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Diagnostic Procedures for Vesiculobullous Lesions: A Review

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Abstract

Vesiculobullous lesions present with varied manifestations. Clinical examination of an intact vesicle and bulla can be quite challenging as the masticatory forces lead to erosions and ulcerations on the surface leading to challenging diagnostic dilemma. Various diagnostic and laboratory procedures can aid in further investigation of the vesiculobullous lesions for a conclusive diagnosis.

Keywords: Bulla; Vesiculobullous; Immunofluorescence; Mucocutaneous; Salt split; Diagnostic tests

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Introduction

Vesiculobullous lesions present protean manifestations. It may present as formation of vesicles or bullae. However, it is uncommon to appraise vesicles or bullae intraoral as they rupture very easily due to masticatory forces and appear as ulcerations and erosions [1]. Vesiculobullous lesions include viral diseases, autoimmune mucocutaneous diseases due to immunologically mediated mechanism and genetic susceptibility. Clinical history and general physical examination play a vital role which includes the presence of vesicles and bullous in any other region of the body like skin, genitilia and eyes as they may present with dermatological manifestations. Due to indistinguishable appearance of the lesions, the diagnosis can be made histopathologically, clinically and immunological methods. Clinical examination involves a thorough examination of the exposed and mucosal surfaces of the body. The oral diagnostician therefore should have a thorough knowledge of the different procedures that can be used for scrutinising the lesions. This article aims to explain various diagnostic tests that can be done for the diagnosis of vesiculobullous lesions.

Nikolsky'stest

It was described by a Russian dermatologist, Piotr Vasiliyvich Nikolsky (1858-1940) who stated that there was blistering or denudation of the epidermis with a moist, shining appearance upon rubbing of the skin of patients with pemphigus foliaceous [2,3].

This is due to a weak relationship between the corneal and granular cell layers on unaffected skin. It is also seen in patients with toxic epidermal necrolysis which was confirmed by Lyell in 1956 [4,5].

A positive Nikolsky sign is an evident ulceration of tissue or blisters in applying mucosal pressure by blowing air or finger pressure. Index finger is used to apply lateral pressure that separates normal appearing epidermis and producing erosion [6].

Nikolsky's sign is classically associated with pemphigus vulgaris. However, other blistering conditions are also known to exhibit this sign including pemphigus foliaceous, paraneoplastic pemphigus, oral lichen planus, mucous membrane pemphigoid, bullous pemphigoid, epidermolysis bullosa, Stevens–Johnson Syndrome, Staphylococcal scalded skin syndrome (SSSS), toxic epidermal necrolysis (TEN), linear IgA disease, lupus erythematous (LE), dermatomyositis chronic erythema multiform and graft-versus-host disease [7].

LE cell phenomenon

The test was first described by Hargraves for the confirmation of systemic LE (SLE). In tissues, the presence of neutrophil or monocyte showing reddish purple amorphous inclusion known as haemotoxylin or LE body. It represents as the degraded nuclear material of an injured cell which has been phagocytised by an intact phagocyte. It occurs due to phagocytosis of apoptotic

bodies induced by autoantibodies and is a pathognomic sign of systemic lupus erythematosus (SLE) [8,9].

Tzanktest

It is relatively a simple and rapid test. It is indicated in viral infections (herpes simplex, varicella and herpes zoster) to identify viral giant cells and the presence of acantholysis for diagnosing pemphigus. [10] Fresh samples should be taken. The suspected area is dried and cleaned and a sterile needle is inserted at the base of the blister.On microscopic inspection, it shows a large round keratinocyte with a hyperchromatic nucleus and peripheral condensation of the chromatin, hazy and prominent nucleoli and abundant cytoplasm known as Tzanck cells [11,12].

Pathergy test

Pathergy phenomenon is defined as a state of altered tissue reactivity that occurs in response to minor trauma. Pathergy test (PT) is an easy to perform skin test to look for the pathergy phenomenon [13]. The cutaneous injury leads to inflammatory response that is more prominent and intense than normal saline and shows release of cytokines from keratinocytes in the epidermis or dermis resulting in a perivascular infiltration observed on skin biopsy [14].

A hairless area on the flexor aspect of the forearms is usually chosen as the test sites. After asepsis of skin with 100% alcohol, 20-G needle tips are blunted using the cap and pricked intradermally at a 45°–90° angle with 0.1ML normal saline. Prick sites were evaluated at 48th hour. Papules of >2 mm in diameter and pustules with or without erythematous halo at any prick site is a positive result. Development of only crusts or needle mark due to the trauma or minimal erythema without papule formation is considered negative. Pathergy test is positive in Behcet's disease [15].

Koebnerphenomenon

It was first described by Heinrich Koebner in 1876. The Koebner phenomenon is defined as the appearance of cutaneous lesions on previously non involved skin following trauma. It is seen in psoriasis [15,16]. It is also seen in vitiligo.

Brocq'sphenomenon

Brocq's phenomenon is the presence of subepidermal hemorrhage on scraping of lichen planus. This is in contrast to the scratching of the surface of lesions of psoriasis, which results in pin-point bleeding [18].

Immunofluorescence

Immunofluorescence (IF) is an immunological histochemical staining technique used for demonstrating the presence of antibodies bound to antigens in tissues or serum. These techniques supplement clinical findings and histopathology in the diagnosis of immunobullous disorders. It was developed by Coons in 1940 with blue fluorescing compound- beta anthracene [19-22].

Techniques- there are three basic types of IF techniques:

1) Direct

2) Indirect

3) Complement techniques

Variants of IF techniques-

1. Salt- Split technique

2. Antigenic Mapping Method

3. Double Staining Method

4. Sandwich Technique

5. Calcium Enhancement Indirect Technique [18].

Interpretations of various diseases (Table 1)

Table 1 Interpretations of various diseases.

Disease	Direct IF	Indirect IF	Salt-Split
PemphiusValgaris	"Chicken wire" or "Fishnet" or "Lacy" pattern of IgG and C3 in extracellular matrix around keratinocytes or spinous cells of epithelium.	"Punctate" or "Granular" fluorescence against circulating antiepithelial cell surface IgG.	--
Bullous Pemphigoid	Deposition of IgG and C3 in a linear band pattern to the basement membrane zone (BMZ) at dermoepidermal junction.	--	IgG1,4 Antibodies bound to the epidermal side/ roof of the split skin. (may also be on both sides).
CicatricalPemphigoid	Linear deposition of IgG and C3 along the BMZ in a homogeneous manner.	--	IgG localized only to the roof.
Linear IgA Disease	Linear deposition of IgA along BMZ	Circulating IgA antibodies against a BM antigen.	--
Epidermolysis BullosaAquisista (EBA)	Linear deposition of IgG, IgA and C3 in BMZ which is more intense and broad than that in pemphigoid.	--	IgG anti- BMZ Antibodies against globular carboxy terminus of Type VII collagen and localized to the dermal (floor) side of the split skin.
Lichen Planus	Characteristic pattern of fibrinogen deposition outlining the BMZ and extending irregularly into superficial lamina propria—"Shaggy" or " Fibrillar" Pattern. C3 positive cytoid bodies in epithelium and superficial connective tissue.	--	--

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