

子宮平滑肌肉瘤轉移至頭皮

— 病例報告暨文獻回顧 —

王淳樺 陳國熏 蕭惠樺* 楊曉芳**
高雄醫學大學 皮膚科 血液腫瘤內科* 病理科**

Uterine Leiomyosarcoma Metastatic to the Scalp

— A Case Report and Review of the Literature —

Chun-Hua Wang Gwo-Shing Chen Hui-Hua Hsiao* Sheau-Fang Yang**

Leiomyosarcoma is an uncommon neoplasm. It occurs more frequently in the uterus, retroperitoneal space, stomach and large vessels. Metastatic leiomyosarcomas to the skin, in general, are extremely rare. Herein, we describe a patient with leiomyosarcomas of uterus who developed multiple cutaneous metastatic leiomyosarcomas on the scalp over the duration of one year. The diagnosis was confirmed by histopathological and immunohistochemical studies, which showed the tumor positively stained for desmin and smooth muscle actin, while negatively stained for cytokeratin γ S-100 and CD117 (c-kit). Distant cutaneous metastases from sarcoma usually occur as a late event and carry a poor prognosis. The course in our patient is somewhat unusual, and she is still alive now, which is about 21 months after the occurrence of skin metastasis. (*Dermatol Sinica* 22 : 69-73, 2004)

Key words: Leiomyosarcoma, Scalp metastases

平滑肌肉瘤是一個罕見腫瘤，較常出現於子宮、後腹壁腔、胃壁或大血管壁中；轉移至皮膚的個案更是罕見。在此吾人提出一個由子宮平滑肌肉瘤轉移至遠處頭皮的病例報告。該病例經由組織病理及免疫組織化學的檢查後(包括 desmin 和 smooth muscle actin 的陽性反應；cytokeratin γ S-100 和 CD117 的陰性反應)確定診斷。肉瘤之遠處皮膚轉移多表示病症末期且癒後不佳，但是該病人在肉瘤遠處皮膚轉移後接受化學治療及規則門診追蹤而繼續存活，距離其頭皮腫塊出現已達 21 個月。(中華皮誌 22 : 69-73, 2004)

From the Departments of Dermatology, Oncology and Pathology**, Kaohsiung Medical University Hospital*

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Reprint requests: Gwo-Shing Chen, M.D., Department of Dermatology, Kaohsiung Medical University, No.100, Shih-Chuan 1st Rd., Kaohsiung, Taiwan, R.O.C.

TEL: 886-7-3208214 FAX: 886-7-3216580

INTRODUCTION

Primary leiomyosarcoma (LMS) of the skin and subcutaneous tissue are rare and account for 2% to 3% of all soft tissue sarcoma.¹ A LMS of the skin is typically presented as a solitary lesion. The lower limbs are the most frequently involved sites, but the scalp, however, is rarely involved. Anatomically, primary LMS of the skin and subcutaneous tissue is situated deep in the dermis or within subcutaneous tissue. It may originate from muscoli arrectores pilorum, muscle coats of vessel walls, or the specialized muscle in the skin of the genitalia.

Metastatic LMS from uterus to lung or liver is not uncommon. Nevertheless, skin metastases from a uterine LMS are quite unusual. Herein we present clinical, histopathological and immunohistochemical findings in a case of multiple scalp metastases from a uterine LMS.

CASE REPORT

A 62-year-old female patient presented with multiple asymptomatic, fleshy to erythematous nodules (0.8 to 1.2 cm in diameter) on the scalp for 16 months (Fig. 1a). Due to absence of discomfort, she did not seek for investigation. A fresh nodule on the scalp appeared (about 1.0 cm in diameter) (Fig. 1b) in



Fig. 1a

Multiple asymptomatic, fleshy to erythematous nodules on the scalp for 16 months.

Fig. 1b

One fresh nodule on the scalp appeared 4 weeks ago.

recent one month and she called at our dermatological outpatient clinics for opinions.

In December 1998, the patient was diagnosed with LMS of the uterus and cervix. Subsequently, she underwent a total hysterectomy and a bilateral salpingo-oophorectomy. Then she received six courses of chemotherapy and had regular follow-up at our GYN outpatient clinics in the following years. She first noticed an asymptomatic nodule on the scalp 16 months ago. The second nodule on her scalp appeared one month later and the third one fol-

Table 1. Summary of Cutaneous Metastatic Leiomyosarcomas

| Case No. | Authors(s) | Sex/ Age(y) | Sites of metastases | Sites of primary tumors | Treatment | Survival after metastases |
|----------|--------------------------------------|-------------|---|-------------------------|---------------------|---------------------------|
| 1 | Gardner ³ | Ns | sacral area, back, scalp | Uterus, stage III | Ns | Ns |
| 2 | Akers and Prazak ⁴ | F/79 | scalp | Retroperi- toneal area | excision | Ns |
| 3 | Pandhi <i>et al.</i> ⁵ | F/40 | scalp, lungs | Labium majus | wide excision, C/T | 46 days |
| 4 | Broderick <i>et al.</i> ⁶ | F/49 | left foot | Uterus, stage I | excision, C/T, R/T. | alive(18m) |
| 5 | Alessi <i>et al.</i> ⁷ | F/64 | scalp, back, lungs, bone | Uterus, stage I | excision, C/T | 20 m |
| 6 | Kinoshita <i>et al.</i> ⁸ | F/62 | generalized skin, liver, lungs, kidneys | Uterus, stage I | R/T, thermotherapy | 5 y |
| 7 | Rao <i>et al.</i> ⁹ | F/63 | anterior abdominal wall, lungs | Uterus, stage III | C/T | 7 m |
| 8 | Present case | F/63 | scalp, lungs, liver | Uterus, stage II | C/T, excision | Alive(21m) |

Abbreviation: Age= age at diagnosis of cutaneous metastatic LMS, Ns= not stated, F= female, C/T= chemotherapy, R/T= radiotherapy.

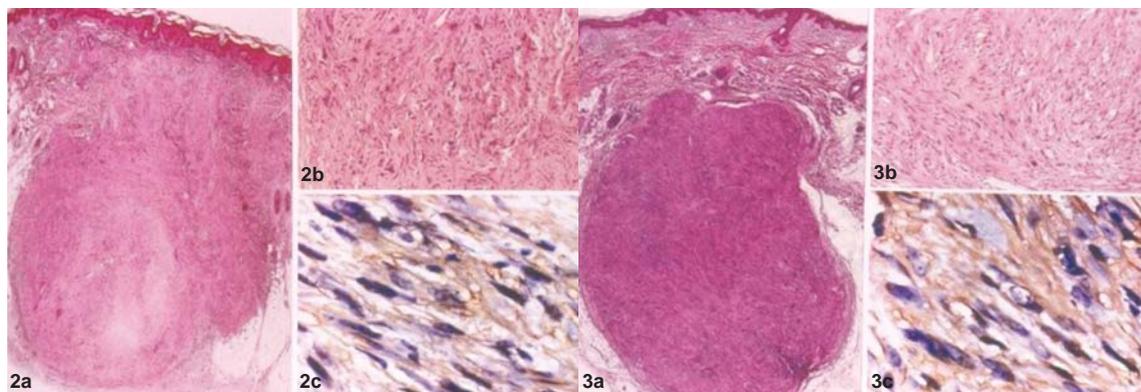


Fig. 2a and 3a

Both nodules showed nodular proliferation of spindle cells in dermis.(H & E stain, x20)

Fig. 2b and 3b

The tumor cells were mainly arranged in irregular and interlacing fascicles. Bizarre cells with pleomorphic and hyperchromatic nuclei were frequently seen.(H & E stain, x200)

Fig. 2c and 3c

Immunohistochemical studies showed positive immunoreactivity for smooth muscle actin, which demonstrated that myofilaments are inside the cells.(smooth muscle actin stain, 400x)

lowed. In April 2002, she sustained abdominal fullness and abdominal sonography showed multiple hepatic tumors, which were suspected to be metastatic tumors. Six months later, due to progressive cough, she came to our oncology clinics for help and was admitted for further management.

The chest radiograph showed multiple metastases in both lungs and the liver biopsy performed later documented metastatic LMS. After that, she noticed a fresh nodule on the scalp and her oncologists consulted our dermatologists to evaluate this condition. Two skin nodules from the scalp were taken, with both older and newer lesions. The histopathological finding of both nodules showed nodular proliferation of spindle cells in dermis. The tumor cells were mainly arranged in irregular and interlacing fascicles. Bizarre cells with pleomorphic and hyperchromatic nuclei were seen (Fig. 2a-b for older lesion; 3a-b for newer lesion). Immunohistochemical studies showed positive immunoreactivity for smooth muscle actin (Fig. 2c & 3c) and desmin but negative immunoreactivity for cytokeratin, S-100 protein and CD117 (c-kit). The diagnosis of cutaneous

metastatic LMS was therefore made. She then received chemotherapy with the regimen of mini-ICE (Ifosfamide + Cisplatin + Etoposide) for six courses at our oncology ward and is currently alive, about 21 months after the first appearance of cutaneous metastatic LMS.

DISCUSSION

Cutaneous metastases have been reported to occur in 0.7% to 9% of patients with malignancies, including leukemia and lymphoma. Of these, various types of sarcomas contribute to 2% to 3%.² Uterine LMSs are aggressive and often lethal cancers. Their location within the myometrium allows for early vascular invasion and potential spread to extrapelvic sites. The median time to recurrence is usually less than 2 years, and up to 90% of patients who perish show distant metastases alone or associated with pelvic recurrence. Most distant metastases occur in lungs and abdomen, while skin, bone and brain are uncommon sites. To the best of our knowledge, only five other cases of cutaneous metastasis from uterine LMS have been reported to date.³⁻⁹ Among them, the scalp was involved in two cases.

Although the scalp as a metastatic site constituted 1.76% of all metastases,¹⁰ careful examination of the skin on whole body, with particular attention to the scalp, should be done when the patient had a history of primary internal malignancy. These lesions may appear in several different forms such as solitary or multiple, cutaneous or subcutaneous nodules. Indeed, the abrupt appearance of cutaneous or subcutaneous nodules should prompt the clinicians to consider the possibility of metastatic lesions, especially when they are multiple, widespread in location, and painless.

The typical histopathology of cutaneous primary or metastatic LMS showed the tumor situate in the dermis or within the hypoderm. In some areas of the nodules, there were spindle-shaped cells with very long nuclei and blunt, rounded ends, partially arranging into fascicles. Most of their nuclei were atypical, and sometimes large cells with bizarre nuclei existed. In other areas, there was a diffuse infiltration of pleomorphic cells in a disordered pattern. Mitotic figures were frequently seen in multiple areas. Immunohistochemical staining revealed that the tumors were positively stained for muscle-specific markers such as actin, desmin, and myosin, but negatively stained for S-100 protein. Nevertheless, we know the histological diagnosis of these lesions is not always so distinct. Metastatic sarcomas may be confused with primary cutaneous tumors, since a variety of metastatic sarcomas may have overlapping histological features.

Clinically, these cutaneous metastatic tumors may be similar to sebaceous cysts or other benign tumors. On hematoxylin and eosin stained sections, the tumors should be differentiated from malignant fibrous histiocytoma, spindle cell type melanoma or gastrointestinal stromal tumor (GIST). Immunohistochemically, the tumor cells from malignant fibrous histiocytoma stained with CD68 and vimentin, but not with smooth muscle actin, CD34, or S-100 protein. The tumor cells from spindle cell type melanoma were stained with S-100 protein, but not with smooth muscle actin. On the other

hand, the tumor cells from GIST were strongly positive for CD117 (c-kit), especially cell membrane accentuation, while negative for desmin or smooth muscle actin. Therefore, the patient should undergo an extensive metastatic evaluation both to determine the extent of disease and to rule out the possibility of synchronous primary LMS. Past history and generalized survey could also help us to differentiate the primary or metastatic tumors.

How the uterine LMS metastasize to the scalp is a matter of conjecture. Scalp metastases appear to spread via a hematogenous route. Some authors considered that tumor invasion of Batson's plexus could bypass the pulmonary circulation, thereby allow embolic metastases to any site draining into the system.¹¹ That hypothesis may also explain the metastases to the head and neck areas.¹²

To date, no consentaneous treatment has been proposed due to the rarity of scalp metastasis from uterine LMS. However, treatment strategies have been applied based on our experiences with other kinds of recurrent uterine cancers. Current recommendations include local excision (if feasible) and combination chemotherapy (doxorubicin or ifosfamide). Radiation and thermotherapy have also been suggested.

From all accounts, distant cutaneous metastasis from sarcoma usually occurs as a late event and carries a poor prognosis. Reingold¹³ stated that the life expectancy from the time of the appearance of metastatic skin nodules to death averages three months. The cutaneous metastatic lesions, by usual standards, are ordinarily biologically aggressive. Nevertheless, the course of metastatic LMS in our patient was somewhat different. The patient is still alive now, which is about two years after the appearance of cutaneous metastasis.

In conclusion, we present an unusual case of uterine LMS metastasizing to the scalp. All physicians and dermatologists should keep this entity in mind despite of its rarity.¹⁴

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