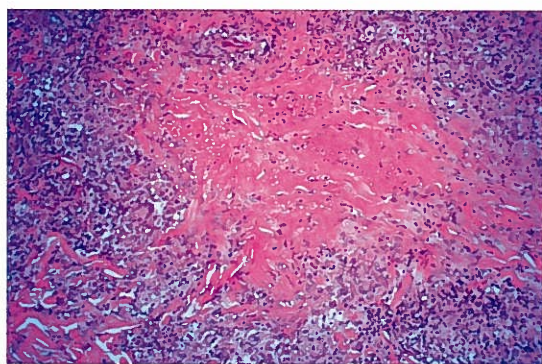


Fig.3. Giant cells and nuclear dust were seen in the palisading granuloma. (HE stain X 100)



Fig.4. Post-treatment picture. (Follow up 6 months later)

TB and chronic pleurisy.

Microscopically, there was focal collagen degeneration (necrobiosis) with the accumulation of lymphocytes, histiocytes and fibroblasts around the necrotic areas in a palisading fashion. Giant cells and nuclear dusts were also seen in the center of the palisading granuloma (Fig. 2,3). Acid-fast staining and Giemsa staining were negative. Alcian blue staining at pH 2.5 revealed a little mucin deposition in the areas corresponding to the collagen degeneration. The clinical picture and histopathological feature suggest that this is a case of granuloma annulare in herpes zoster scar. The patient received 0.1% triamcinolone intralesional injection for 4 times, but got little improvement. Then the patient used some unknown topical herbs by himself and got some improvement 6 months later. (Fig. 4).

DISCUSSION

The occurrence of a new skin disorder exactly at the site of another unrelated skin disease that had already healed was first described in 1955 by Wyburn-Mason.¹⁶ He described a series of 26 patients whose malignant tumors (i. e., basal cell carcinoma, squamous cell carcinoma, and breast carcinoma) developed at the site of a previous herpes zoster (25 cases) or herpes simplex (1 case) lesion. Granuloma annulare in herpes zoster scar was first reported by Guill and Goette in 1978.³ From 1955 to 1993, there are 58 reported cases of herpes zoster scar developing other skin disorder. Sixteen cases of them were granuloma annulare. Other diseases included tuberculoid (1 case)¹⁷ and sarcoid granuloma (2 cases),^{18,19} Kaposi's sarcoma (2 cases),^{20,21} pseudolymphoma (2 cases),^{22,23} granulomatous

vasculitis (1 case),²⁴ tinea (2 cases),²⁵ angiosarcoma (1 case),²⁶ Bowen's disease (1 case),²⁷ lymphoma (1 case),²⁸ leukemia cutis (1 case)²⁹ and acne (1 case).³⁰ Besides, granuloma annulare perforans occurring in herpes zoster scar with Lennert's lymphoma was reported by Krahl et al in 1993.³¹

Until now, the true etiology of granuloma annulare developed from herpes zoster scar still remains as a mystery. First, the granuloma annulare arose as a result of an atypical delayed hypersensitivity immune reaction to herpes zoster/varicella viral antigens or a tissue antigen altered by the virus.⁶ Serfling et al³² used PCR technique to detect varicella-zoster virus DNA in the site of granuloma annulare formation. They concluded that the VZV DNA sequences could be detected in the granuloma that occurred early (less than 1 month) after resolution of herpes zoster, but not in those that occurred later (more than 1 month). Zanolli et al suggested that cutaneous lesions of herpes zoster produced a focus of dermal injury that triggered the cellular immune response.⁹ Krahl et al used immunohistochemical studies and showed marking of cellular infiltrate, mostly for CD3 (pan-T), CD11 and CDw14 (monocyte). T lymphocyte were mostly of the CD4 positive subset.³¹ Umbert and Winkelmann maintain that histologic, ultrastructure, histochemical, direct immunofluorescent findings, and the evidence of a circulating macrophage migration inhibition factor (MIF) in patients with granuloma annulare suggest that a cell-mediated immune response may be the dominant pathologic event.³³ Second, there is growing evidence that there are bi-directional interaction between the nervous system and the immune system and that secretion of neuropeptides

from sensory nerve fibers in the skin has a variety of effects on mast cells, T lymphocytes, monocytes, and endothelial cells.³⁴ Third, previous disease produced endothelial traps for circulating immune complex (CIC) and /or produced a source of antigen for CIC and /or resulted in reduced clearance of CIC. Recent reports have emphasized damage to collagen and elastic fibers in granuloma annulare, although it remains unclear whether this damage initiate or is a sequela of previously unexplained inflammatory events.⁹

Review of the reported cases, the age of most patients was between 50 and 75 years old. The sex ratio of F : M was about 2 : 1. The onset varied from weeks to years after resolution of herpes zoster. Clinically, multiple rice-grain to pea-sized, shiny, flesh-colored to erythematous papules and irregular circinate plaques were seen. The histologic character of granuloma annulare in herpes zoster scars is similar with idiopathic granuloma annulare as seen in our case. The results of the treatment varied with intralesional or topical steroid. We concluded that granulomatous reactions are modulated by the immune status of the host, the individual genetic background, and by the dynamic stage of granuloma formation. This may explain the morphological variety of granulomatous reactions reported after varicella-zoster infection.⁶

REFERENS

1. Beer WE, Jones EW : Granuloma annulare following tuberculin Heaf tests. *Trans ST Johns Hosp Dermatol Soc* 52 : 68, 1966.
2. Fisher I : An unusual histologic change seen in the intracutaneous tuberculin reaction. *J Invest Dermatol* 23 : 233-235, 1954.
3. Guill MA, Goette DK. : Granuloma annulare at site of healing herpes zoster. *Arch Dermatol* 114 : 1383, 1978.
4. Klein P, Levy RS. : Granuloma annulare after varicella. *Arch Dermatol* 120 : 578, 1984.
5. Packer RH, Fields JP, King LE. : Granuloma annulare in herpes zoster scar. *Cutis* 34 : 177-179, 1984.6. Friedman SJ, Fox BJ, Albert HL. : Granuloma annulare arising in herpes zoster scars. Report of two cases and review of the literature. *J Am Acad Dermatol* 14 : 764-770, 1986.
7. Shiedler SJ, Richards M. : Granuloma annulare arising after herpes zoster. *J Am Acad Dermatol* 15 : 1049-1050, 1986.
8. Kleber R, Landthaler M, Burg G. : Postzosterisches granuloma annulare. *Hautarzt* 40 : 110-111, 1989.
9. Zanolli MD, Powell BL, McCalmont T, et al. : Granuloma annulare and disseminated herpes zoster. *Int J Dermatol* 31 : 55-57, 1992.
10. Hayakawa K, Mizukawa Y, Shiohara T, et al. : Granuloma annulare arising after herpes zoster. *Int J Dermatol* 31 : 745-746, 1992.
11. Muhlbauer JE : Granuloma annulare. *J Am Acad Dermatol* 3 : 217-230, 1980.
12. Moyer DG : Papular granuloma annulare. *Arch Dermatol* 89 : 41-45, 1964.
13. Curwen W : Granuloma annulare, multiple, suggesting insect bite reaction. *Arch Dermatol* 88 : 355-356, 1963.
14. Klein P, Levy RS : granuloma annulare. *Arch Dermatol* 120 : 578, 1984. (Letter to editor)
15. Ward WH : Warts and granuloma annulare. *Br Med J* 2 : 1484, 1956
16. Wyburn-Mason R. : Malignant change arising in tissues affected by herpes. *BMJ* 2 : 1106-1109, 1955.
17. Fisher G, Jauorski R. : Granuloma formation in herpes zoster scars. *J Am Acad Dermatol* 16 : 1261-1263, 1987.
18. Bisaccia E, Scarborough DA, Carr RD. : Cutaneous sarcoid granuloma formation in herpes zoster scars. *Arch Dermatol* 119 : 788-789, 1983.
19. Redondo P, Espana A, Sola J, et al. : Sarcoid-like granulomas secondary to herpes simplex infection. *Dermatologica* 185 : 137-139, 1992.
20. Niedt GW, Prioleau PG : Kaposi's sarcoma occurring in a dermatome previously involved by herpes zoster. *J Am Acad Dermatol* 18 : 448-451, 1988.
21. Roth JS, Grossman ME. : Linear Kaposi's sarcoma in HIV disease. *J Am Acad Dermatol* 29 : 488, 1993.
21. Sanchez JL, Mendez RP. : Cutaneous pseudolymphoma at the site of resolving herpes zoster. *Arch Dermatol* 117 : 377, 1981.
23. Wolff HH, Wendt V, Winzer M. : Cutaneous pseudolymphoma at the site of prior herpes zoster

- eruption. Arch Dermatol Res 279 (Suppl) : S52-S53, 1987.
24. Langenberg A, Yen B, Leboit PE. : Granulomatous vasculitis occurring after cutaneous herpes zoster despite absence of viral genome. J Am Acad Dermatol 24 : 429-433, 1991.
25. Wolf R, Wolf D. : Tinea in a site of healed herpes zoster (Isoloci Response) . Int J Dermatol 24 : 539, 1985.
26. Hudson CP, Hnano R, Callen JP. : Cutaneous angiosarcoma in a site of healed herpes zoster. Int J Dermatol 23 : 404-407, 1984.
27. Claudy AL, Chignol MC, Chardonner Y. : Detection of herpes simplex virus DNA in a cutaneous squamous cell carcinoma by in situ hybridization. Arch Dermatol Res 281 : 333-335, 1989.
28. Aloï FG, Appino A, Puiatti P. : Lymphoplasmacytoid lymphoma arising in herpes zoster scars. J Am Acad Dermatol 29 : 652-654, 1990.
29. Pujol RM, Matias-Guiu X, Planaguma M, de Moragas JM. : Chronic lymphocytic leukemia and cutaneous granuloma at sites of herpes zoster scars. Int J Dermatol 29 : 652-654, 1990.
30. Stubbings JM, Goodfield MJD. : An unusual distribution of an acneiform rash due to herpes zoster infection. Clin Exp Dermatol 18 : 92-93, 1993.
31. Krahl DMD, Hartschuh WMD : Granuloma annulare perforans in herpes zoster scars. J Am Acad Dermatol 29 : 859-62, 1993.
32. Serfling U, Penneys NS, Zhu WY, et. al. : Varicella-zoster virus DNA in granulomatous skin lesions following herpes zoster. A study by the polymerase chain reaction. J Cutan Pathol 20 : 28-33, 1993.
33. Umbert P, Winkelmann RK : Histologic, ultrastructure, and histochemical studies of granuloma annulare. Arch Dermatol 113 : 1681-1686, 1977.
34. Farber EM. : Psychoneuroimmunology and dermatology. Int J Dermatol 32 : 93-94, 1993.