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## Photo Vignette

### Zosteriform lichen planus after herpes zoster: report of a new case of Wolf's isotopic phenomenon and literature review

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## Abstract

The Wolf's isotopic phenomenon corresponds to the occurrence of a skin disease at a body site affected previously by a different, already healed dermatosis. We report a 74-year-old man who presented with a zosteriform eruption consisting of erythematous-scaly, slightly pruritic papules on the right flank some weeks after herpes zoster (HZ) had healed on the same area. Histologic examination showed typical changes of lichen planus, confirming the diagnosis of post-HZ zosteriform lichen planus (ZLP). The lesions regressed with topical steroid treatment. Zosteriform lichen planus (ZLP) is one example of Wolf's isotopic phenomenon appearing after HZ. So far, only 17 cases have been reported in the literature. The precise pathogenesis of ZLP is not well known, although persisting viral proteins could be responsible for the hypersensitivity reaction. We review and discuss the salient clinicopathologic features of this rare entity based on a thorough literature review.

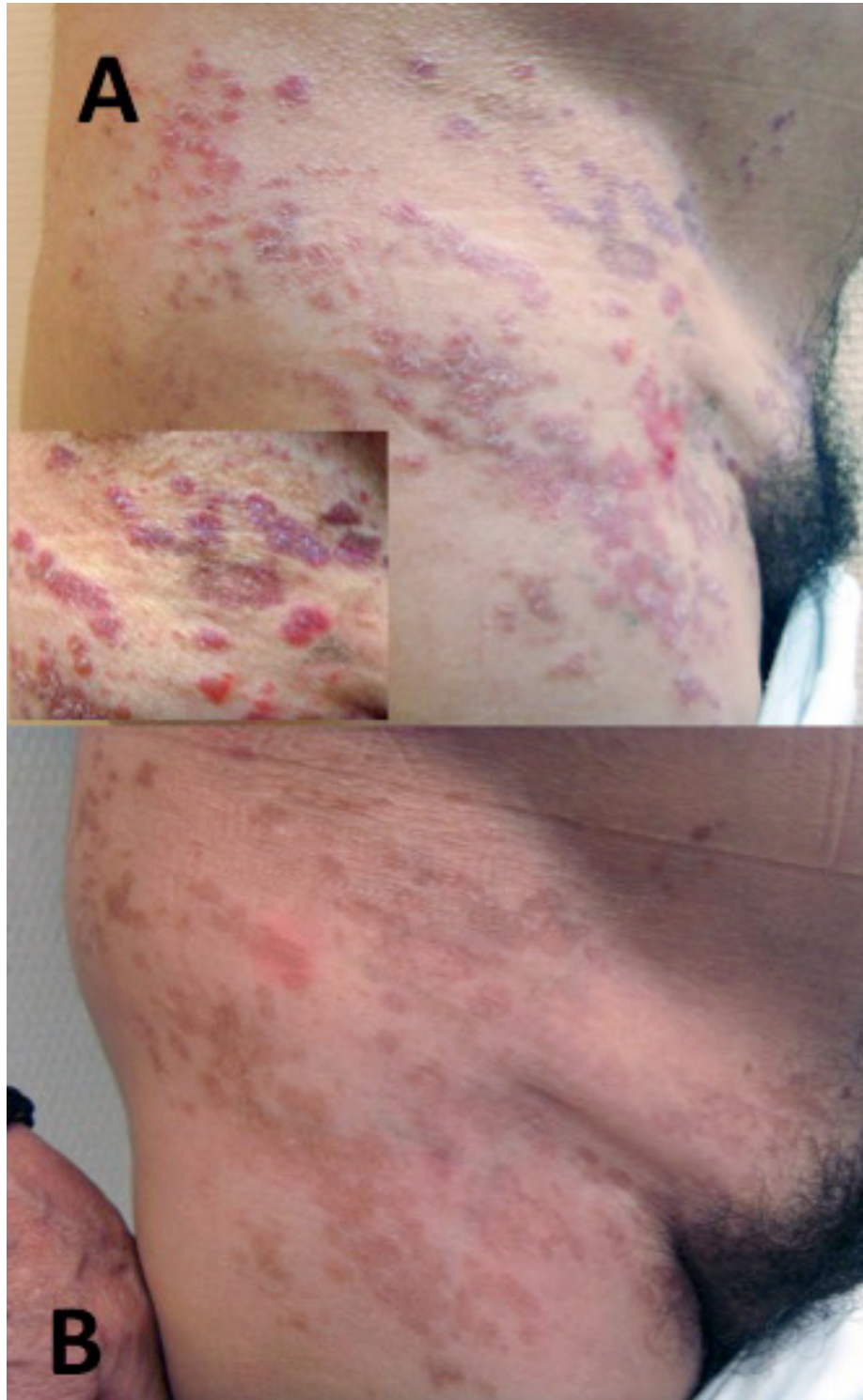
## Introduction

The term « isotopic phenomenon » (from the Greek *ισον* : equal, *τοπος* : site) was coined by Wolf et al in 1995 [1] and refers to the occurrence of a skin disease at a body site affected previously by another unrelated and already healed dermatosis. It is different from the Koebner (or isomorphic) phenomenon, describing the appearance of the same disease at another location (from the Greek *ισον*: equal, *μορφή*: aspect) [1,2]. The isotopic phenomenon was in fact first described in 1955 by Wyburn-Mason, a neurologist who reported 26 patients who developed malignant tumors at the site of a previous herpes zoster (HZ) or herpes simplex infection [3]. Since then, several dermatoses have been reported to occur following HZ ; they include squamous- and basal-cell carcinomas, leukemic/lymphomatous infiltrates, Kaposi's sarcoma, angiosarcoma, metastases from internal malignancies, granulomatous dermatoses (including granuloma annulare, granulomatous vasculitis, sarcoidal granuloma and granulomatous folliculitis), comedones, xanthomatous changes, acneiform eruption, allergic contact dermatitis, eosinophilic dermatosis, dermatophytosis and viral warts [1,2,4]. Lichen planus following HZ as an expression of the isotopic phenomenon has only rarely been described. We report here a new typical case and review the relevant literature.

## Case synopsis

A 74-year-old French man was referred to us for an eruption of the right flank that had developed progressively after HZ was diagnosed by his family physician and treated with topical acyclovir and oral valacyclovir several weeks prior to consulting us. The eruption consisted of red-violaceous scaly papules arranged in zosteriform plaques over the right flank, the right side of the pubis, and the right inguinal fold (Figure 1A). The lesions were mildly pruritic but not painful. No other skin or mucosal lesions were found. The patient recalled having developed HZ over the same body area 10 years before; this had healed uneventfully following systemic therapy. His past medical history additionally included tuberculous meningitis at the age of 10 years treated successfully with streptomycin. Family history was non-contributory.

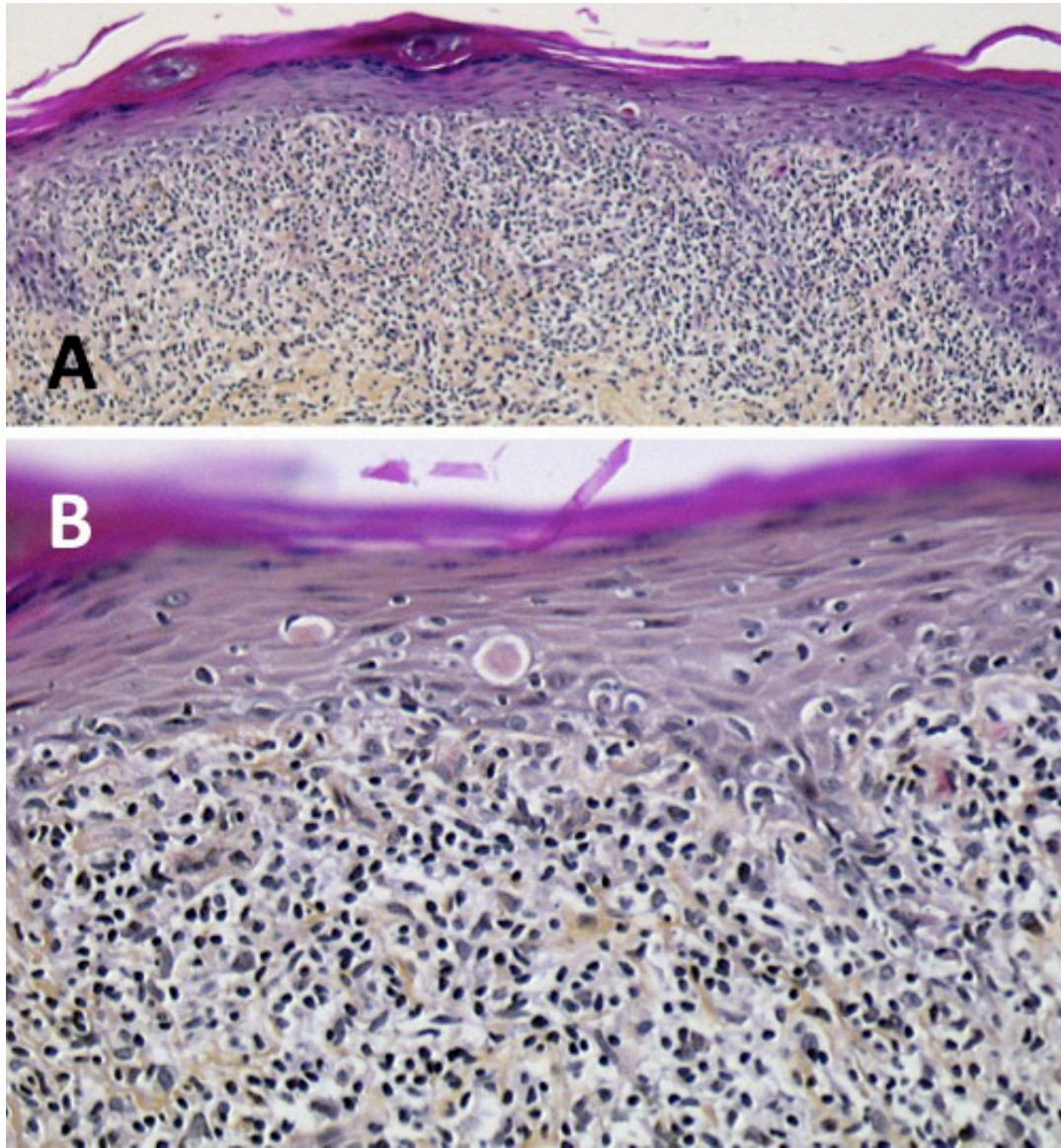
Routine laboratory tests showed raised values of ESR, CRP, and fasting blood glucose. The patient had IgG (but not IgM) antibodies against HSV1 and VZV/HZV (titer 663 IU/mL), showing he had specific immunity to VZV/HZV. Serological tests for HBV and HCV were negative.



**Figure 1.** A. Zosteriform eruption over the flank and pubis : Inset: close-up view showing red-violaceous, scaly papules B : After a 3-month treatment with potent local steroids the lesions regressed leaving residual hyperpigmentation.

A skin biopsy taken from a papule of the flank showed hyperkeratosis (mostly orthokeratotic), hypergranulosis, acanthosis with large spinous layer keratinocytes, lymphocytic exocytosis, basal-cell layer vacuolization, presence of colloid bodies in the lower epidermis and a band-like, dense (lichenoid) infiltrate in the upper dermis made of lymphocytes admixed with some melanophages (Figs. 2A-B). PAS staining was negative. These findings were diagnostic of lichen planus (LP). The patient was

treated with local applications of a potent steroid (clobetasol) during one month. Two months later the lesions had regressed leaving residual, slightly pigmented, asymptomatic macules (Figure 1B).



**Figure 2.** A : Microscopic examination of a skin biopsy shows typical pathologic findings of lichen planus, i.e. orthokeratotic hyperkeratosis, acanthosis, hypergranulosis, and a dense band-like subepidermal infiltrate in the upper dermis (hematoxylin-eosin-saffron stain, original magnification X40). B: On higher magnification, colloid bodies and lymphocytic exocytosis can be seen within the epidermis (hematoxylin-eosin-saffron stain, original magnification X100).

## Discussion

Zosteriform lichen planus (ZLP) is a rare clinical appearance of LP. Its remarkable dermatomal distribution enables clinicians to link it to a preceding episode HZ. Our literature review yielded only 17 such cases with pathological confirmation of LP (Table I). They include 11 men and six women, aged 25-76 years (mean 51.2) [5-17]. ZLP has a predilection for the trunk and legs. The delay between HZ and LP onset is highly variable, ranging from 15 days to 5 years (mean 12.6 months). No concomitant medical conditions were reported, with the exception of one patient with glioblastoma [16] and one with HIV infection [4]. Of note, some similar cases that comprised histologically a mixed lichenoid dermatitis with a granulomatous component [18] were not included in this review as they are not typical examples of LP.

**Table 1.** Clinical features of patients with post-zoster zosteriform lichen planus (nm : not mentioned)

Reference	Age/sex	Delay	Location
4	30/M	4 years	trunk
5	42/M	2 months	lumbar/abdominal
6	40/M	nm	back
7	65/F	nm	left buttock
8	42/F	nm	right side of the body (T6-T12, L1-L4, S1-S2)



9	71/M	6 months	left side of the trunk
10	76/M	2 months	trunk (T11)
11	35/F	2 months	left flank, breast, arm
12	25/M	2 weeks	left groin
13	64/F	nm	left shoulder
14	44/F	5 weeks	left scapular region
15	55/M	nm	left lower limb
16	68/M	6 weeks	right thorax (T10, T11)
17	39/M	5 years	left upper thigh (L2)
17	76/M	12 weeks	left lower leg (L5)
17	26/F	nm	leg (S1)
present case	74/M	several weeks	right flank/pubis

The pathogenesis of this variant of LP appearing in a dermatome previously affected by HZ remains unclear. LP results from a T-cell-mediated autoimmune damage to basal keratinocytes that express altered self-antigens on their surface [19]. Of the many potential exogenous antigens, attention has been focused on the role of viruses, particularly hepatitis C virus (HCV), human herpesvirus (HHV-6), and HHV-7. Indeed, in oral forms of LP, HCV-RNA has been detected by PCR in 93% of lesions and HHV-6 in 67-100% by *in situ* hybridization or immunohistochemistry [19]. Regarding ZLP resulting from WIP, the etiologic agent likely to be involved is varicella-zoster virus (VZV) [5-17]. The presence of VZV antigens and/or DNA in cases of zosteriform isotopic phenomenon was searched for in some studies. In granulomatous lesions of isotopic reactions, Requena et al. [3] could not detect viral genome by PCR. Nikkels et al. [20] studied early granulomatous reactions after cutaneous VZV infections and detected immunohistochemically in all five patients VZV glycoproteins in cells abutting altered vessels, but the corresponding genomic sequences were found by *in situ* hybridization in similar locations in only one of these patients. They concluded that the major viral envelope glycoproteins, rather than complete viral particles, triggered granuloma formation following VZV infection. Regarding ZLP, Mizukawa et al. [17] detected immunohistochemically VZV antigens in the eccrine epithelium of the zosteriform lesions. It seems therefore likely that the isotopic response results from an immune reaction to keratinocytes antigenically altered by the viruses, rather than to a response to the viruses themselves. Moreover, it has been shown that VZV antigens can persist in the eccrine epithelium long (up to 2.5 years) after clinical resolution of HZ, when VZV DNA is no longer detected [21], probably explaining the long delay that can be observed between HZ resolution and ZLP onset. Besides persisting VZV antigens, other factors potentially involved include immunological dysregulation, cutaneous nerve affection, neuropeptide secretion, and altered microcirculation, rendering HZ scars a *locus minoris resistentia*, favoring the expression of (latent) LP [4]. Although nerves are not directly involved in the pathogenesis of LP arising in herpetic scars, an indirect influence of the nervous system through an interaction with the immune system remains possible because there are bidirectional interactions between the nervous system and the immune system. For instance, neuropeptides released from cutaneous sensory nerves can exert various effects on mast cells, T lymphocytes, monocytes, and endothelial cells [1,22].

Although clinically similar, ZLP should not be confused with linear lichen planus (LLP) because the two forms are distinct [23,24]. In LLP, the lesions develop secondary to trauma (isomorphic phenomenon) and less commonly spontaneously. They may follow the lines of Blaschko, whereas isotopic ZLP follows the dermatomal distribution of a peripheral cutaneous nerve and its branches. Furthermore, contrasting with ZLP, VZV antigens are not detected in LLP [17]. One case of « isotopic LP » possibly related to a dental amalgam was actually LLP because the arrangement of lesions was not zosteriform, but followed the lines of Blaschko [25-28]. Finally, some papers reported cases of ZLP without preceding HZ [29-39]. These were not included in this review for they do not represent examples of isotopic phenomenon.

ZLP is usually treated with topical and intralesional corticosteroids. The lesions regress with a post-inflammatory pigmentation within 4-5 months [11,13].

In conclusion, ZLP as an expression of Wolf's isotopic phenomenon, is rare and its pathogenesis remains still poorly understood. The detection of VZV-DNA within the lesions probably depends on their age, as only early lesions contain viral genome, whereas viral antigens can persist much longer. It seems likely that persisting viral proteins, even in minute amounts, rather than the viral genome, are responsible for this hypersensitivity reaction (additionally to other possible immunological, neural, or vascular triggers that remain to be studied).

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