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Case Report

Wolf's Isotopic Response in a Post Herpes Zoster Patient Forming Superficial Basal Cell Carcinoma

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Abstract

Basal cell carcinoma (BCC) is a common cutaneous malignancy in Caucasians but has a low incidence in Indian skin. Most commonly, BCC is found in sun-exposed areas, with intermittent ultraviolet exposure as a major risk factor. Although rarely fatal, BCC can cause tissue damage if left untreated. Varicella zoster virus affects both nerve endings and skin, thereby presenting as a rash that may resolve with persisting pain as a symptom. Wolf's isotopic response (WIR) phenomenon is the formation of a new unrelated disease in the area of a previously healed disease. A 72-year-old housewife with a clinical history of resolved herpes zoster on the scalp presented with an erythematous, atrophic lesion with crusting and fissuring. The post-herpetic neuralgia gradually resolved, but the lesion was not responding to any form of treatment. The histopathological examination demonstrated a picture consistent with superficial basal cell carcinoma. The neurotransmitters released by the nerve endings during an episode of varicella alter the immune control process. This can be a probable cause of a second, unrelated disease, i.e., viral activation in a specific ganglion may alter local immunity, therefore triggering a neoplastic transformation.

Keywords

Wolf's Isotopic Response Phenomenon, Basal Cell Carcinoma, Varicella Zoster

1. Introduction

Basal cell carcinoma is a common cutaneous malignancy affecting one in five Americans, though the incidence of BCC in Indian skin is low. [1, 2] Gross differences are noted in the percentage of skin cancer in the Asians (2-4%) and Blacks (1-2%) as compared to the Caucasians (35-40%). [3] Major contributory risk factors include intermittent rather than constant ultraviolet (UV) exposure, and a possible role of arsenic and pesticides. [2] Most commonly, BCC is found on the sun-exposed areas, typically presenting as a gradually increasing, shiny, pink- or flesh-coloured papule or a nodule with surface telangiectasias. [1] Although rarely fatal, it can cause tissue destruction if not treated or if the treatment is delayed. Varicella simplex viruses are epidermoneurotropic viruses that affect both skin and nerve endings. These viruses and the neurotransmitters released by the nerve endings cause changes in the immune control process. [4] This can cause formation of a dermatosis in an area previously affected by varicella virus that has now completely healed. This is called Wolf's isotopic response. [5] Although such presentations are rare and underreported, this case report highlights the importance of regular follow-up in these patients.

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2. Case Presentation

A 72-year-old housewife presented to our clinic with a history of herpes zoster (HPZ) involving the mandibular division of the trigeminal nerve (V3), with severe neuralgic pain on the left side of the scalp in October 2021. The herpetic lesions had resolved within three weeks with anti-viral treatment prescribed by a dermatologist. Two to three weeks later, she had complaints of the formation of a single, progressive lesion at the same site. She had consulted a dermatologist before presenting to us, where she was diagnosed as a case of post-herpetic neuralgia (PHN) with sebopsoriasis. The patient had been put on 100mg gabapentin for PHN and 0.05% clobetasol with sertaconazole nitrate cream on alternate nights. After four months, the patient presented to us with a single lesion associated with brown crusting and pain on the left side of the scalp (Figure 1). The PHN had slowly reduced, but the lesion had a nil to negligible response to the previous medication. The lesion was well defined, 4x4 cm in size, erythematous, associated with adherent brownish crusting, fissuring, and atrophy. She was put on seratconazole nitrate cream daily, ciclopirox and zinc pyrithione shampoo twice weekly, oral itraconazole 100mg twice daily for 3 weeks, and oral vitamin B12 supplements. It was also observed that the patient had female pattern hair loss and had complaints of photo-sensitivity; hence, an oral biotin supplement was also added. The patient showed no improvement after three weeks. Hence, topical salicylic acid ointment was added along with the previous treatment to remove the crust for dermoscopy. Leaf-like, bulbous extensions forming the border of the lesion, along with well-defined grey-brown dots scattered within the lesion, were observed. (Figure 2) The patient was counselled for a skin biopsy from the border of the lesion with differential diagnosis of basal cell carcinoma, cutaneous sarcoidosis, lichen simplex atrophicus, and actinic porokeratosis. Histopathology revealed increased pigment deposits, mitosis, and an increased basaloid cell proliferation with retraction artefact at the dermo-epidermal junction (DEJ). These features are diagnostic for BCC. (Figure 3) The patient was referred to an oncology surgeon for wide excision of the lesion with full-thickness skin grafting from the lateral aspect of the left thigh under general anaesthesia. The patient visited us about a month later with contact pustulosis due to neomycin ointment on the recipient site, which resolved after treatment with 10 days of oral doxycycline. (Figure 4).

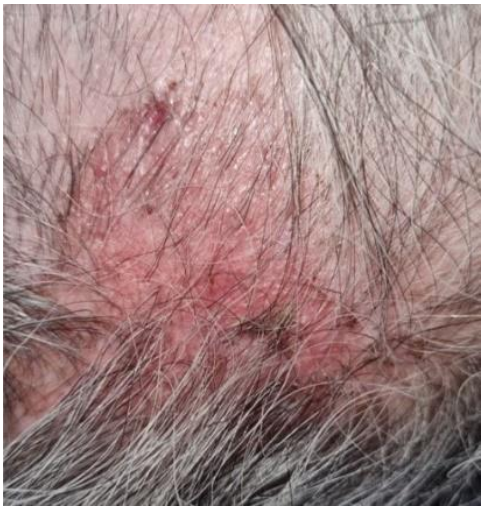

Figure 1. *A single lesion on the left side of the scalp with brown crust and associated pain.*

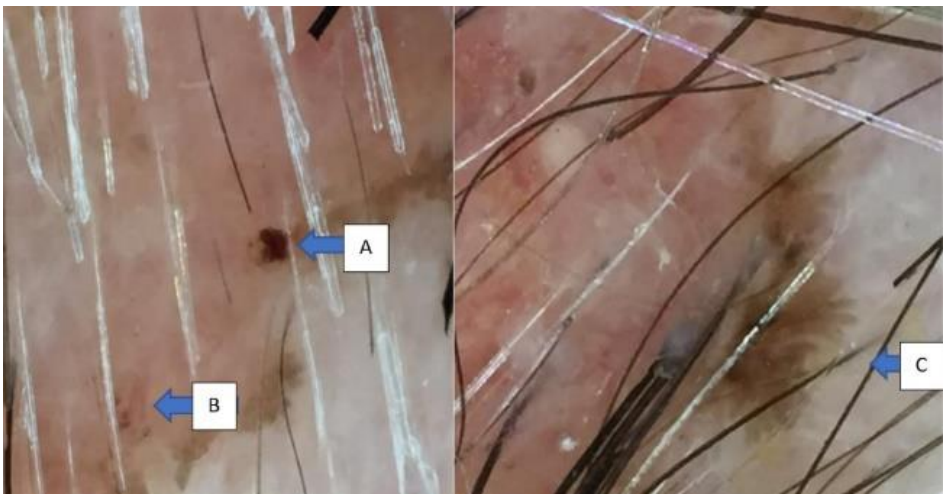

Figure 2. *Dermoscopic findings: well-defined grey-brown dots scattered within the lesion (arrow A and arrow B). Leaf-like (Maple leaf-like), bulbous extensions forming the border of the lesion (arrow C). Maple leaf-like areas and brown to blue-grey dots and globules are among the classic BCC-associated dermoscopic features.*

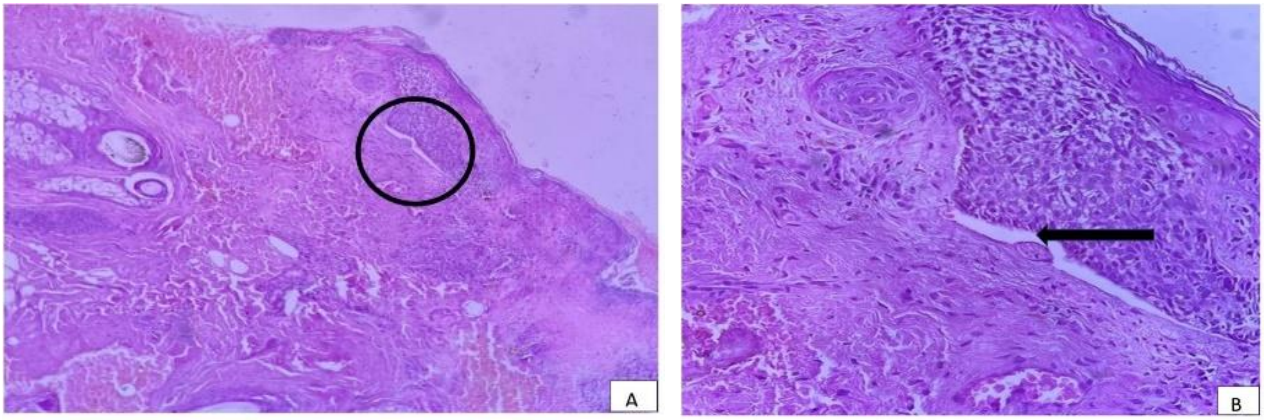

Figure 3. *Skin biopsy from the border of the lesion. (A) Haematoxylin and Eosin stain, 40X scanner view. (B) Haematoxylin and Eosin stain, 100X: increased pigment deposits, mitosis, and an increased basaloid cell proliferation with retraction artefact at dermo-epidermal junction (DEJ).*

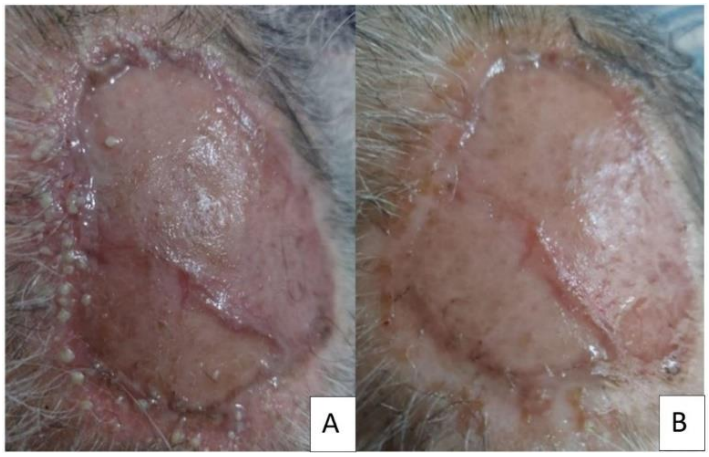

Figure 4. *(A) Contact pustulosis due to neomycin ointment on the recipient site. (B) Resolution of contact pustulosis after treatment with 10 days of oral doxycycline.*

3. Discussion

Table 1. *Reported cases of diseases demonstrating Wolf's isotopic response.*

Primary disease	Secondary lesions
Herpes simplex virus infection [6]	Urticaria
Herpes zoster virus infection [7, 9, 11, 12]	Chronic GVHD, Acquired perforating folliculitis, Granuloma annulare, acne and comedones, lichen planus, Morphea, linear IgA disease, fungal granuloma, psoriasis, squamous cell carcinoma, basal cell carcinoma, herpetiform pemphigus
Dermatophytosis [6]	Lichen planus
Scrofuloderma [6]	Herpes Simplex Virus infection
Contact dermatitis [9, 13]	Bullous lichen sclerosis et atrophicus, Lichen planus

Wolf's isotopic response (WIR) describes the occurrence of a new, unrelated disease at the same location as a previously healed disease. [5] Various diseases have been reported to demonstrate WIR (Table 1). HPZ is the most common pri-

mary disease to induce WIR. [7] Although the pathogenesis remains unclear, several theories have been proposed. Wolf *et al* suggested that two diseases affecting the same area can be a reason for the decrease in the local resistance of that area, and such an event can be caused by two different unrelated stimuli (e.g., HPZ on exposed area due to viral activation in a particular ganglion, followed by carcinoma due to previous sun exposure). [5] Viral, vascular, immunologic, as well as neural hypotheses have been suggested for WIR. Some authors believe that an exaggerated immune response to viral antigens, immune complex deposits, or altered local antigens might play a role in the mechanism of WIR. This might be due to the long-term immunologic changes caused by the primary disease that make the skin vulnerable to the second disease. [5] In HPZ, the nerves might not be directly involved in the pathogenesis of the second disease, but the influence of the nervous system through interaction with the immune system can be a cause. Secretion of neuropeptides from sensory fibres in the skin affects the mast cells, T lymphocytes, monocytes, and endothelial cells. [8] Wang *et al* evaluated 24 patients with WIR post HPZ and proposed that the mechanism of neuro-immune destabilization at the site of HPZ is caused by the continuous immunological effect of the persisting viral DNA. [9] The new dermatosis can be anything ranging from a granulomatous reaction to a malignancy and vascular tumors. [10] There have been a few case reports of formation of BCC after HPZ. Formation of nodular BCC six months after HPZ has been reported. [11] (Figure 5).

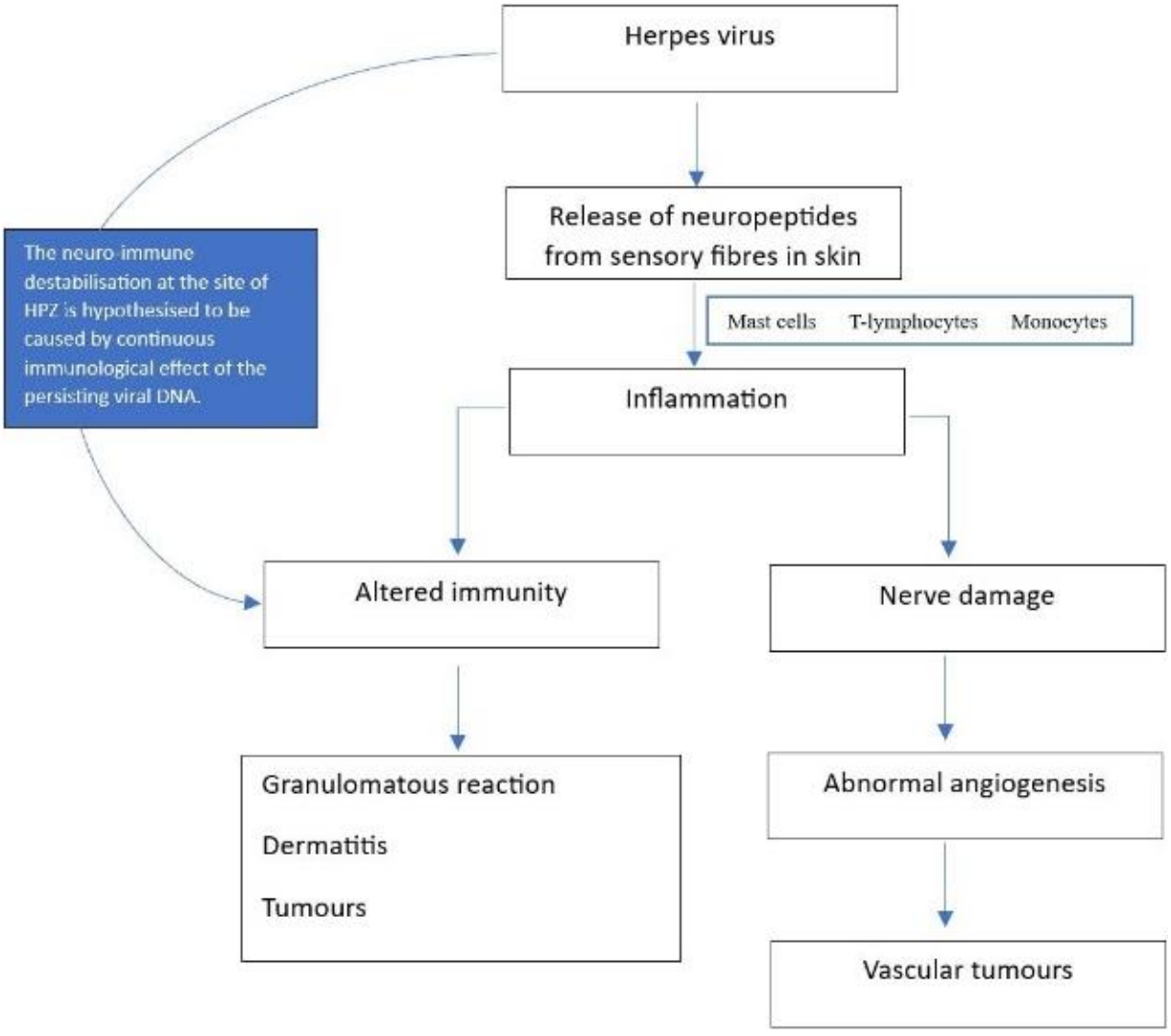

Figure 5. *Suggested hypothesis of pathogenesis of Wolf's Isotopic Response.*

Superficial BCCs commonly occur on the trunk with a predilection for shoulders, chest, or back. Sometimes multiple lesions can be present. They are particularly slow growing, often flat, well-demarcated, pink to red in colour, scaly macules or plaques which may have telangiectasias. Clinically, the lesions can appear similar to inflammatory dermatoses such as eczema or psoriasis. Therefore, one should consider the diagnosis of superficial BCC in case of a persistent, erythema-

tous, and scaly plaque. There are also pigmented variants of superficial BCC. Portions of superficial basal cell carcinomas can evolve into nodular BCC over time. [1, 4] There have been various cases reporting the formation of BCC and other malignancies secondary to a previous lesion or trauma (Table 2).

Table 2. *Reported cases with neoplasms presenting as secondary lesions.*

Primary disease	Secondary lesions
Herpes Zoster [10, 11, 13-17]	BCC and Bowenoid papulosis Acute myeloid leukemia
Vitiligo [18]	BCC
Nevus sebaceous [19]	BCC
Hirudiniasis [20]	BCC
History of trauma (burn, sharp or blunt trauma, varicella scars, vaccination sites) [21-23]	SCC and SCC
Chronic radiodermatitis [24]	BCC

The presence of a treatment-resistant dermatosis on the same site as HPZ, and dermoscopic findings indicative of superficial BCC, prompted a skin biopsy in our patient. WIR is a known entity in dermatology, but the patho-mechanism of this phenomenon remains elusive. There are a few case reports demonstrating WIR post HPZ forming BCC, hence making this a rare case report worth noting. Such case reports become pertinent is elucidating further studies on the pathology of WIR.

Abbreviations

BCC	Basal Cell Carcinoma
UV	Ultraviolet
HPZ	Herpes Zoster
PHN	Post-Herpetic Neuralgia
DEJ	Dermo-Epidermal Junction
WIR	Wolf’s Isotopic Response

Declaration

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient (s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Conflicts of Interest

The authors declare no conflicts of interest.

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