以低劑量Vinblastine病灶內注射有效地治療龜頭之傳統卡波西肉瘤

—病例報告—

李淑芬　王德華　李玉雲
國立成功大學附設醫院 皮膚科部

Classical Kaposi's Sarcoma of the Glans Penis Effectively Treated with Low-dose Intralesional Vinblastine Injection

—A Case Report—

Shu-Fen Lee　Tak-Wah Wong　J. Yu-Yun Lee

Classical Kaposi's sarcoma (KS) is a multicentric cutaneous and extracutaneous vascular neoplasm predominantly affecting older individuals, immunosuppressed patients and homosexual men. Although KS of the genitalia is not rare event, it is challenging to treat multiple KS of the glans penis. Localized KS may be treated by excision, radiation, cryotherapy and intralesional injection of interferon-alpha or cytotoxic chemotherapy. Although intralesional injection of vinblastine has been used to treat oral KS successfully, little is known about its efficacy in treating glanular KS. We report a 56-year-old man with isolated, classical KS involving his glans penis. The tumors were treated with 6 biweekly intralesional vinblastine injections (0.2 mg/ml, 1 ml/dose) after regional anesthesia. The tumors showed about 70% reduction in size after one injection and were almost completely resolved after 4 treatments. There was no obvious side effect. The patient remained tumor-free 18 months later. The favorable response in our case suggests that intralesional low-dose vinblastine injection could be an effective alternation for treating glanular KS. (Dermatol Sinica 20：218-222, 2002)

Key words: Kaposi's sarcoma, Vinblastine, Glans penis

傳統卡波西肉瘤爲一可侵犯皮膚及內臟器官之多發性惡性血管腫瘤，通常好發在年紀較大的病人、免疫力低下者或同性戀者。雖然發生在生殖器之卡波西肉瘤並不罕見，但對位於龜頭部位之多發性卡波西肉瘤在治療上則有其特殊的考量及困難處。一般而言，局部之卡波西肉瘤可以用手術切除、放射線治療、冷凍治療、及病灶內注射干擾素或其他化學藥物等來治療。雖然病灶內注射vinblastine對位於口腔之卡波西肉瘤的治療效果極佳，但

From the Department of Dermatology, National Cheng-Kung University Hospital
Accepted for publication: January 29, 2002
Reprint requests: Tak-Wah Wong, M.D., Department of Dermatology, National Cheng-Kung University Hospital, 138 Sheng-Li Road, Tainan, Taiwan 704　TEL: 886-6-2353535 ext. 5417　FAX: 886-6-2766180　E-mail: tehwa.wang@rosewellpark.org

此種治療方式對位於龜頭之卡波西肉瘤的療效如何則未知。本文報告用此方法治療一例局限於龜頭之傳統卡波西肉瘤的治療經驗。病人於局部麻醉後，接受每兩週一次、共六次病灶內注射vinblastine(濃度爲每毫升0.2毫克，每次注射1毫升)；病灶在接受一次治療後，即縮小70%，而在連續四次治療後即幾乎完全消失。治療過程中並無明顯的副作用出現，之後追蹤十八個月並無復發現象。鑑於此病例之治療經驗，病灶內注射低劑量vinblastine可能是治療龜頭部位之卡波西肉瘤的另外一種好的療法。(中華皮誌20：218-222, 2002)

INTRODUCTION

Kaposi's sarcoma (KS) is a multicentric cutaneous and extracutaneous vascular neoplasm. It is currently classified into 4 different subtypes, including classic KS, endemic African KS, KS in iatrogenically immunosuppressed patients, and KS associated with acquired immunodeficiency syndrome (AIDS).[1] In classical KS, the lesions usually first appear on the lower extremities and only rarely affect the penis at the beginning. HIV-associated KS on the penis was involved in about 20% of the patients, although less than 3% of such patients have the first lesion in that location.[2] Treatment of KS depends on the extent, location and clinical subtype of the disease. Localized KS may be treated by surgical excision, radiotherapy, cryotherapy and intralesional injection of interferon-alpha or cytotoxic chemotherapy. Some experimental treatments such as photodynamic therapy[3] and systemic cimetidine[4] also showed positive results. We report a patient with glanular classical Kaposi's sarcoma, which was successfully treated with low-dose intralesional vinblastine injections.

CASE REPORT

A 56-year-old Taiwanese married man presented to our clinic with two slowly enlarging nodules on the glans penis for a 2-month duration. He denied fever, chills or body weight loss. The past history was significant for cutaneous lymphoma of the neck which was successful treated by radiotherapy and chemotherapy 10 years ago.

Physical examination revealed a moderately

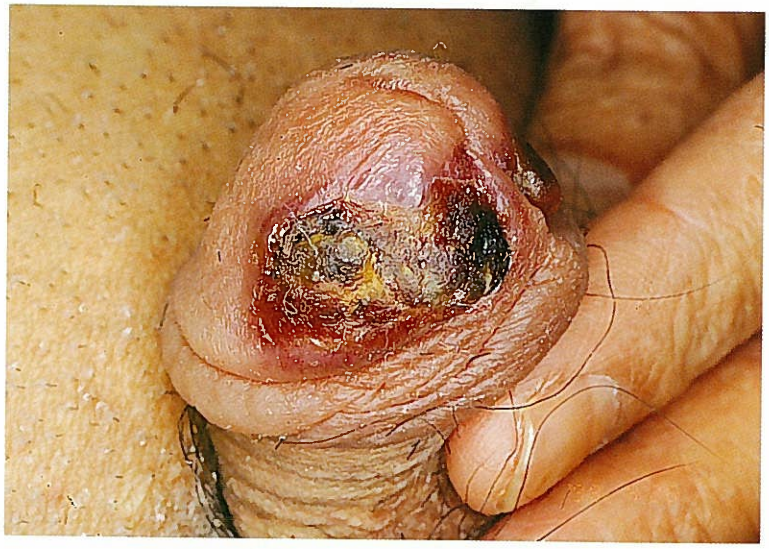

Fig. 1
Two 1-2cm, ulcerated, indurated violaceous nodules are present on the glans penis.

nourished man with no palpable lymphadenopathy or hepatosplenomegaly. Two ulcerated, non-tender, 1-2cm violaceous nodules (Fig. 1) were noted on his glans penis. Laboratory examinations including chest X-ray, complete blood cell counts and CD4, CD8 lymphocyte counts were all within normal limits. Although he had solicited prostitutes in China and Taiwan in the past two years, both himself and his wife were negative for HIV antibody in 2 successive months. Under the impression of recurrent cutaneous lymphoma, a skin biopsy was performed. Histopathologically, there was proliferation of spindle cells and numerous irregular, jagged vascular channels lined incompletely by flat endothelial cells throughout the reticular dermis (Fig. 2). The diagnosis of plaque stage Kaposi's sarcoma was made.

Patient refused surgical excision or radiotherapy and preferred intralesional injections. Since he was only able to come for treatment every other week, intralesional vinblastine (0.2mg/ml, 1ml/dose) was given biweekly after regional anesthesia with 2% lidocaine injected to the root of the penis. Vinblastine sulfate, 0.2mg/mL in normal saline solution, was injected using a U-100 insulin syringe. The dosage approximately was 0.1 mL/cm^2 of lesion surface area. Multiple injections were made depending on the size of the lesion and the solution was injected superficially to result in blanching of the lesions. About 70% reduction of the tumor was noted after the first treatment (Fig. 3). Only some residual small papules were left after the second injection (Fig. 4.). Minimal lesions remained after 4th injection (Fig. 5). Two additional injection sessions were given to complete the treatment. The patient tolerated the treatment well and there was no ulceration and hyperpigmentation locally. The patient remained lesion-free18 months post-treatment by telephone follow-up.

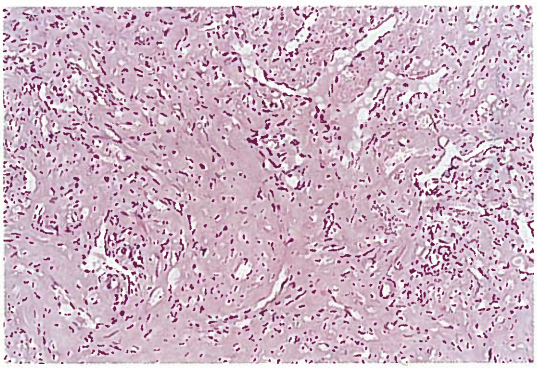

Fig. 2
Histopathology reveals proliferation of spindle cells in association with numerous irregular, jagged vascular channels lined incompletely by flat endothelial cells throughout the reticular dermis. (H & E stain, x40)

DISCUSSION

Treatment of KS depends on the subtype, extent and localization of the disease. Conant *et al.*[5] recommended local therapy for KS when the following criteria are fulfilled: 1) a

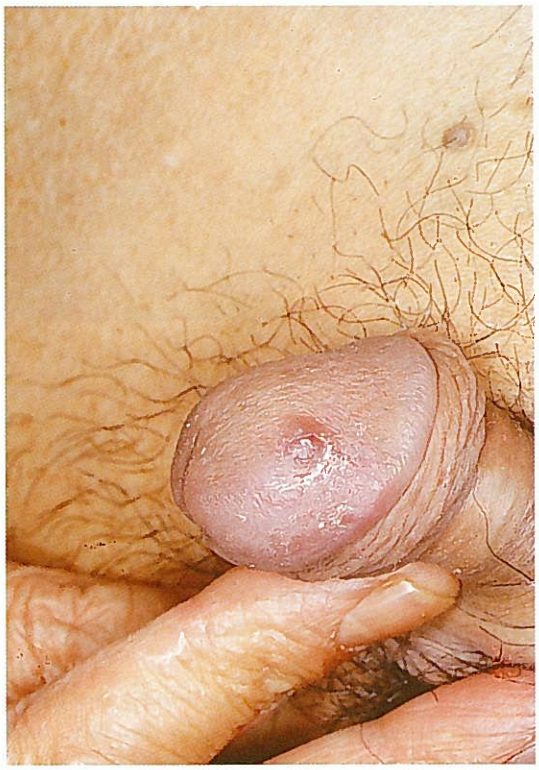

Fig. 3
About 70% reduction of KS tumor is noted after the first intralesional vinblastine injection.

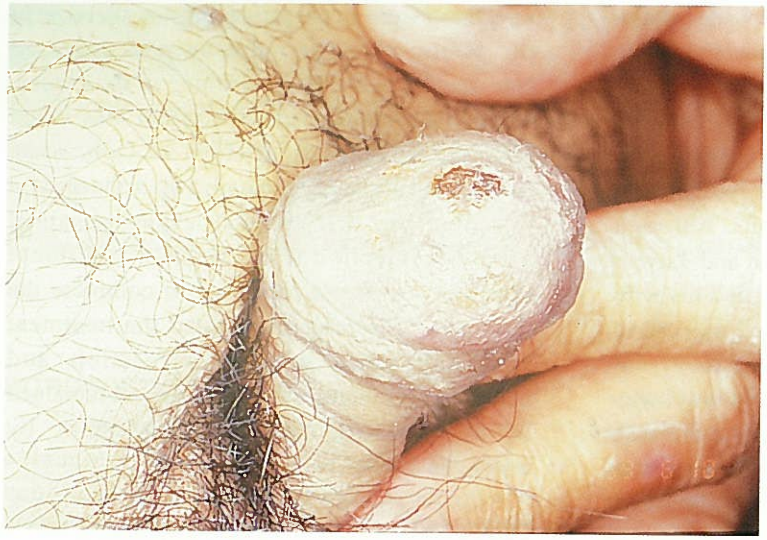

Fig. 4
Small residual KS lesions are left after the second intralesional vinblastine injection.

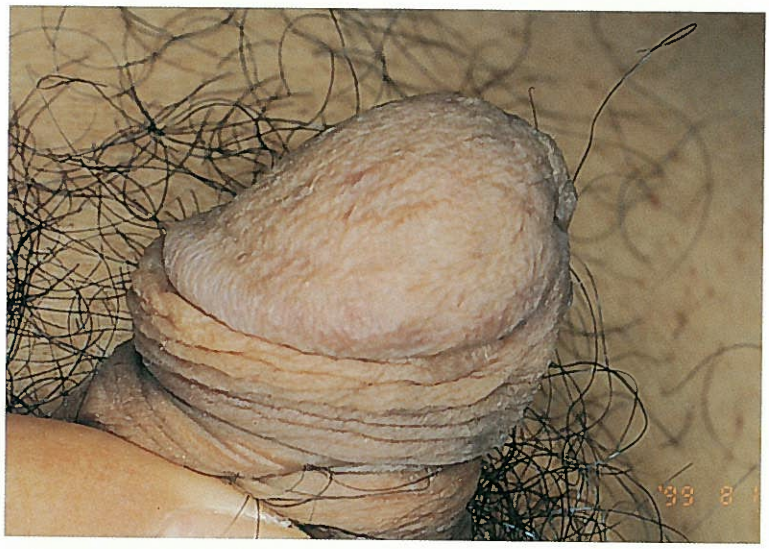

Fig. 5
No obvious KS lesion is noted after 6 biweekly intralesional vinblastine injections.

"manageable" number of lesions involving the integument, 2) an "acceptable" rate of new lesions formation, and 3) no evidence of significant or increasing internal lesions; or 4) troublesome individual lesions in patients with progressive KS being treated with aggressive systemic therapy.

Local treatments including surgical excision, radiotherapy, cryotherapy and intralesional injection of interferon-alpha or cytotoxic chemotherapy are effective with variable successful rates. However, surgical treatment can cause disfigurement of the penile lesion, thus would not be a good choice in this location. Radiotherapy has a high response rates approaching 100% with complete remission rates of 54-85%.[2] However, radiodermatitis, ulceration and fibrosis are common side effects.[6] In addition, fractional radiations should be performed daily. Cryotherapy with liquid nitrogen spray has produced a 85% response rate, especially in deeply violaceous, 1- to 2-cm nodules on the head and neck.[3] Pain, blistering and need for wound care are the drawbacks of

this type of treatment. Photodynamic therapy was reported to be beneficial to cutaneous KS.[3] Intralesional interferon is highly effective in treating KS lesions of the skin, conjunctiva, and oral cavity. However, in comparison with intralesional vinblastine, interferon requires more treatment sessions, and is 10 to 100 times more expensive.[7]

Vinblastine is an antimitotic agent; it acts by disrupting microtubules and blocking mitosis in metaphase. In dermatologic practice, this agent is used primarily as intralesional injection, usually 0.1 to 0.2 mg/ml, for cutaneous and oral lesions of Kaposi's sarcoma with 88% complete or partial clinical response.[8] Some authors use one injection only, whereas others recommend injections every 2 to 4 weeks until complete response is seen. The side effects of intralesional vinblastine are usually limited to pain, ulceration and hyperpigmentation at the injection site. Fortunately, our patient was free of these adverse effects, probably due to the low dosage of vinblastine used.

In summary, we described a glanular isolated classical KS was effectively treated by intralesional low-dose vinblastine therapy. The therapeutic response in our case suggests that intralesional low-dose vinblastine injection could be a well-tolerated and effective alternative treatment for glanular KS.

REFERENCES

1. Rappersberger K, Stingl G, Wolff K: Kaposi's sarcoma. In: Freedberg IM, Eisen AZ, Wolff K, *et al.*, eds. Dermatology in General Medicine. 5th ed. New York: Mcgraw-Hill, 1195-1204, 1999.
2. Lowe FC, Lattimer DG, Metroka CE: Kaposi's sarcoma of the penis in patients with acquired immunodeficiency syndrome. J Urol 142: 1475-1477, 1989.
3. Mitsuyasu RT: Update on the pathogenesis and treatment of Kaposi sarcoma. Curr Opin Oncol 12: 174-180, 2000.
4. Calvieri S, Fattarossi A: Cimetidine for Kaposi's sarcoma. Clin Exp Dermatol 10: 499-501, 1985.
5. Conant MA, Galgazzory G, Illeman L: Intralesional vinblastine (Velban) treatment of lesions of Kaposi's sarcoma. Presented as a poster at the Fifth International Conference on AIDS, Montreal, Canada, 290: 335, 1989.
6. Piedbois P, Frikha H, Martin L, *et al*: Radiotherapy in the management of epidemic Kaposi's sarcoma. Int J Radiation Oncology Biol Phys 30: 1207-1211, 1994.
7. Johnson RA, Dover JS: Cutaneous manifestation of human immunodeficiency virus disease. In: Fitzpatrick TB, Eisen AZ, Wolff K, *et al.*, eds. Dermatology in General Medicine. 4th ed. New York: Mcgraw-Hill, 2648-2650, 1993.
8. Shupack JL, Lai IW, Washenil K: Topical cytotoxic agents. In: Freedberg IM, Eisen AZ, Wolff K, *et al.*, eds. Dermatology in General Medicine. 5th ed. New York: Mcgraw-Hill, 2768-2772, 1999.