Squamous Cell Carcinoma of the Scalp Arising from Chronic Discoid Lupus Erythematosus with Scarring Alopecia

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Neoplasms have rarely been reported in lesions of lupus erythematosus (LE) and have included basal cell carcinoma (BCC), squamous cell carcinoma (SCC), and atypical fibroxanthoma. We here report a case of SCC of the scalp arising from a patch of scarring alopecia secondary to chronic discoid lupus erythematosus (DLE). Surgical excision of the tumor with a 1cm margin was performed, showing a deeply invasive SCC extending to the deep fascia. A series of staging investigations were undertaken, including positron emission tomography (PET) scan, which revealed high risk of metastasis to the cervical lymph nodes. Although malignant transformation of chronic DLE lesions is uncommon, a high index of suspicion and need for continued surveillance is still warranted. A SCC arising from a chronic inflammatory scar such as seen in this case should be regarded as a high risk tumor with greater invasive and metastatic potential, and requires careful staging, greater excision margin, possible adjunctive treatments, and closer follow-up. In addition, since PET is a noninvasive and whole-body imaging modality that can detect both regional lymph node and distant organ metastases, it may be clinically useful in the staging of high-risk SCC patients. (Dermatol Sinica 25: 165-170, 2007)

Key words: Squamous cell carcinoma, Discoid lupus erythematosus, Scarring alopecia

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INTRODUCTION
Squamous cell carcinoma (SCC) is a locally invasive neoplasm of the skin that occasionally gives rise to distant metastases. We here report a patient with SCC of the scalp developing from a lesion of chronic discoid lupus erythematosus with scarring alopecia. The possible pathogenesis is discussed, together with implications for staging, treatment and prognosis.

CASE REPORT
A 77-year-old Taiwanese female had a history of discoid lupus erythematosus involving her face and scalp for about 40 years, previously treated with topical steroids (fluocinonide cream). Over the last 10 years, the lesions of discoid lupus erythematosus on her scalp had gradually turned into a large area of scarring alopecia. She came to the Dermatology outpatient clinic of our hospital with a 6 month history of a growing hyperkeratotic plaque on her scalp. This was associated with contact bleeding but not pain or pruritus. There was no history of frequent sun exposure or chronic arsenism.

On physical examination, a large area of hypopigmented scarring alopecia was noted on her scalp. Near the center of the patch of alopecia was a 3cm × 3cm brown, firm, hyperkeratotic plaque with central ulceration and crusting (Fig. 1a). The patient’s face showed hypopigmented atrophic plaques on bilateral cheeks from previous DLE (Fig. 1b). Enlarged cervical lymph nodes were palpable on the right side. Chest, cardiovascular, and abdominal examinations were normal.

An incisional biopsy was diagnostic of SCC. It showed strands and islands of eosinophilic cells growing from the epidermis down into the dermis. The cells were well keratinized, with formation of horn pearls. Pleomorphism, nuclear hyperchromasia, and numerous mitotic figures were seen. The superficial epidermis showed hyperkeratosis, parakeratosis, and the presence of serum crust. The patient was subsequently admitted to our dermatology ward for further survey and surgical

Fig. 1
(a) A 3cm × 3cm brown, hyperkeratotic plaque with central ulceration and crusting arising from a large area of scarring alopecia on the scalp. (b) The patient’s face showed hypopigmented atrophic plaques on bilateral cheeks from previous DLE.

Fig. 2
Histological examination of the excisional surgical specimen at low-power confirmed a deeply invasive squamous cell carcinoma (hematoxylin-eosin stain x1).
Following admission, the scalp SCC was completely excised surgically with a 1 cm margin down to deep fascia, and the specimen sent for examination by frozen section. The lateral margins were clear of tumor cells, but the deep margin was involved. A second excision was performed with removal of the underlying periosteum and exposure of bone, and pathological examination showed the deep margins of the periosteum to be free of tumor cells. The scalp surgical wound was left to heal by secondary intention.

Histological examination of the excisional surgical specimen confirmed a deeply invasive squamous cell carcinoma (Fig. 2). Sections of skin adjacent to the tumor (Fig. 3) showed epidermal atrophy, effacement of the rete ridges, focal basal layer vacuolization, and absent melanin pigment at the dermoepidermal junction. The dermis showed fibrosis, patchy lymphoplasmacytic infiltration, mucin deposition, absence of hair follicles and sebaceous glands, and replacement of follicles by follicular scars. This was consistent with scarring alopecia.1, 2

The patient had previously undergone skin biopsy of the scalp 10 years ago for suspected discoid lupus erythematosus. Review of this pathological specimen showed features consistent with DLE (Fig. 4). There were hyperkeratosis of the stratum corneum with follicular plugging, thinning and flattening of the stratum malpighii, hydropic degeneration of basal cells, and a predominantly lymphocytic infiltrate along the dermal-epidermal junction, as well as around hair follicles and other appendages. Direct immunofluorescence had also revealed granular IgG deposition along the dermal-epidermal junction.

During the patient's inpatient stay, blood tests including complete blood count and biochemical parameters, and C3/C4 levels were within normal limits. Antinuclear antibody (ANA) titer was 1:80. Tumor markers including squamous cell carcinoma antigen, alpha-fetoprotein (AFP), tissue polypeptide antigen (TPA), carcinoembryonic antigen (CEA), CA125, and CA19-9 were not elevated. Radiological and nuclear imaging including plain radiography of the chest, abdominal ultrasound, and bone scan revealed no evidence of metastatic disease. However, a cervical computed tomography scan revealed enlarged right cervical lymph nodes. In addition, a positron emission tomography scan was performed, which showed right cervical lymphadenopathy (2.5 cm in size) with central necrosis and high grade radionuclide activity, highly suspicious of lymph node metastases (Fig. 5a). There was no
evidence of distant organ metastasis. A lymph node biopsy was recommended, but the patient refused further invasive investigations or management due to advanced age.

Following discharge from hospital, the patient was regularly followed up at our Dermatology outpatient clinic, and the surgical wound on her scalp healed well by secondary intention (Fig. 6). Eight months after scalp surgery, the right cervical lymph node remained enlarged clinically. A repeat PET scan was performed 8 months post-surgery, which showed a slight further enlargement of the right cervical lymph node (2.8 cm in size). In addition, a slight further increase in high grade radionuclide activity (about 18% increase) was noted in the right cervical lymph node (Fig. 5b).

DISCUSSION

Squamous cell carcinoma is a locally invasive neoplasm of the skin that occasionally gives rise to distant metastases. A variety of factors may predispose to squamous cell carcinoma, including precursor lesions (such as actinic keratosis and Bowen’s disease), ultraviolet exposure, ionizing radiation, environmental carcinogens (such as arsenic and aromatic hydrocarbons), human papilloma virus, immunosuppression, and scars. Historically, SCC has been associated with both burn scars and chronic ulcers.

Development of SCC in lesions of DLE has been observed rarely. The majority of early reports were from white populations, but subsequently this complication has been described in black patients. The scarcity of reports of Orientals with SCC arising from DLE lesions may be a result of under-reporting or may indi-
cate a real genetic difference in susceptibility. A review of patients with chronic DLE and SCC revealed a latent period of 7-30 years between the onset of chronic DLE and the development of SCC, with a median of 18 years.

While cutaneous SCC is usually easily treatable, it has the potential to recur locally and even metastasize, then leading to significant morbidity and mortality. Therefore, it is important to identify those tumors that are more aggressive and require further staging, closer follow-up and possible adjunctive treatments such as micrographic surgery, lymphadenectomy, or radiation therapy. The course of squamous cell carcinoma arising from actinically damaged skin is relatively less aggressive, with a metastatic rate of 2 to 6%, while SCC originating in scars is high risk, with metastatic rates approaching 40% in some studies. SCCs arising from chronic DLE were found to have a 21% recurrence rate and 31% metastatic rate.

SCC is regarded as ‘high risk’ under certain situations, including location on the ear, lip, or scalp, diameter larger than 2cm, depth greater than 4mm, tumor involvement of bone, muscle or nerve, tumor arising in a scar, poor differentiation, rapid growth, patient immunosuppression, and absence of inflammatory infiltrate. The patient as described in this report is regarded as high risk because of large diameter and depth of lesion, scalp location, and having originated from a scar.

SCCs developing from scars are high risk for a number of reasons. Poor vascularization and lymphatic supply of scar tissue allows SCCs to grow without the usual limitation by the person’s immunologic resistance. The scar therefore represents an immunologically privileged site, with the scar impeding natural immunosurveillance. Patients with a lymphocytic infiltrate around the tumor were more likely to survive since they had mounted an immunologic attack on the tumor and restricted its spread. Our pathological specimen showed a moderate peri-tumoral lymphocyte infiltrate, indicating that a certain degree of immunosurveillance may still be active in limiting the spread of SCC in this patient.

SCCs that are regarded as high risk require more aggressive management. Surgical excision necessitates a 4 mm margin for low-risk SCCs with depth < 2 mm, and 6 mm margin for lesions with depth > 6 mm or diameter > 1 cm. In addition, careful formal staging is required for high risk SCCs, including CT or MRI, Gallium scan, PET scan, and sentinel lymph node biopsy or radical lymph node dissection. More frequent patient follow-up is also required. In our case, cervical CT scan and PET scan revealed high risk of right cervical lymph node metastasis. A repeat PET scan 8 months after surgery showed a slight further increase in size and radionuclide activity in the right cervical lymph node, and a progression of cervical lymph node metastatic disease was suspected.

We propose several factors which may predispose this patient to the development of SCC. Firstly, DLE represents a chronic inflammatory skin condition with repetitive injury (by inflammatory cells) and regeneration of the basal layer of the epidermis, which may increase the likelihood of neoplastic transformation. Secondly, the combined presence of alopecia and post-inflammatory hypopigmentation (with a decrease in protective melanin) predispose the skin to ultraviolet damage. We believe that the first mechanism (chronic inflammation and scarring) may play a more important role in tumorigenesis in this patient since she denied frequent sun exposure in the past.

In recent years, whole-body 18F-fluorodeoxyglucose positron emission tomography (FDG PET) has emerged as a valuable imaging modality in clinical oncology, which has had a great impact on the diagnosis, staging, provision of prognostic information, assessment of therapeutic response, and early detection of recurrence in various cancers. The clinical use of FDG PET is based on the premise that cancer cells exhibit a higher glycolytic rate than do non-neoplastic cells. Since glucose metabolism is greatly increased in malignant tumors, PET has a high sensitivity and high negative predic-
tive value.\textsuperscript{16,17}

However, there have been only a few reports of FDG PET in cutaneous cancers, except for melanoma and lymphoma. In a study of 12 cases of SCC, Cho et al.\textsuperscript{18} found that PET imaging accurately detected primary lesions as well as lymph node and distant organ metastases. They therefore concluded that PET is useful as a baseline workup study for patients with cutaneous SCC, and suggested further comparative studies on the cost-effectiveness between sentinel lymph node biopsy and PET in SCC patients.\textsuperscript{19} Since FGD PET is noninvasive and a whole-body imaging modality that can detect not only regional lymph nodes but also distant organ metastases, it may be clinically useful in the baseline workup of high-risk SCC patients.

This report illustrates the importance of continued monitoring of patients with DLE for possible development of cutaneous malignancies such as squamous cell carcinoma. SCCs arising from chronic DLE scars have greater invasive and metastatic potential, and therefore require more careful staging, greater excision margin, possible adjunctive treatments, and closer follow-up. Since skin cancers generally have low metastatic potential (except for melanoma), staging with PET scan is rarely required. However, PET may be clinically useful in the management of a subset of patients with high risk cutaneous SCCs (such as those arising from chronic inflammation and scars).

REFERENCES