

Nikolskiy's Sign - A Review

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ABSTRACT

Autoimmune skin disorders sometimes are characterized by acantholysis, or loss of the normal epithelial cell-to-cell adhesion within the skin(8). Clinically, these disorders present with blistering of the skin and include the pemphigus and pemphigoid groups of disorders. On visual inspection only, these skin conditions are difficult to diagnose and may be confused with other types of skin disorders. Nikolskiy's sign is a well described clinical sign that can be helpful in differentiating some of the autoimmune skin disorders and even determining their prognosis(9). This article presents the original description of Nikolskiy's sign given by Piotr Vasiliyevich Nikolskiy in 1894, along with various different interpretations of Nikolskiy's sign and numerous terminologies used in the literature by a number of clinicians.

1. Background

Nikolskiy's sign, seen in patients with pemphigus vulgaris, has been a subject of much confusion since it was initially reported. The sign is significant for diagnosis, prognosis and follow-up of patients with autoimmune blistering diseases like pemphigus.

2. Discussion

Surprisingly, there have been numerous modifications of the actual Nikolskiy sign, originally described by Piotr Vasiliyevich Nikolskiy in 1894. Nikolskiy described this phenomenon of skin fragility as comprising three variants: 1) the ability to remove the horny layer of the skin far beyond the preexisting erosion, extending to a great distance on the normal-appearing skin, by pulling the remnant of the roof of a ruptured blister; 2) the ability to remove large strips of horny layer from visibly normal skin areas at the periphery of existing lesions by lateral pressure with a finger; and 3) the ability to dislodge the horny layer of apparently normal skin, revealing the moist surface of the underlying layer (1).

Thereafter this sign was considered the main diagnostic criterion for diagnosis of pemphigus. In 1957, Wilhelm Lutz suggested "if one carefully presses upon a blister, it will enlarge within the epidermis in the direction of the periphery due to mechanical pressure of the blister fluid in the acantholytic epidermis". He also suggested a sign which he referred to as the Nikolskiy phenomenon "if carefully rubbed on an uninvolved area of skin, the superficial layers of the skin will move and a blister will form after some time" (2).

Nikolskiy's phenomenon described here by Sir Wilhelm Lutz is different from the original description by Nikolskiy, who never mentioned formation of a blister by rubbing off the uninvolved skin. However, the usage of Nikolskiy's name had added to the confusion.

In 1960, Gustav Asboe-Hansen described a similar sign, which is referred to as blister spreading sign or Asboe-Hansen sign. He described it as the enlargement of bullae by finger

pressure in patients with pemphigus vulgaris, pemphigus foliaceus, pemphigus vegetans, and bullous pemphigoid (3), which is similar to the initial description by Lutz in 1957.

Later in the second half of the twentieth century, Nikolay Dmitriyevich Sheklakov modified the classic description of Nikolskiy sign and introduced the term "marginal Nikolskiy sign". He suggested that application of lateral pressure to a pre-existing lesion using a cotton-tipped swab, tongue depressor, or a pencil eraser, leads to lateral extension of the bulla. He also described the sign of perifocal sub epidermal separation, which is known as "Sheklakov sign" (4,5).

Adding further to the confusion, Fassmann and others have described Nikolskiy's sign in two forms: direct and indirect. The direct Nikolskiy's sign refers to wrinkling of apparently healthy skin under pressure with subsequent exposure of a macerated lesion. The indirect Nikolskiy's sign refers to an increase in size and release of its content through the surrounding epidermis when pressure is applied to a bulla (6). Braun-Falco and colleagues have mentioned variants of Nikolskiy's phenomenon, which were originally described by Lutz, as phenomena I & II. Nikolskiy's phenomenon-I refers to the application of lateral pressure to apparently normal skin in the vicinity of a vesicle resulting in removal of the upper layers of the epidermis.

Nikolskiy's phenomenon-II refers to the extension of a blister into apparently normal skin as a consequence of applying direct pressure to an intact blister (7). Keeping in mind Nikolskiy's original report, two different phenomenon based on the same mechanism occur because of destruction of desmosomal attachments by antibodies against desmosomal antigens.

The first phenomenon is Nikolskiy's sign that involves rubbing off or shearing of the epithelium by slight friction on apparently normal skin or mucosa, and the second is the so-called bulla spreading sign (Asboe-Hansen sign) resulting from application of pressure to, and extension of the bulla. Although the latter phenomenon was first described by Lutz, it has gained popularity as the Asboe-Hansen sign. The use of

various different terminologies for the phenomenon resulting from presence of antibodies against desmosomal antigens adds only to further confusion. Therefore consistency in the use of these terms is recommended

Nikolsky's sign may have prognostic value in patients with bullous skin diseases. One study described 2 distinctly different versions of the sign: the so called "wet" Nikolsky's sign, in which a moist, glistening base of eroded skin is seen after pressure is exerted on the skin; and the so-called "dry" Nikolsky's sign, in which a dry base of eroded skin is seen after pressure is exerted on the skin. In patients with active pemphigus vulgaris,

a wet sign is expected, whereas the presence of the dry sign may indicate reepithelialization beneath a pemphigus blister, which could signify healing and thus be a favourable finding.

3. Summary

Nikolsky's sign is a well known clinical sign classically associated with the pemphigus group of disorders but also occurring in other autoimmune dermatologic conditions. The lack of standardization regarding how exactly to elicit the sign has limited its usefulness, but it remains an interesting sign to observe and interpret.

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