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Letter to the Editor

Post Herpes zoster dermatome/s – A therapeutic ground for cutaneous T-cell lymphoma (CTCL) & Stevens–Johnson syndrome/toxic epidermal necrolysis (SJS/TEN)

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The term isotopic response was coined by Wolf et al. in 1995 to describe the occurrence of a new skin disease at the site of a previous, unrelated and already healed cutaneous disorder [1]. Dermatome/s that have been infected by herpes zoster virus become breading sites for a subsequent development of heterogeneous skin disorders, the occurrence of which generate the well-defined 'Wolf's post-herpetic isotopic response' [2,3].

Alongside the large number of cases of post-herpetic isotopic response, there are also few reports of generalized skin disorders which spared exactly the cutaneous areas that had been subjected to herpes zoster virus infection [4]. These peculiar observations, apparently pave the way to introduce a new entity called isotopic nonresponse (Wolf's post-herpetic isotopic nonresponse') [3,4].

So far only four cases have been described in medical literature that could be categorized under Wolf's post-herpetic isotopic nonresponse' related to post herpetic dermatome sparing cutaneous T-cell lymphoma (CTCL) and Stevens–Johnson syndrome/ toxic epidermal necrolysis (SJS/TEN) (Table 1) [5-7].

Immune reactions associated with CTCL

CTCL is characterized by the accumulation and clonal proliferation of malignant, epidermotrophic, CD4+/ CD45ro+ (Helper/Memory) T lymphocytes that interact with keratinocyte within the lesion. These keratinocytes are atypical in that they express ICAM-1 plus MHC-11. They also produce increased amount vascular permeability and increase the effectiveness of other keratinocytes attractants for lymphocytes, such as IL-8. Thus, these lesional keratinocytes have an enhanced ability to interact with epidermotrophic, malignant T lymphocytes, which tend to produce a T helper-2 cell cytokine profile [8].

There is evidence that CTCL cells may home to the epidermis as a result of their interaction with LC (an immature member of the dendritic cell lineage). Dendritic cells (OKT6+, now CD1a+) were interspersed among the dermal and epidermal infiltrates of CTCL has been described by Chu et al [9]. Various other researchers have shown that epidermotropic lymphocytes are closely associated with LCs [10,11].

Immune reactions associated with SJS/TEN

SJS/TEN is categorized as a cytoplasmic immune reaction targeted at the destruction of keratinocytes expressing foreign antigens. In both erythema multiforme and TEN, epidermal keratinoytes express intercellular adhesion molecule-1 (ICAM-1) and major histocompatibility complex-1 (MHC-1) antigens [10]. Cytotoxic T lymphocytes (mainly CD8) expressing the skin homing receptor and cutaneous lymphocyte antigen is the major effector cell in this process. It has been proposed that drug or their metabolites act as haptens, and drug-specific CD 8 cells secrete interferon-gamma which facilitate keratinocytes antigenic to produce tumour necrosis factor-alpha (TNF α), Fas ligand (FaSL), interleukin-6 (IL-6) and IL-10. TNF-alfa up-regulates expression of MHC-1 and MHC-11 molecules, which increase exposure of keratinocytes to

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Table 1: Summary of the reported cases relevant to Wolf's post-herpetic isotopic nonresponse sparing CTCL & SJS/TEN

Case no.	Age & sex of patient	Herpes Zoster affected dermatome	Interval between Herpes zoster and	Second cutaneous disease	Site involved (sparing site)
1.Twersky et al 2004. [5]	58 Male	Left T8	3 weeks	Cutaneous T cell lymphoma	Left side abdomen
2. Kannangara et al 2008 [6]	62 Male	Left C3–C4	3 months	Cutaneous T cell lymphoma	Left upper arm & anterior chest
3. Kannangara et al 2008 [6]	53 Female	Left V1, V2	2 months	SJS-TEN	Left upper face
4. Tenea D 2010. [7]	39 Female	Right T8-T9	4 weeks	SJS	Right lower abdomen

cytotoxic T cells (CTLS) [12]. Cytotoxic T lymphocytes can induce apoptosis through perforin/granzyme caspase cascade leads to cell destruction [13,14].

Proposed mechanisms of post herpetic dermatome/s sparing TEN/SJS & CLCL

One possible mechanism states that Immunohistochemistry of the previous zoster lesion showed a notable reduction in LC in the area clinically spared by the CTCL. If an LC-Tcell interaction is essential to proliferation of the lymphomatous cell line perhaps the decrease in LC in the previous herpes zoster dermatome leads to less epidermotropism of CTCL to the local area concern [6].

The second proposed theory is that down-regulation of MHC-1, MHC-11 and ICAM-1 expression in HZV-infected keratinocytes has been proved [15]. Thus, the reduction or inhibition of ICAM-1 expression on keratinocytes by HZV most probably attenuates the keratinocytes to function as antigen-presenting cells and inhibit its role in LFA-1/ICAM- 1-mediated T-cell response. This down-regulation would have probably prevented the SJS-TEN and CTCL involving on previously HZV-affected area [6].

Considering existing facts I would like to state that Post Herpes Zoster dermatome/s eventually behave as a therapeutic ground for dermatosis like CTCL and SJS/TEN. As clinicians we should emphasize more weight on this unique phenomenon and encourage researches who are engaging in discovery of new pharmaceuticals for these two serious skin diseases to turn eyes to proposed mechanism for this skin reaction.

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