The Koebner phenomenon

Koebner phenomenon is the appearance of new skin lesions on areas of cutaneous injury in otherwise healthy skin, also known as the isomorphic response (meaning Greek – equal shape). Lesions seen in Koebner phenomenon adopt the same clinical and histological features as the patient's original skin disease. In a true Koebner response, lesions are not secondary to seeding of infectious agents, allergic or irritant reactions (Boyd and Nelder, 1990).

Clinical features

Lesions secondary to Koebner phenomenon can be seen in patients without pre-existing skin conditions and therefore may pre-date the appearance of skin disease. This can assist in clinical diagnosis or alert the clinician to potential skin disease when taking a history.

Patients with Koebner phenomenon also exhibit an 'all or nothing' response (Pedace et al, 1969). A patient exhibiting Koebner lesions on sites of trauma can therefore be cautioned regarding potential reoccurrence at sites of injury or scars. Similarly, a patient with a linked pre-existing condition, such as psoriasis, who does not exhibit Koebner phenomenon to known stimuli, will not exhibit Koebner phenomenon to any cutaneous injury.

Response time and severity of Koebner lesions in psoriasis are variable. In psoriasis, time to appearance of Koebner lesions can vary between 10 to 20 days following cutaneous trauma, with a range of 3 days to 2 years (Shelley and Arthur, 1958). Intensity of lesions can be classified into four grades of response (*Table 1*) (Bizzozero, 1931; Weiss et al, 2002).

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Triggers

Koebner phenomenon triggers include burns, trauma, friction, insect bites, surgical incisions and therapies such as ultraviolet or irradiation (Weiss et al, 2002) (*Table 2*).

Pathogenesis

Pathogenesis remains uncertain and several mechanisms have been postulated, mainly through experimental studies in patients with psoriasis. Histologically, lesions arising in Koebner phenomenon are identical to primary lesions. Trauma-induced lesions in psoriasis will thus also exhibit a T-cell mediated reaction, keratinocyte proliferation, protein synthesis and angiogenesis. How this process is elicited following Koebner stimulus is controversial, but theories include immune, vascular and growth-factor mediated mechanisms (Camargo et al, 2013).

Immune-mediated hypotheses suggest that the primary event may include production of antibodies against the stratum corneum such as α2-microglobulin leading to epidermal hyperplasia (Burch and Rowell, 1965; Camargo et al, 2013). Patients with Koebner phenomenon have a significant increase in CD4:CD8 although the importance of this is unknown (Baker et al, 1988; Camargo et al, 2013). It has been postulated that high CD8 may have an inhibitory role and higher CD4 may lower the threshold for production of plaques.

Histopathologically, psoriasis lesions reveal dilated capillary loops with increased permeability. This is also seen in trauma-induced lesions. It has been suggested that microvascularity can be altered following trauma leading to lesions in a similar fashion (Eddy et al, 1964; Camargo et al, 2013). In support of this, vasoconstrictors such as adrenaline inhibit the Koebner phenomenon.

Nerve growth factor in psoriasis plays an important role in keratinocyte proliferation, angiogenesis, and T-cell activation and migration. Over-regulation of nerve growth factor in basal keratinocytes together with keratinocyte proliferation has been demonstrated in psoriatic plaques induced by trauma, suggesting a possible role in Koebner phenomenon (Raychaudhuri et al, 2008; Camargo et al, 2013).

Fibroblast growth factor within the basal layer and dermal matrix induce a proliferative response in keratinocytes and endothelial cells. In Koebner phenomenon, theories suggest that trauma could result in an increase in fibroblast growth factor leading to appearance of psoriasiform lesions (Sharpe et al, 1989; Camargo et al, 2013).

Which of these immune, vascular or growth-mediated mechanisms play a prime role in pathogenesis is still uncertain and further insight into pathogenesis via the various underlying dermatoses is awaited.

Table 1. Intensity of response in Koebner phenomenon

Koebner response	Intensity
Maximal	Lesions develop across the entire area of injury
Minimal	Lesions develop in focal areas of trauma
Abortive	Lesions appear, but vanish spontaneously after 12–20 days
None	No lesions appear with injury

Table 2. Triggers of Koebnerization

Trauma	Lacerations: surgical incisions, needle scarification, knife injuries
	Excoriation, friction: shaving
	Bites: animal, insect
	Burns: thermal, electrodessication
	Freezing, cryotherapy
	Pressure: orthotics, pressure ulcers, nail manicure
Allergic, irritant or drug reactions	Positive patch test reaction
	Tattoo-associated skin reactions
	Bacillus Calmette–Guérin (BCG), influenza vaccinations
	Hair spray, hair dye allergy
	Iodine reaction
Other	Variety of dermatoses
	Phototherapy, ultraviolet damage
	Immunosuppression
	Irradiation

From Weiss et al (2002)

Associated conditions causing Koebner phenomenon

Koebner phenomenon is most commonly encountered in the context of psoriasis. Around 25% of psoriasis patients have experienced Koebner lesions, most often in patients with unstable psoriasis, young age of onset or who are emotionally distressed. There is a seasonal predominance towards winter, possibly because of the lack of the sun's protective factor. However, no significant correlation with disease activity or severity has been found (Sagi and Trau, 2011).

Koebner phenomenon is most commonly associated with psoriasis but true Koebner phenomenon can also be seen with lichen planus and vitiligo. A true Koebner response, as defined by Boyd and Nelder (1990), should be reproducible and not relate to infectious or allergic or irritant agents. However, Koebner-type lesions have been reported at trauma sites with several dermatoses and these are termed a pseudo-Koebner response (related to seeding of infectious agents such as molluscum contagiosum, or skin breakdown, e.g. pyoderma gangrenosum) or occasional or questionable responses where not all criteria for a true Koebner phenomenon are met (Boyd and Nelder, 1990; Weiss et al, 2002) (*Table 3*).

Table 3. Skin conditions linked to Koebner phenomenon as per Boyd and Nelder (1990) classification

Classification	Examples
True Koebnerization	Psoriasis
	Lichen planus
	Vitiligo
Pseudo-Koebnerization	Viral warts
	Molluscum contagiosum
	Pyoderma gangrenosum
Occasional lesions	Darier's disease
	Erythema multiforme
	Behçet's disease
	Kaposi's sarcoma
	Lichen sclerosis
Questionable trauma-induced processes	Pemphigus vulgaris
	Bullous pemphigoid
	Eczema
	Lichen nitidus
	Dermatitis herpetiformis

Clinical significance

In an examination setting or at the bedside, evidence of the Koebner phenomenon can often give a clue to the underlying diagnosis. Its presence without any pre-existing condition can lead to early diagnosis, allowing preventative measures to be used.

Apart from its importance in clinical diagnosis, the Koebner phenomenon signifies activity of the disease. Its presence of should guide the general physician to advise avoidance of physical trauma or chemical irritants, carefully consider the need for surgical procedures and treat underlying or concurrent diseases (Sagi and Trau, 2011).

In postgraduate examinations, cases are usually encountered in the short cases or clinical consultation setting where a full consultation is required. This will usually be a patient with psoriasis but lichen planus or vitiligo, which are directly linked to Koebner phenomenon, may also be present. This article details how to approach these conditions and Koebner phenomenon.

Psoriasis

Psoriasis affects 1–2% of the UK population. It classically presents with well-defined erythematous plaques with silvery white scale over limb extensor surfaces, scalp, navel and behind the ears. It is important to examine all extensor surfaces in a patient with suspected psoriasis and then move on to other areas. Examine for psoriatic arthropathy and nail changes including nail pitting, onycholysis, transverse ridging and subungal hyperkeratosis. Look carefully for plaques over sites of trauma or surgical scars and see if the Koebner phenomenon is present (*Figure 1*) (Weiss et al, 2002).

Disease-specific pathogenesis with psoriasis that can contribute to Koebner phenomenon involves reactive abnormal epidermal proliferation and inflammation (mainly T-cell mediated) (Camargo et al, 2013).

Vitiligo

Vitiligo affects 0.5–1% of the population, and occurs in all races. In half of sufferers, pigment loss begins before the age of 20 years. It presents with well-demarcated areas of depigmentation, which can affect any part of the skin or mucous membrane. Hair in the affected area will also be depigmented. Histologically, vitiligo shows partial or complete loss of melanocytes. Koebner phenomenon in patients with vitiligo has a predilection for areas that are subjected to repeated trauma or friction, e.g. bony prominences, extensor surfaces of elbows, knees and forearms, dorsal aspects of hands and fingers (van Geel et al, 2012) (*Figure 2*).

Lichen planus

Lichen planus is characterized by pruritic violaceous, flat-topped polygonal papules covered with fine white striae found predominantly on flexor surfaces. There is often associated scalp and buccal mucosa involvement and nail changes such as nail dystrophy and longitudinal ridging. Lichen planus also exhibits Koebner phenomenon and thus these lesions can also be found along cutaneous injury sites such as scratch marks and scars (Weiss et al, 2002).

Figure 1. Koebner phenomenon in psoriasis. Patient with end-stage renal failure, who developed lesions of psoriasis on areas adjacent to arteriovenous fistulae.

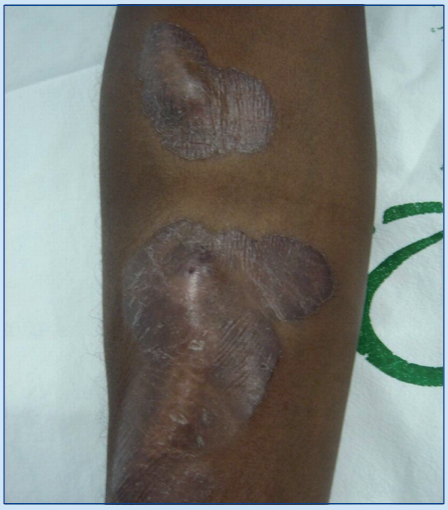
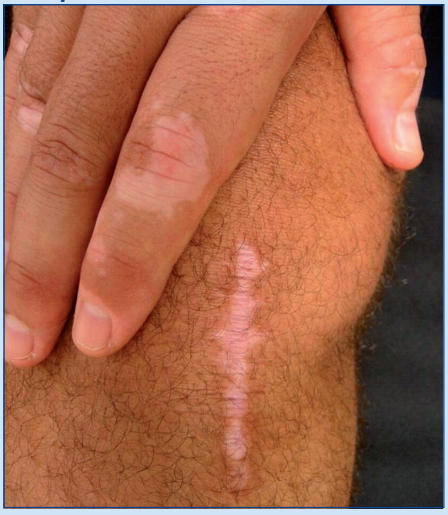


Figure 2. Koebner phenomenon in vitiligo: isomorphic lesion after trauma.



Other conditions that can affect scar sites

Several dermatoses and manifestations of multisystem diseases may appear in sites of trauma or scars. It is important to be aware of the following differential diagnoses in a postgraduate examination setting:

Pathergy

Pathergy is most commonly described in Behçet's disease and pyoderma gangrenosum, and has been associated with Sweet's syndrome. It is characterized by non-specific pustules or papules developing on sites of trauma. Development of a monocytic infiltrate can be seen on histopathology, elicited via a pathergy test which leads to the production of an erythematous papule at the site of a skin prick and intradermal injection of saline solution. A positive pathergy test is one of the minor criteria for the diagnosis of Behçet's disease by the International Study Group diagnostic criteria for Behçet's disease. Lesions in pathergy therefore develop a non-specific pustular reaction, whereas in Koebner phenomenon, lesions have the characteristics of the underlying skin disease (Camargo et al, 2013).

Reverse Koebner phenomenon

There is a disappearance of dermatosis following local trauma (Camargo et al, 2013).

Scar sarcoidosis

This uncommon cutaneous manifestation of sarcoidosis is characterized by thickening of existing or old scars and tattoo sites secondary to infiltration. Histology shows non-caseating granulomas consistent with sarcoidosis. Scar sites can become thickened, nodular, firm or erythematous to touch (Merola and Callen, 2014).

Dermographism

Dermographism ('writing on the skin') is a manifestation of physical urticaria where sites of rubbing or stroking of skin produces erythema and linear wheal along the site of injury. This tends to appear within 5–10 minutes and can persist up to 30 minutes, although more delayed forms have been identified (Laube, 2014).

Addison disease

Hyperpigmentation in Addison disease is usually generalized but can be prominent on sun-exposed areas of skin, extensor surfaces, knuckles, elbows, knees, palmar creases, mucous membranes and scars formed after disease onset. Scars formed before disease onset are not affected as this pre-dates elevation of adrenocorticotropic hormone.

Management

Management of Koebner phenomenon relies on prevention, although this may not always be possible. General advice includes avoiding scratching, limiting exposure to irritants and avoiding sunburn. Elective surgery or procedures should be performed when skin disease is stable or in remission. Treatment of the associated skin condition may help suppress Koebner lesions. Steroids do not prevent Koebner phenomenon. Certain inhibitory mechanisms of Koebner phenomenon have been postulated (Sagi and Trau, 2011). Topical application of white soft paraffin or bland ointment has an inhibitory effect on Koebner phenomenon. Other methods include application of pressure, e.g. pressure dressing, bandage or suction. Vasoconstrictors such as adrenaline have also been suggested to inhibit Koebner lesions (Sagi and Trau, 2011).

Once further insight into the pathogenesis of Koebner phenomenon is obtained, it may be possible to investigate further treatment options through targeting responsible mediators.

Conclusions

We are yet to fully understand the pathogenesis of the Koebner phenomenon. With links to such a wide variety of conditions, the general physician should be aware of the clinical diagnosis, management, referral and decisions related to therapy or surgery. **BJHM**

KEY POINTS

- Koebner phenomenon, or the isomorphic response, is the appearance of new skin lesions with the same clinical and histological features as pre-existing skin disease on areas of trauma in uninvolved skin.
- In an examination, look for Koebner phenomenon in patients with psoriasis, lichen planus and vitiligo.
- Associated conditions include pyoderma gangrenosum, molluscum contagiosum, lichen sclerosis, Darier's disease and erythema multiforme.
- Management includes advising prevention strategies, performing surgical procedures when skin disease is stable and treatment of the associated skin condition.
- Other conditions that may present on scar or trauma sites include pathergy (e.g. in Behçet's disease), reverse Koebner phenomenon, hyperpigmentation in Addison disease, dermographism and scar sarcoidism.

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