IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 19, Issue 4 Ser.9 (April. 2020), PP 01-03
www.iosrjournals.org

Exploring Nikolsky's Sign

Dr Nikkhiel Diwaan[1], Dr Rashmi Sapkal[2], Dr KamanaKureel[3], Dr Sabah Pathan[4], Dr AadiaMujawar[5], Dr Shraddha Supnekar[6], Dr Husna Patel[7]

1Department of Oral Medicine and Radiology, M. A. Rangoonwala Dental College and Research Centre, Pune 411001
2Reader, Department of Oral Medicine and Radiology, M. A. Rangoonwala Dental College and Research Centre, Pune 411001
3Post graduate student, Department of Periodontology, Late Shri YashwantraoChavan Memorial Dental College and Research Centre, Ahmednagar 414003
4Ex undergraduate student, M. A. Rangoonwala Dental College and Research Centre, Pune - 411001
5Ex undergraduate student, M. A. Rangoonwala Dental College and Research Centre, Pune - 411001
6Senior lecturer, Department of Oral Medicine and Radiology, M. A. Rangoonwala Dental College and Research Centre, Pune- 411001
7 Senior lecturer, Department of Oral Medicine and Radiology, M. A. Rangoonwala Dental College and Research Centre, Pune - 411001
Corresponding Author: Dr Nikkhiel Diwaan

Date of Submission: 10-04-2020 Date of Acceptance: 24-04-2020

I. Introduction

The Russian dermatologist Pyotr Vasiliyevich Nikolskiy (1847-1897), was the first to explain Nikolsky sign when he was working on a thesis on pemphigus in 1895. He referred this sign to as a weak bond between epidermal layers on normal areas between the lesions appearing on a normal skin surface[1]. Practically, on application of a tangential pressure in the normal area adjacent to the lesion, a new blister forms due to the peeling of the epidermis[2]. The sign is spelt as Nikolsky and not Nikolskiy after its demonstrator.

Nikolskiy described 3 ways of eliciting the sign [3, 4, 5]

1) The tag remaining around the blister can be stretched for a longer distance even on normal mucosa.
2) Lateral pressure exerted by a finger on a normal mucosal surface near an existing lesion can form a new lesion.
3) A new lesion can be elicited by stretching the epidermis on a normal healthy appearing mucosa

Several conditions like toxic epidermal necrolysis, Steven – Johnson syndrome, oral lichen planus, staphylococcal scalded syndrome (SSS), Bullous mucous membrane pemphigoid, other variations of pemphigus, second or third degree burns, bullous impetigo and epidermolysis bullosa [6]are known to demonstrate Nikolsky sign.In the oral cavity the bullae or blisters rupture easily due to frictional activity. Hence Nikolsky sign can be elicited by pressure on the mucosa by finger or blunt instrumentor by air pressure [7].

Sign of Nikolskiy & related signs

Clinical Nikolsky's sign:

Nikolsky's sign (Clinical Nikolsky's sign) is observed when a new blister forms on application of tangential pressure on or adjacent to the lesion thus separating the upper epidermal layer from the lower[2, 8]. This results due to the acantholysis occurring below the normal appearing mucosa and the lesional mucosa as well[1]. Lyell, in 1956, confirmed the findings of Nikolskiy [9]during an endoscopic procedure.

Bulla spread sign:

Appearance of an irregular bulla from an intact bulla margin resulting from unidirectional pressure is referred to as Lutz sign or Bulla spread sign [10]. This is seen in Pemphigus vulgaris and in other subepidermal blistering conditions.

Asboe Hansen sign:

This is a variant of the bulla spread sign [11]and wasexplained by Danish physician. Gustav Asboe- Hansen. A small and tense bulla appears on pressure to a blister which may be seen in acute stage of bullous lichen planus

along with Nikolsky sign.[6, 12]. This test is negative in Hailey Hailey disease and SSS as the blister is very fragile and ruptures very easily[13].

Sheklakov sign/False Nikolskiy sign:
In sub-epidermal blistering disorders, when the roof of the ruptured blister is sheared, the erosion extends on the adjacent normal skin. These are referred to as False Nikolsky's sign or Sheklakov's sign[6]. These erosions are smaller in size and have a rapid healing capacity.

Microscopic Nikolsky's sign:
The subclinical variant of Nikolsky sign is microscopic Nikolsky sign where only microscopic changes are observed with minimal evident changes as only the intercellular adhesions are weakened on eliciting clinical Nikolsky's sign[6]. This can prove of help in cases where immunofluorescence test is not accessible as concluded by Hameed and Khan[14]. In a study by Barzegari M. et. al.[8] it was postulated that microscopic Nikolsky sign is a representative of generalized disease state.
Marginal and Direct Nikolsky's sign:
When the normal skin surrounding an established lesion is rubbed, the erosion extends, which can be referred to as "Marginal Nikolsky's sign"[6]. Similarly, if a lesion is elicited distant to the original lesion it can be quoted as "Direct Nikolsky's sign". The latter representative of a severe form of pemphigus and is the first to disappear on initiation of treatment.
Wet and Dry Nikolsky's sign:
A Nikolsky sign is referred to as wet when a moist or glistening base is seen in the new lesion and it is referred to as dry when the eroded base of the new lesion is dry[6].In inactive Pemphigus vulgaris, when there is re-epithelialisation below the blister, the appearance is dry[2].
Modified Nikolsky's sign:
On pressure application the blister extends on the peripheries and is referred to as the "modified Nikolsky's" sign. This new blister doesn't show epithelial regeneration[14].
Variations in Nikolsky sign:
Ghoneim S. et. al. reported Nikolsky sign in a patient with skin Bullous Pemphigoid, which is a rarity in bullous dermatosis[15]. The sign was noticed during an endoscopic investigation where shearing pressure lead to the formation of a new bullae.The sign may also be elicitable in the rare ichthyosis bullosa of Siemens, where it is termed the `Mauserung phenomenon' [16].
Nikolsky phenomenon:
Sir Wilhelm Lutz, described Nikolsky I phenomenon, as appearance of new lesion after a while due to the movement of superficial layers of the epithelium on the area adjacent to the lesion whereas Nikolsky II phenomenon was referred to as new lesion appearing on normal skin[17]. The superficial epidermis is detached from the dermis in Nikolsky phenomenon[18]. A positive Nikolsky phenomenon is indicative of lower disease activity in pemphigus vulgaris[19].
Pseudo-Nikolskiy sign/Epidermal peeling sign:
The appearance of a new lesion on the erythematous adjacent surface of the lesion, observed due to necrosed adjacent epidermis is termed as Pseudo Nikolsky sign [12, 20]

Pathophysiology

The intercellular cohesions between epidermal cells is loosened or lost leading to loss of attachment between each other. This feature can be noticed in acantholysis and is termed as Nikolsky sign. This can be observed in the affected region as well as intact mucosal surfaces presenting as erosions or ulcers on the surfaces. Nikolsky sign is characteristically seen in intra-epidermal lesions, so can be one of the diagnostic criteria to differentiate between intra epidermal and sub- epidermal lesions [21].

Nikolsky's sign is usually positive in diseases with intraepidermal acantholysis and typically negative in diseases with dermo-epidermal separation, thus helping to distinguish pemphigus from bullous pemphigoid [6]

Histopathology in conditions where Nikolsky sign is positive

The epidermis may be lost entirely or may show necrosis due to separation in t**oxic epidermal necrolysis**[22](TEN)**.** In **pemphigusvulgaris**, suprabasilar epidermal acantholysis[6] may be observed with intact keratinocytes at the floor of the lesion giving a 'tomb stone appearance'[23]. **Staphylococcalscaldedsyndrome** shows intraepidermal splits suggestive of subcorneal acantholysis, characteristically in stratum granulosum[24]. Fewer acantholytic cells and inflammatory cells are seen. The lesions develop on the entire body, with the peeling of epithelium on slight touch.The melanin pigmented spinous layer remaining after the peeling of the granular layer may be attributed to the pigmentation seen in Nikolsky sign. This helps to differentiate between

SSS and TEN[24]. Inflammatory cells aggregate in the dermis with subcorneal acantholytic cells[6] in the epidermis with degenerating keratinocytes is noted in the **bullous form of Impetigo**[6]. In **Epidermolysis Bullosa**[25], vesicles are seen intraepidermally and the variations in skin separation may be helpful to distinguish between various forms of the condition.The subcorneal layer of epidermis may show acantholysis[6, 26]in **Pemphigus Foliaceus** with moderate number of acantholytic cells. The roof may show layers of Malphigian cells.**Paraneoplastic pemphigus**shows epidermal acantholysis with vacuolar changes in the basal layer of the epidermis[27]. **Benign mucous membrane pemphigoid**shows subepidermal blistering with neutrophil and eosinophil infiltrate in the dermis[28]. **Lichen planus**in the form of lichenoid reaction shows basal cell layer degeneration with lymphocytic infiltration at the dermoepidermal junction[29].

Role of Nikolsky sign:

Nikolsky sign can differentiate between intraepithelial and subepithelial lesions as it is evident only in intraepithelial conditions [2]. It can also be used to evaluate the progress of the disease or as a prognostic marker as it cannot be elicited as the disease improves in condition[3]. Reappearance of the sign during a course of treatment to suggest an alternative treatment approach may be considered that the lesion is reappearing[12].

Conclusion:

Nikolsky sign is a dermatological sign seen in multiple autoimmune disorders. There is lack in standard eliciting procedures, so the use of this sign has limited applications. Although the lackof standardization regarding how exactly to elicit the sign haslimited its usefulness, but it remains an interesting sign toobserve and interpret.

References:

[1]. Channual J, Wu JJ. The Nikolskiy sign. Arch Dermatol. 2008; 144:1140.
[2]. Urbano FL. Nikolsky's Sign in Autoimmune Skin Disorders. Hosp. Physician 2001; 37:23-4.
[3]. Uzun S, Durdu M. The specificity and sensitivity of Nikolsky sign in the diagnosis of pemphigus. J. Am. Acad. Dermatol. 2006; 54(3):411‑ 5.
[4]. Polifka M, Krusinski PA. The Nikolsky sign. Cutis 1980; 26(5):521‑ 526.
[5]. Doubleday CW. Who is Nikolsky and what does his sign mean? J. Am. Acad. Dermatol. 1987; 16(5 Pt 1):1054‑ 5.
[6]. Seshadri D, Kumaran MS, Kanwar AJ. Acantholysis revisited: Back to basics. Indian J. Dermatol. Venereol. Leprol. 2013; 79(1):120‑ 6.
[7]. Rastogi V, Sharma R, Misra SR, Yadav L. Diagnostic procedures for autoimmune vesiculobullous diseases: A review. J. Oral Maxillofac. Pathol. 2014; 18(3):390-7.
[8]. Barzegari M, Valikhani M, Esmaili N, Naraghi Z, Nikoo A, Kamyab K. et. al. Microscopic Nikolsky's sign: Is it useful for diagnosis of pemphigus vulgaris?. Iran J Dermatol 2008; 11(2):64‑ 6.,8.
[9]. Arndt KA, Feingold DS. The sign of Pyotr Vasilyewich Nikolsky. N Engl J Med. 1970 May; 282(20):1154-5.
[10]. Grando SA, Grando AA, Glukhenky BT, et al. History and clinical significance of mechanical symptoms in blistering dermatoses: A reappraisal. J Am AcadDermatol 2003; 48(1):86-92.
[11]. Odom RB, James WD, Berger TG. Cutaneous lymphoid hyperplasia, cutaneous T-cell lymphoma, other malignant lymphomas, and allied diseases. In: *Andrews' Diseases of the Skin: ClinicalDermatology*. 9th ed. Philadelphia: WB Saunders; 2000.p. 918-42.
[12]. Sachdev D. Sign of Nikolskiy and related signs. Indian J. Dermatol. Venereol. Leprol. May – June 2003; 69(3):243-4.
[13]. Kaur S, Singh M, Radotra BD, Sehgal S. Positive Nikolsky's and bulla-spread signs in acute bullous lichen planus. Arch Dermatol 1987; 123(9):1122-3.
[14]. Hameed A, Khan AA. Microscopic Nikolsky's sign. Clin. Exp. Dermatol. 1999 Jul; 24(4):312-4.
[15]. Ghoneim S, Shah A, Calderon Al.: Esophageal Nikolsky's Sign: A Rare Finding in a Patient with Bullous Pemphigoid Case Rep. Gastroenterol. 2019 Oct; 13(3):445–449
[16]. Griffiths WAD, Judge MR, Leigh IM. *Disorders of keratinisation*. In: Champion RH, Burton JL, Burns DA, Breathnach SM, editors. Rook Textbook of dermatology. 6th ed. London: Blackwell Science; 1998. p. 1483-588.
[17]. Salopek TG. Nikolsky's sign: is it 'dry' or is it 'wet'? Br J Dermatol 1997 May; 136(5):762‑ 7
[18]. Adya KA, Inamdar AC, Palit A. A simple and succinct simulation of Nikolsky phenomenon and sign. Indian Dermatol. Online J. (Epub ahead of print) (cited 2020 Apr 3). http://www.idoj.in/preprintarticle.asp?id=276565.
[19]. Juneja M. Nikolskiy sign revisited. J. Oral Sci. 2008 Jun; 50 (2):213-4.
[20]. Valia AR, Valia RG. Vesiculobullous disorders. In: IADVL *Textbook and atlas of dermatology*. 2nd ed. 2001. p. 857-905. Mumbai: Bhalani Publishing House.
[21]. Soni AG. Nikolsky's sign - A clinical method to evaluate damage at epidermal-dermal junction. J Indian Acad. Oral Med. Radiol. 2018; 30(1):68-72.
[22]. Weidner N, Cote RJ, Suster S, Weiss LM. 2009. *Modern Surgical Pathology* , II ed. Elsevier Inc. http://doi.org/10.1016/B978-1-3966-2.X0001-X
[23]. Barr RJ. Cutaneous cytology. J. Am. Acad. Dermatol. 1984 Feb; 10(2 Pt 1):163-80.
[24]. Seneviratne J. Letter to the Editor: Nikolsky's sign in staphylococcal scalded skin syndrome: A new diagnostic clue to the level of epidermal split.Indian Journal of Pediatric Dermatology; Jan- Apr 2012: 13, (1): 51-52.
[25]. Fine JD. Pathology and Pathogenesis if Epidermolysis Bullosa. In Lin AN, Carter DM (eds) *EpidermolysisBullosa*. 1992. Springer, New York, NY. https://link.springer.com/chapter/10.1007/978-1-4612-2914-8_3
[26]. Furtado TA. Histopathology of Pemphigus Foliaceus. *AMA Arch. Derm.* 1959; 80(1):66–71. doi:10.1001/archderm.1959.01560190068010
[27]. Sehgal VN. Paraneoplastic pemphigus/ paraneoplastic autoimmune multiorgansyndrome. Int. J. ofDermat. 2009 Feb; 48(2) : 162-169. https://doi.org/10.1111/j.1365-4632.2009.03995.x
[28]. Tolaymat L, Hall MR. *Cicatricial Pemphigoid*. [Updated 2019 Nov 17]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2020 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK526120/
[29]. Weedon D. *Weedon's Skin Pathology*. III ed. 2009. Elsvier. Churchhill Livingstone 2010.