

“Enthralling Diagnostic Pearls”

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Abstract: “Oral health is a mirror of general health”. Certain signs manifested in head and neck region including oral cavity serve as an imperative clue in diagnosing systemic disorders. These manifestations serve as clinical pearls in leading the clinician towards appropriate management of the disorder. The present review discusses some of the significant signs which act as clinical guide.

Keywords: Oral manifestations, systemic disorders, clinical guide.

I. Introduction

The word diagnosis means “*thorough knowledge*”, it is the greatest task and a key to successful clinical practice. Hence a thorough knowledge regarding various presenting signs and symptoms is of utmost importance to a clinician for precise diagnosis and management of a disease. This present article reviews various fascinating “*SIGNS*” which in *medical lexicon* refers to an objective physical finding observed by an examiner. Only signs presenting as a cutaneous or mucosal eruptions that are visible, palpable, or elicited by direct manipulation, and dermatologic signs associated with oral involvement are included herein.

Asboe-Hansen sign

Asboe-Hansen sign was described in 1960 by Gustav Asboe-Hansen (1917–1989) a Danish dermatologist[1]. The fascinating history of discovery of mechanical symptoms in blistering dermatoses was recently reviewed by Grando and colleagues[2]. Asboe-Hansen sign is also known as *blisterspread sign*, which refers to the ability to enlarge a blister in the direction of the periphery by applying mechanical pressure on the roof of the intact blister spreading of a blister into a clinically normal skin when lateral pressure is applied on the edge of a blister[2].

Angular blister formation is thought to be associated with intraepidermal acantholytic diseases (eg, pemphigus), whereas rounded blister formation is associated with subepidermal acantholytic diseases (eg, bullous pemphigoid)[3]. It is also observed in bullous drug eruptions. Importantly, the sign is different from Nikolsky's sign (reviewed below).

Auspitz sign

Heinrich Auspitz an Austrian dermatologist (1835–1886) is credited for the Auspitz sign, the term is a misnomer. Both Devergie Jeune (1860) and Hebra (1845) observed this clinical sign before Auspitz, as did Robert Willan (1808), Joseph Plenck (1776), and Daniel Turner (1736)[4].

Auspitz sign refers to the appearance of a red, glossy surface with pinpoint bleeding on removal of the scale by scraping or scratching. This occurs as a result of removal of overlying suprapapillary epithelium with subsequent rupture of dilated dermal capillaries. Although importantly Auspitz sign is neither sensitive nor specific for psoriasis[5] as it occurs in other skin conditions, including Darier's disease and actinic keratosis[3].

Battle's sign

Battle's sign is named after an English surgeon, William Henry Battle (1855–1936). It occurs after fracture of the base of the skull in the posterior cranial fossa. Blood accumulates beneath the fascia and causes discoloration at the mastoid process. Battle's sign is highly specific and predictive for the basal skull fracture[3].

Cluster of jewels sign

Cluster of jewels sign also termed string of pearls or rosettes sign. It refers to an early stage of chronic bullous disease of childhood when new lesions appear at the margin of older ones resembling a cluster of jewels[6].

Dubois' sign

Dubois' sign is shortening of the little finger associated with congenital syphilis[7]. This feature is seen occasionally as a late stigma of the disease. It may be associated with other stigmata of congenital syphilis such

as Hutchinson’s triad (deafness, keratitis, and pointed teeth), perioral rhagades, optic atrophy and broad-based saddleback nose[3].

Flag sign

Flag sign refers to horizontal alternating bands of discoloration in the hair shafts corresponding to periods of normal and abnormal hair growth. The discoloration may be reddish, blonde, gray, or white depending on the original hair color. The flag sign may be seen in patients with nutritional deficiencies such as kwashiorkor and with certain medications such as intermittent high dosage of methotrexate or following chemotherapy[8]. Patients with ulcerative colitis may also manifest the flag sign[3].

Forchheimer’s sign

Forchheimer’s sign refers to an enanthem of red macules or petechiae confined to the soft palate in patients with rubella. The sign presents in up to 20% of patients during the prodromal period or on the first day of the exanthema[3].

Gorlin’s sign

Robert James Gorlin, an American oral pathologist and geneticist described Gorlin’s sign for the first time. It is seen in patients with Ehlers-Danlos syndrome. It is used to describe the ability to touch the tip of the nose with the extended tongue[3].

Hoagland’s sign

Hoagland’s sign is early and transient bilateral upper lid edema occurring in patients with infectious mononucleosis. The sign is usually present only for the first few days of the clinical presentation of the illness[9].

Hutchinson’s nose sign

Hutchinson’s nose sign refers to the presence of vesicles occurring on the tip of the nose in patients with herpes zoster. This presentation indicates that the nasociliary branch is affected and that eye involvement may be present or forthcoming; therefore an ophthalmologic assessment is necessary for these patients[10].

Jellinek’s sign

Jellinek’s sign refers to eyelid pigmentation occasionally seen in hyperthyroidism. The hyperpigmentation is secondary to increased corticotrophin levels and may also occur on other areas of the face but usually spares the buccal mucosa[3].

Necklace of Casal sign

It refers to hyperpigmentation occurring on the neck owing to pellagra. The “necklace” can extend as a broad collar-like band around the entire circumference of the neck[11].

Nikolsky’s sign

Historical Perspective of Nikolsky’s sign

Piotr Vasilyewich Nikolsky (1858-1940) was a Russian dermatologist who studied at the University of Kiev and published a thesis on Pemphigus in 1895[12]. Nikolsky first described the sign that bears his name in 1896. He related how, after rubbing the skin of patients who had Pemphigus Foliaceus there was a blistering or denudation of the epidermis with a glistening moist surface underneath. According to his explanation, the skin showed a weakening relationship and contact between the corneal (horny) and granular layers on all surfaces even in places between the lesions. Nikolsky’s observations were later confirmed by Lyell in 1956 who described Nikolsky’s sign in patients with toxic epidermolysis necrolysis[12].

Variants of Nikolsky’s sign

As recently reviewed by Grando and colleagues, two variants of Nikolsky’s sign exist[2]. **Marginal sign** refers to the ability to split the epidermis of the skin beyond the preexisting erosion by pulling the remnant of a ruptured blister or rubbing at the periphery of existing lesions. On the other hand, **direct sign** refers to the ability to split the epidermis on skin areas distant from the lesions by lateral pressure with a finger. Both variants are observed in pemphigus vulgaris, pemphigus foliaceus, and staphylococcal scalded skin syndrome. In contrast to Asboe-Hansen sign, these are negative in autoimmune subepidermal blistering diseases (eg, bullous pemphigoid) and the bullous drug eruptions, erythema multiforme, Stevens-Johnson syndrome, and toxic epidermal necrolysis[2].

One study described two distinctly different versions of sign the so called “wet” Nikolsky’s sign, in which moist glistening base of eroded skin is seen after pressure is exerted on the skin as seen in active pemphigus, and “dry” Nikolsky’s sign in which a dry base of eroded skin is seen after pressure is exerted on the skin which indicates repithelisation beneath a pemphigus blister, which could signify healing[14].

Pseudo-Nikolsky’s sign refers to the ability to peel off the entire epidermis by lateral pressure (rubbing) only on the erythematous skin areas; it is present in the bullous drug eruptions but is negative in pemphigus and autoimmune subepidermal blistering diseases. Recently Uzun and Durdu reported that Nikolsky’s sign is moderately sensitive but is highly specific in the diagnosis of pemphigus[15].

Pyotr Vasilyewich Nikolsky’s described various ways of eliciting the sign[16,17]

(1) The stratum corneum, when pulled, can be stripped off over large areas, and it is possible to displace the stratum corneum of healed skin and,

(2) Healthy uninvolved skin by rubbing.

Clinical utility of Nikolsky’s sign

Nikolsky’s sign can be provoked in other conditions such as paraneoplastic pemphigus, oral bullous lichen planus, mucous membrane pemphigoid, epidermolysis bullosa, linear IgA disease, lupus erythematosus, dermatomyositis, chronic erythema multiforme, graft-versus-host disease[18], toxic epidermal necrolysis, staphylococcal scalded skin syndrome, bullous impetigo, and mycosis fungoides[12].

Raccoon sign

It is a useful feature indicative of basilar skull fracture. The condition is seen as periorbital ecchymosis from subconjunctival hemorrhage, which occurs secondary to blood dissecting from the disrupted skull cortex to the soft tissue of the periorbital region[19].

Russell’s sign

It is seen in patients with bulimia nervosa owing to repeated contact of the *incisor teeth* with the skin and during self-induced vomiting[20]. It refers to the lacerations, abrasions, and callosities that are found on the dorsum of the hand overlying the metacarpophalangeal and interphalangeal joints[20].

Shawl sign

It is seen in patients with dermatomyositis and is characterized by confluent, symmetric, macular violaceous erythema on the posterior shoulders and neck, giving a distinctive shawl-like appearance[3].

Slapped cheek sign

Slapped cheek sign is seen in children with fifth disease as confluent, erythematous, edematous plaques on the cheeks[21]. This manifestation is often the first skin change seen in patients with fifth disease. As the facial rash begins to fade over 1 to 4 days and erythematous macules, papules begin to appear on the trunk, neck and extensor surfaces of the extremities[3].

Tin-tack sign

It is also known as carpet tack sign, is a useful clinical feature in diagnosing discoid lupus erythematosus[22]. Hyperkeratotic scales extending into the follicular infundibulum creates keratotic spikes when viewed from the scale’s undersurface resembling a carpet tack. Other conditions in which tin-tack sign has been reported include cutaneous B-cell lymphoma[23], seborrheic dermatitis[24], lichen planus[25] and pemphigus foliaceus[26].

II. Conclusion

A *multitude of signs* exist in medical literature and an exhaustive list is difficult to elaborate. Many signs are based on the morphology or physical characteristics of the lesions. The eponymous nature of some signs highlights the rich chronicle of oral lesions associated with dermatological lesions. These signs help in narrowing the differential diagnosis. It is crucial for a clinician to take into account that these signs are rarely pathognomonic and each is associated with inherent sensitivity and specificity. Hence these signs are to be utilized as adjunctive clinical guide for successful practice.

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