

In Shortly about Skin Pathology

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Abstract

Pathology is the science of disease. It represents the connection between basic sciences and clinical medicine, whose goal is to study structural and functional changes in the cells and tissues of organs or organ systems involved in a certain disease. Pathology, as a science of diseases, in addition to studying morphological changes, also studies the mechanisms of occurrence and development of reactions in cells and tissues under the influence of harmful factors that cause the disease. When studying the origin and development of the pathological process and disease, the cause that initiated the pathological process and the mechanisms involved in its development must be taken into account. It is therefore important to know that, by studying cells, tissues, and body fluids using microbiological, immunological, and biochemical methods, pathology assists physicians in clinical practice in making diagnoses and appropriate treatment of diseases. In skin pathology, diseased states are skin tumors and other skin diseases.

Keywords

Skin, Dermatology, Skin Diseases, Pathology

1. Introduction

What could be easier than the diagnosis of skin disease [1]? The pathology is before your eyes! Why then do nondermatologists have such difficulty interpreting what they see? There are three reasons. First, there are literally hundreds of cutaneous diseases. Second, a single entity can vary in its appearance. A common seborrheic keratosis, for example, may have a smooth, rough, or eroded surface and a border that is either uniform or as irregular as a melanoma. Third, skin diseases are dynamic and change in morphology. Many diseases undergo an evolutionary process: herpes simplex may begin as a red papule, evolve into a blister, and then become an erosion that heals with scarring. If hundreds of entities can individually vary in appearance and evolve through several stages, then it is necessary to recognize thousands of permutations to diagnose cutaneous entities confidently. What at first glance appeared to be simple to diagnose may later appear to be simply impossible.

Dermatology is a morphologically oriented specialty. As in other specialties, the medical history is important; however, the ability to interpret what is observed is even more important. The diagnosis of skin disease must be approached in an orderly and logical manner. The temptation to make rapid judgments after hasty observation must be controlled.

The skin is an optimal organ for studying fundamental principles of pathology because lesions on its surface are readily apparent and easily biopsied [2]. Except for diseases of highly specialized tissues (e.g., those of the alveolus), all classes of disease are seen in the skin. Some diseases, such as the blistering ones, are manifested only in the skin (and occasionally the mucous membranes).

Many cutaneous diseases have only minor symptoms and some have no symptoms at all. Few are lifethreatening, and many are self-limited. However, even self-limited, asymptomatic cutaneous diseases are often of great concern

to the patient. For example, the symptoms of acne are systemically minor, but the disease can change a life. Although scalp hair is unneeded, baldness may cause considerable distress.

Dermatopathology and genetics are two very important parts of the field of dermatology [3]. Both allow physicians to be better able to diagnose and treat their patients more appropriately. Dermatopathology gives a better look at what is happening in the skin at a microscopic level. It allows the dermatopathologist or pathologist to better identify the cause of the patient's lesion. With further advances in staining along with other forms of technology such virtual slides, non-invasive techniques, and smartphone applications it will be interesting to see what the future holds in regards to the number of punch and shave biopsies and frozen sections performed in the dermatology office and what new advancements in the skin field will be made over the next few decades. Other questions to consider with these advances in technology is how will cost affect these procedures and how will they be reimbursed via insurance companies.

A skin biopsy is simple to perform [4]. Interpretation of that skin biopsy, particularly in the context of a patient with a skin eruption who is on multiple medications, has undergone or is undergoing chemotherapy or radiation, can be a challenge. Inflammatory skin diseases pass through stages of evolution and therefore the histologic findings in a skin biopsy vary with the stage of the disease. Disparate entities may share histologic features and the final diagnosis often rests with the clinical-pathologic correlation. At early stages, some inflammatory conditions may not have evolved entirely diagnostic histologic features. Nonetheless, one may expect that an experienced dermatopathologist anticipates such issues and, in the context of a detailed clinical history, can compile a report that is diagnostically relevant and helps guide patient care.

2. Surgical Pathology

Despite technological advances in diagnostics, the art of clinical medicine still lies in the recognition and interpretation of clinical signs and symptoms [5]. In no field is this more apparent than dermatology. In particular, the dermatologist has acquired skills for the detection of the most representative lesions of any skin disease—the so-called “elementary lesions”—and a precise evaluation of their color, size, border, thickness, number, and topography, as well as the pruritus, pain or tenderness that may be associated with them. This analytic approach to clinical diagnosis is a complex cognitive process complementary to a global, more intuitive process; the latter probably represents the ground of daily dermatological practice and allows the non-specialist to recognize most skin lesions and diseases, provided they have already seen them before. However, the “global” approach may reach its limit in unusual diagnostic situations. Such a situation may be encountered, for example, in countries where a massive campaign for the detection of leprosy has been conducted by general practitioners, nurses or other field agents who had received basic minimal instruction for the detection of leprosy lesions. As the prevalence of this disease progressively decreased due to the efficacy of these campaigns, so did the teams' diagnostic capabilities, due to a lack of clinical experience and awareness of the differential diagnosis when confronted with a larger variety of skin lesions. This example also reminds us that, whatever the diagnostic approach (global or analytic), the negative and positive predictive values of any clinical sign or group of signs vary with the prevalence of the disease being sought.

A correct diagnosis sets the patient and clinician along an appropriate treatment path [6]. At the same time, there is an understanding that surgical pathology processes and laboratories are complex systems that offer ample opportunity to make mistakes. Errors occur for a variety of reasons. Some occur because of poor processes, some occur because of a lack of knowledge, some occur due to carelessness, and some occur because of external stresses. Trying to evaluate every possible source of error can be daunting. By breaking down the system into segments and evaluating each segment, errors can be more easily classified, analyzed, and addressed.

Surgical pathology is a laboratory discipline of testing that has a defined test cycle of preanalytic, analytic, and postanalytic. Preanalytic and postanalytic challenges of specimen identification and processing as well as report generation and delivery are similar to processes that occur in clinical laboratories. The specimens in surgical pathology are unique and many times cannot be obtained a second time as can be done with blood or urine specimens. The procedures to obtain surgical pathology specimens are also far more complex making it unpalatable to lose, mislabel, or mishandle a specimen.

3. Skin Mechanics

The mechanical properties of skin are of importance to prevent damage and maintain good feel [7]. For example, mechanical properties influence skin's resistance to laceration during impact injury. They are important indicators of pathological situations. Precise knowledge of the mechanical properties of skin is also of interest to plastic

surgeons in designing the size, shape, and orientation of skin grafts. The mechanical properties of skin are affected by the level of hydration. Extensibility and viscoelasticity are markedly influenced by the water content of the stratum corneum, which is the top layer of skin. The main objective of the application of skin cream is to assist the stratum corneum in restoring lost moisture. Many macroscale studies have focused on the mechanical properties of skin with and without skin treatment such as elastic-plastic deformation behavior, hardness, Young's modulus of elasticity, time dependent creep, and relaxation properties. Nanoscale studies using an AFM and nanoindenter have focused on the mechanical properties of skin with and without cream treatments.

4. Psyche

Skin is the largest organ of the body, and is the only organ visible to others and exposed to the external environment [8]. It is, therefore, obvious that any pathology of the skin could have an impact on the psychology of the person. The more extensive the disease and the more chronic it is the greater the psychological effect on the person. Stress can affect any organ of the body such as myocardial infarction, gastric ulcers, irritable bladder, irritable bowel syndrome, etc. The effect of psyche on the skin can be studied under the following two headings:

- The effect of skin disease on the psyche
- The effect of the psyche on the skin

4.1 The effect of skin disease on the psyche

A number of skin disorders can lead to emotional trauma such as psoriasis, atopic dermatitis, ichthyosis, acne, hair disorders such as alopecia, etc [8]. Acne affects young adults; this can lead to low self-esteem, antisocial behavior, stress, depression, and even suicide. Eczema of the hands can lead to loss of work; this monetary loss leads to its associated problems. A number of skin disorders can be precipitated by stress such as acne, herpes simplex, psoriasis, alopecia areata, discoid eczema, pompholyx, etc.

4.2 The effect of the psyche on the skin

A number of skin disorders can be due to the emotional trauma suffered by a patient [8]. Patients inflict damage to their skin for complex reasons including to get more attention from the people around them. The skin is the organ to vent out these emotions.

5. Disorders

Interpretation of clinical signs on the skin in the context of underlying pathological processes is very important topic in dermatology. This helps the reader develop a deeper understanding of the subject and should form some guiding principles that can be used as tools to help assess almost any skin eruption [9]. Clinically, cutaneous disorders fall into three main groups:

- 1) Those that generally present with a characteristic distribution and morphology that leads to a specific diagnosis—such as chronic plaque psoriasis, basal cell carcinoma and atopic dermatitis.
- 2) A characteristic pattern of skin lesions with variable underlying causes—such as erythema nodosum and erythema multiforme.
- 3) Skin rashes that can be variable in their presentation and/or underlying causes—such as lichen planus and urticaria.

Malignant change can occur in any cell in the skin, resulting in a wide variety of different tumours, the majority of which are benign. Recognition of typical benign tumours saves the patient unnecessary investigations and the anxiety involved in waiting to see a specialist or waiting for biopsy results. Malignant skin cancers are usually only locally invasive, but distant metastases can occur. It is important therefore to recognize the early features of lesions such as melanoma and squamous cell carcinoma before they disseminate.

The majority of skin diseases, however, do not signify any systemic disease and are often considered 'harmless' in medical terms. However, due to the very visual nature of skin disorders, they can cause a great deal of psychological distress, social isolation and occupational difficulties, which should not be underestimated. A validated measure of how much skin disease affects patients' lives can be made using the Dermatology Life Quality Index (DLQI). A holistic approach to the patient both physically and psychologically is therefore highly desirable.

6. Toxicity

Substances may affect the skin in many ways, which may result in a variety of adverse effects [10]. Clinically

observable pathological skin conditions are as manifold as their underlying mechanisms. Local effects on the skin include corrosion, irritation and sensitization. Corrosion is defined as an irreversible destruction of the skin, whereas irritation implies reversible damage that is mostly caused by inflammation. However, substances may not only induce inflammation directly (i.e. by irritation), but also by immunemediated processes (i.e. by sensitization). Allergic contact dermatitis is the clinical manifestation of skin sensitization, i.e., the immunemediated inflammation of the skin. It requires repeated dermal contact with the substance, whereas direct irritation and corrosion are typically acute effects that are already observed after one single contact. Additionally, some substances may elicit local dermal effects only upon simultaneous irradiation with UV or visible light, thereby causing either phototoxicity (photoirritation or, *in vitro*, photo-cytotoxicity) or photoallergic reactions (with the frequently used but misleading overarching term for all UV- and visible light-facilitated effects, 'photosensitivity').

In most substance or product safety legislations, the identification of potential hazards of substances arising from incidental skin contact or intended topical application is a core requirement. The Globally Harmonized System of Classification and Labelling of Chemicals (GHS) that has been implemented—albeit with modifications—in the EU Regulation on the classification, labelling and packaging of substances and mixtures distinguishes three types of local dermal effects with the following categories and hazard phrases: skin corrosion (Category 1, corrosion H314), skin irritation (Category 2, irritation H315, and Category 3, mild irritation H316) and skin sensitization (Category 1, sensitization H317). Additionally, repeated exposure may cause skin dryness or cracking (EUH066) has been laid down in the EU as further skin-related hazard phrase. All hazard categories may be sub-categorized by potency levels (e.g. Sub-categories 1A, 1B and 1C for 'Category 1, corrosion', and Sub-categories 1A and 1B for 'Category 1, sensitization', with the latter sub-categorization based upon human evidence or the potency of effects observed in animals). Notwithstanding, the GHS does not require sub-categorization, and it may indeed not improve the ensuing risk management measures.

7. Cell Death

Tumor growth occurs when the cellular birth rate exceeds the death rate [11]. Control of cell growth is important in the process of normal development and tissue homeostasis, and in pathological conditions such as neoplasia. Growth arrest and cell death are also important in normal and neoplastic growth.

Inactivation of apoptosis is a hallmark of cancer, an obligate ritual in the malignant transformation of normal cells. By inactivating apoptosis, cancer cells enhance their chances of survival and increase their resistance to chemotherapeutic agents. Because apoptosis is a genecontrolled process, it is susceptible to genetic manipulation for therapeutic purposes, such as in cancer treatment. The acquisition of resistance to apoptosis is important in the transition from normal melanocyte to melanoma. Apoptosis is, in fact, critical for epidermal homeostasis, representing a key protective mechanism removing premalignant cells that have acquired mutations.

Melanoma is the most aggressive form of skin cancer, notoriously resistant to current modalities of cancer therapy and known to be a tumor with an elevated metastatic ability. Although today melanoma is more often diagnosed in an early stage of disease and therefore shows a better overall survival, when tumor cells are detected in the regional lymph node, the patient has a poorer prognosis. One of the earliest events in melanoma progression involves the unregulated proliferation of melanocytes. In this stage of melanoma progression, the cells lose their ability to maintain the cell-cycle controls that function in normal unstimulated melanocytes. This loss of cell-cycle control can lead to sustained proliferation, decreased apoptosis, or both. It also has been reported that melanocytes displayed a broad expression of apoptotic inhibitors to maintain their longevity, at the cost of the nonelimination of damaged cells, thus resulting in a high probability of developing melanoma.

In addition to signs and symptoms at the sites of primary and metastatic disease, cancer can produce manifestations in sites that are not directly affected by the disease [12]. Such manifestations are collectively referred to as paraneoplastic syndromes. Some of these manifestations are caused by the elaboration of hormones by cancer cells, and others result from the production of circulating factors that produce hematopoietic, neurologic, and dermatologic syndromes. These syndromes are most commonly associated with lung, breast, and hematologic malignancies.

8. Society

Skin diseases affect a significant proportion of the population and can seriously impact on a person's health and well-being [13]. They can affect how a person undertakes their activities of living as well as how they interact with others and how others interact with them. Each time a healthcare professional interacts with those they care for, they are observing the patient's skin as they undertake care activities; it is essential therefore that they have an

understanding of the function of the skin so as to recognise problems that can occur. There are several areas of practice where the healthcare professional will come into contact with those who experience problems of the skin and they are ideally placed to offer these people support with respect to some of these conditions.

Some skin conditions have the potential to cause stigma, such as eczema and psoriasis; the healthcare professional, as advocate, can correct any misunderstanding concerning contagion and help to improve the individual's social well-being. Often appearance and image are associated with success and achievement, and the blemish-free individual represented in the media (in many Western societies) is the image to which many strive; however, this is not always possible for those with skin conditions. Society places much emphasis on physical appearance and for those who have skin problems this can become increasingly challenging. People with skin problems may experience difficulties in other aspects of their lives, e.g., from a sexual relationship perspective, and also concerning issues associated self-esteem and self-concept—altered body image can have a profound effect on the individual, their partner and their family.

9. Conclusion

The skin is not a uniform surface and on it we can find changes of increased or decreased pigmentation or changes that are above or below the level of the surrounding skin. Most skin changes are benign and do not need to be removed. A small number of changes are skin tumors. An experienced dermatologist can make a diagnosis with a high degree of certainty, but only a pathologist, after the change has been removed, can say with certainty what the change is. The patient should talk with a dermatologist about possible pathological diagnoses and possible additional procedures which are possible after the final diagnosis, the risks of the procedure and some conditions that may affect the procedure itself, such as blood pressure, medications that may affect blood clotting, allergies, smoking, scars etc. For the success of the procedure and for making a decision on the procedure, it is crucial to realistically assess its necessity and the expected result.

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