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CASE REPORT
Reconstructive

High Aggressive Herpetiform Squamous Cell Carcinoma

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We describe a highly aggressive squamous cell carcinoma that presents in a dermatome pattern shortly following shingles and review the literature on herpetiform lesions. *(Plast Reconstr Surg Glob Open 2015;3:e522; doi: 10.1097/GOX.0000000000000475; Published online 23 September 2015.)*

LITERATURE REVIEW

We review the literature on varicella zoster virus (VZV), its oncogenic potential, and cutaneous malignancies presenting as herpetiform lesions.

VZV is a member of the herpesviridae family. It is known to cause 2 distinct clinical entities: varicella and herpes zoster. The virus infects dorsal root ganglia and remains latent until reactivated. Herpes zoster typically presents with pain in a dermatome followed by a maculopapular rash, which evolves into vesicles and then pustules. This rash usually dries with crusting in 7–10 days.[1]

It is well documented that several members of the herpesviridae family are oncogenic: herpes virus type 8,[2] Epstein-Barr virus (EBV),[3] cytomegalovirus (CMV), and herpes simplex virus types 1 and 2 (HSV 1 and 2).[4] CMV, EBV, and HSV 1 and 2 all induce transformation in culture,[5] and HSV 2, CMV, and EBV have been reported with human malignancies.[2–4]

VZV has also been shown to induce transformation in mammalian cells in vitro.[6] An animal model study demonstrated oncogenic effects of VZV and its products on the mouse cervical cells.[4] However, there is no epidemiological evidence to suggest that VZV is an oncogenic virus.[4]

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There are several cases of initially diagnosed primary internal cancers developing cutaneous zosteriform metastases.[7–14] This is a very rare presentation, with internal malignancies only developing cutaneous metastases in 2.5%–5% of cases.[9] The rate of zosteriform metastases is rarer still.[15]

The literature describes only one case of squamous cell carcinoma (SCC) that has occurred at the site of previous herpes zoster. This scalp SCC developed several months after the initial shingles episode[16] and was diagnosed as a Marjolin ulcer.

The exact mechanism of zosteriform metastasis is unknown, but a number of theories are speculated, such as perineural lymphatic spread,[17] surgical implantation,[18] "Koebner-like" reaction (decreased immunity) at the site of prior herpes zoster infection,[19] and spread via fenestrated vessels of the dorsal root ganglia.[20]

The literature grossly describes internal malignancy with cutaneous metastases as the likely cause of zosteriform carcinomas, but there is little detail regarding VZV and cutaneous malignancy.

CASE REPORT

An 86-year-old man presented with an 8-week history of a nodular herpetiform lesion over a right T5-7 dermatomal distribution not crossing midline (Fig. 1), with prodromal neuralgia.

His medical history includes bowel cancer—resected in 1998, preauricular melanoma—excised in 2006, and lower lip SCC—excised in 2010 with postoperative radiotherapy.

His local medical officer diagnosed him clinically with shingles at 2 weeks, but at 6 weeks post onset, the lesion was biopsied and revealed a moderately differentiated SCC, and he was

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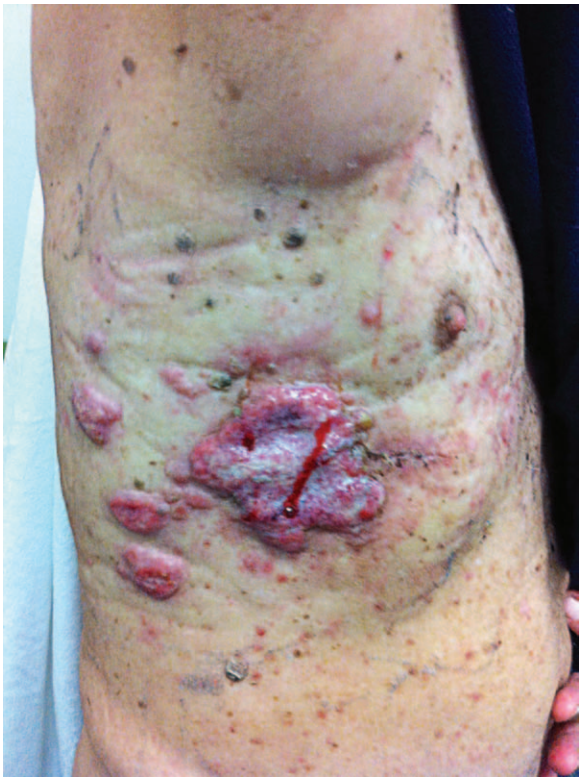

Fig. 1. Right T5-7 dermatome lesion prior to excision 10 weeks after initial onset.

referred to the Gold Coast Hospital, Plastic Surgery Department.

Wide local excision with 1-cm margin was performed with split-thickness skin graft repair. The lesions spanned 140 mm with the largest lesion measuring 94×82×12 mm (Fig. 1).

Histology revealed invasive SCC with extensive lymphovascular invasion throughout with a lesser degree of perineural invasion invading to a depth of 10 mm, with some areas of tumor bearing numerous small vesicles within the epidermis and surface ulceration. Viral serology was performed on the specimen, but there was no evidence of herpes zoster virus present at this late stage.

A staging computed tomography was performed—revealing pulmonary nodules and right axilla lymphadenopathy.

Fine needle aspiration of the axilla lymph node revealed well-differentiated SCC. Multidisciplinary team meeting and patient's wishes decided not for further surgical treatment, chemotherapy, or radiotherapy.

DISCUSSION

This case is unique, presenting with a massive, rapidly growing lesion within the dermatomal distribution of previous clinically diagnosed shingles and metastasizing in a very short period of only 8 weeks.

The typical shingles presentation in this case that describes resolving neuralgia 4 weeks post onset favors shingles rather than perineural invasion causing neuralgia.

In light of such a short latency period, an alternative explanation is that this was an SCC presenting as a zosteriform lesion with perineural invasion causing neuralgia. The pathologist highlighted the SCC's extensive lymphovascular invasion throughout which he described as clinically mimicking shingles, which would lend support to this theory. However, the neuralgia resolved, while the lesion persisted, challenging this hypothesis.

This may have been a dermal metastases from the previous lip SCC that metastasized to the lung and then manifested as a dermal metastasis. This explanation is made less probable by absent cervical lymphadenopathy on staging CT, clear excision margins, and postoperative radiotherapy treatment. However, in 15% of cases, distant metastasis is possible without regional lymphadenopathy.[22]

The metastasis and the involved axillary node highlight the aggressive nature of this SCC and also support the theory of this large lesion being the primary SCC and the cutaneous zosteriform metastasis theory less likely.

We raise the question of VZV inducing SCC. VZV comes from the herpesviridae family well known for its link to cancer in humans.[2–4] Additionally, animal models have proved its oncogenic potential.[4] This case and the case described by Mishra and Raji[16] challenge current epidemiological studies regarding VZV's cancer causing potential in humans.

Alternatively, the Koebner phenomenon is a valid explanation, describing VZV and SCC arising simultaneously in these dermatomes with the concurrent immunosuppression of the VZV contributing to uncontrolled metastasis of the SCC.[20]

The timeline of presentation, where active croppings of vesicles for polymerase chain reaction assay analysis had resolved, makes it difficult to prove definite prior VZV; however, the clinical findings were classical. Skin cancers typically take longer than 7–10 days to develop or at least become clinically evident; hence, making true VZV diagnosis as a prelude to skin cancer is challenging. The patient in this case report was serologically tested postoperatively to further support the diagnosis of shingles. Immunoglobulin G antibodies to VZV were proven; however, even this cannot unequivocally prove that the lesion was VZV but does add weight to the diagnosis.

The natural history of malignancies presenting in a prolonged timeframe makes any laboratory-based

diagnosis of precursor VZV difficult. Clinical diagnosis is, therefore, the most reliable tool in documenting previous VZV.

In the authors' opinion, if VZV is not the primary oncogenic agent, then it was innate in the evolution of this highly aggressive SCC in the shingles' affected dermatomes, as suggested by the Koebner phenomenon.[20]

CONCLUSIONS

This case report highlights the possibility of VZV's oncogenic potential in humans as already established in animal models.[4] After our experience with this case, we would recommend early biopsy of suspicious lesions arising in a zosteriform distribution. Early complete excision of carcinoma is recommended, as it may represent a more aggressive variant than the "common SCC." CT staging should also be considered, as the lesion could represent the cutaneous manifestation of widespread metastasis.

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