Pathology of skin diseases

A study from Western Saudi Arabia

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ABSTRACT

الأهداف: وصف النمط النسيجي للأمراض الجلدية في المرضى الذين يراجعون مستشفى جامعة الملك عبد العزيز في المنطقة الغربية، المملكة العربية السعودية، ومقارنة البيانات المتوفرة لدينا مع البيانات المنشورة سابقا من جميع أنحاء العالم ومن المملكة العربية السعودية.

الطريقة: أجريت دراسة استرجاعية لجميع خزعات الجلد والتي استقبلها في قسم علم الأمراض في مستشفى جامعة الملك عبد العزيز، جدة، المملكة العربية السعودية خلال الفترة من يناير 2005م إلى ديسمبر 2010م وتنفيذها. تم تقسيم التهاب السبلة الشحمية مع النوع الورمي إلى نوع صباغي وغير صباغي. بينما يتم تقسيم النوع الورمي إلى الأنواع التالية: التهاب الجلد، الالتهاب، وعائي، حويصلي فقاعي، أمراض الأنسجة الداعمة، تنكسي، ايضي، وصبغي.

النتائج: تم استعراض ما مجموعه 360 خزعات الجلد (360). للخروج من هذه كانت 207 (57.5%) غير الأمراض الجلدية الأورام، بينما 153 (42.5%) وكانت كل من الأورام غير الورم (M : F نسبة قدرها 1.3:1). والأورام (M:F 1 نسبة 1.2) كانت فئات أكثر شيوعا في الإناث منها في الذكور بين فئة الأورام غير، والنوع الأكثر شيوعا تشخيص المرض كان الأمراض الحويصلية الفقاعية46 (22.2%)، تليها التهاب الجلد 30 (14.5%). وقد تم تقسيم هذه الفئة إلى 31 الأورام الصباغية (20.3%) و 122 (79.7%) غير الصباغية الأورام. كل فئات الأورام وغير الأورام كانت الأكثر شيوعا في الفئة العمرية من 46 عام فما فوق.

خاتمة: تعد أمراض الحويصلية الفقاعية، التهابات الجلد والالتهاب الأمراض الورمية الأكثر شيوعا والأورام الحميدة غير الصباغية من الأوام الأكثر شيوعا. كما أن انتشار الأورام والأمراض الجلدية غير الورمية يزيد مع زيادة العمر.

Objectives: To describe the histopathological pattern of skin diseases in patients from the western region of Saudi Arabia and to compare this with previously published data from other regions in Saudi Arabia and worldwide.

Methods: A retrospective review of all skin biopsies received and reported by the Department of Pathology, King Abdulaziz University Hospital, Jeddah, Kingdom of Saudi Arabia between January 2005 and December 2010. Neoplastic and non-neoplastic category were divided into melanocytic and non-melanocytic subcategories. Non-neoplastic category was divided into the following subcategories: dermatitis, infection, vascular, vesiculobullous, connective tissue disease, drugs, panniculitis, non-infectious granuloma, degenerative, metabolic, and pigmentary.

Results: Three hundred and sixty skin biopsies were reviewed. Out of these, 207 (57.5%) were non-neoplastic skin diseases, while 153 (42.5%) were neoplastic. Both non-neoplastic (female to male ratio of 1.3:1) and neoplastic (female to male ratio of 1.2: 1) categories were more common in females than in males. Among the non-neoplastic category, the most common diagnosed subcategory was vesiculobullous disease (n=46, 22.2%), followed by dermatitis (n=30, 14.5%). The neoplastic category was divided into melanocytic (n=31, 20.3%) and non-melanocytic neoplasms (n=122, 79.7%). Both neoplastic and non-neoplastic categories were most common in the age group of 46 years and older.

Conclusion: Vesiculobullous diseases, dermatitis, and infections are the 3 most common non-neoplastic skin diseases and the most common neoplastic are benign non-melanocytic neoplasms. The prevalence of neoplastic and non-neoplastic skin diseases in general increases with age.

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Skin disorders are quite common and may be the cause of considerable morbidity especially in older people. Correct diagnosis is paramount for early treatment.[1] The incidence of skin disease differs widely in various geographical locations and is influenced by many factors such as environmental and racial, genetic, nutritional, hygienic and others.[2] Additionally, the knowledge and expertise of the treating dermatologist and the diagnosing pathologist play an important role in reporting such cases. There are a few published reports on the pattern of skin disease in general,[3-6] and most, if not all data published is based on clinical studies rather than histopathological ones. In the present study, the histopathological pattern of skin diseases in all skin biopsies received and reported by the Pathology Department of King Abdulaziz University Hospital is reviewed, and results compared to those from within Saudi Arabia and around the world.

Methods. A retrospective cross sectional review of all skin biopsies received and reported by the Department of Pathology at King Abdulaziz University Hospital between January 2005 and December 2010 was carried out. The study was performed by reviewing the computerized database of the pathology department. Cases with incomplete pathological material were excluded from this study. This review has been carried out in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans. Ethical approval for this study was obtained from the King Abdulaziz University Hospital Ethics Committee.

All related pathological material of these skin biopsies are retrieved and studied by one of the dermatopathologist; and the pathological findings were categorized into the following diagnostic categories:[7] neoplastic and non-neoplastic with neoplastic category further divided into melanocytic and non-melanocytic subcategories. Non-neoplastic category was further divided into the following subcategories: dermatitis, infection, vascular, vesiculobullous, connective tissue disease, drugs, panniculitis, non-infectious granuloma, degenerative, metabolic, and pigmentary. Other non-specific skin changes not included in the above 11 major subcategories of the non-neoplastic category were grouped under the diagnostic category of miscellaneous. Difficult cases or cases with vague diagnosis were reassessed by 2 dermatopathologists, and a consensus diagnosis obtained.

Demographic data such as age and gender were retrieved from the medical records of these patients. The diagnostic categories and subcategories were further studied and divided according to gender distribution and distribution in different age groups as follows: 0-15 years, 16-30 years, 31-45 years, 46 years and older. Results are tabulated and data analysis was carried out using Microsoft Excel sheets.

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Results. Three hundred and sixty skin biopsies were reviewed and reported by the Pathology Department in King Abdulaziz University Hospital, Jeddah, Kingdom of Saudi Arabia. The age of patients ranged from 2 months to 93 years old. Of these, 207 (57.5%) were non-neoplastic skin diseases, while 153 (42.5%) were neoplastic. Both non-neoplastic (female to male ratio of 1.3:1) and neoplastic (female to male ratio of 1.2: 1) categories were more common in females than in males. Among the non-neoplastic category, the most common diagnosed subcategory was vesiculobullous disease, followed by dermatitis. Both infections and vascular disease accounted for 21 (10.1%) each. Connective tissue disease was diagnosed and non-infectious granulomas were detected. Pigmentary disorders accounted for 5 cases, while panniculitis were detected in 4 cases. Both degenerative and metabolic disorders were equally detected in 2 cases each. The summary are shown in **Table 1**.

In the vesiculobullous category of non-neoplastic skin diseases, 28 cases were of the secondary lesions (60.8%) while 7 cases were bullous pemphigoid (15.2%) and 6 cases (13%) subepidermal vesiculobullous disease. The remaining diseases were accounted for by one case (2.2%) each: Pemphigus vulgaris, Pemphigus foliaceus, erythema multiforme, intradermal and suprabasal vesiculobullous disease. In the dermatitis category of non-neoplastic skin diseases, both lichen planus and psoriasis were the most common diseases (11 cases each, 36.7%). Four (13.3%) cases of Pityriasis lichenoides chronica, 3 cases (10%) of Prurigo nodularis , and one case (3.3%) of persistent pigmented purpuric dermatitis were detected.

In the infection category of non-neoplastic skin diseases, viral infections were the most commonly diagnosed infection (n=8, 38%), followed by fungal infections (n=3, 14.3%), leishmania (n=3, 14.3%), and non-specific bacterial infections (n=3, 14.3%). Two (9.5%) cases of leprosy were encountered. Necrotizing granulomatous inflammation and arthropod bite were detected as one case each (4.8%).

Most of the vascular category of non-neoplastic skin diseases was leuckocytoclastic vasculitis (n=18, 85.6%), while secondary vasculitis, urticarial vasculitis, and Sweet's syndrome, each accounted for one case (4.8%). Morphea represented the most common category in connective tissue disease (n=7, 50%), followed by lupus erythematosus (n=6, 42.9%). One case of dermatomyositis was encountered (7.1%).

The neoplastic category was divided into 31 melanocytic (20.3%) and 122 (79.7%) non-melanocytic neoplasms. Two cases out of the 31 melanocytic lesions (6.5%) were malignant melanoma, while 29 cases (93.5%) were benign melanocytic neoplasms (benign nevi). Among the non-melanocytic neoplasms, 91 (74.6%) were benign epithelial and non-epithelial neoplasms while 31 (25.4%) were malignant (**Table 2**). The benign non-melanocytic neoplasms (n=91) were divided as follows: squamous neoplasms (n=29, 31.9%), vascular neoplasms (n=9, 9.8%), histiocytic neoplasms (n=5, 5.5%), neural neoplasms (n=5, 5.5%), fibrous neoplasms (n=36, 39.6%), and adnexal neoplasms (n=7, 7.7%). The non-melanocytic malignant neoplasms (n=31) were as follows: squamous cell carcinoma (n=11, 35.4%), basal cell carcinoma (n=11, 35.4%), and skin lymphoma (n=9, 29%).

The skin biopsies are further divided according to the various age groups (**Tables 3 & 4**) and both neoplastic and non-neoplastic categories in general were most common in the age group of 46 years and older. The most common non-neoplastic skin disease in the pediatric age group of 0-15 years was vesiculobullous diseases (n=6, 24%) followed by vascular (n=4, 16%), infection (n=3, 12%), dermatitis and metabolic lesions (n=2, 8%), and finally panniculitis, pigmentary lesions and non-infectious granulomas (n=1, 4%). No connective tissue, drug or degenerative diseases were identified in this age group. Five cases (20%) were of the miscellaneous subcategory. The most common non-neoplastic skin disease in the age group of 16-30 years old were vesiculobullous diseases 8 cases (15%), followed by dermatitis and infection (n=7, 13.2%). The other diagnostic categories were less common. No

Table 1 - Frequency and percentages of non-neoplastic skin diseases.

Non-neoplastic skin diseases	n	(%)
Vesiculobulous	46	(22.2)
Dermatitis	30	(14.5)
Infection	21	(10.14)
Vascular diseases	21	(10.14)
Connective tissue diseases	14	(6.8)
Non infectious granulomas	10	(4.8)
Drugs	9	(4.3)
Pigmentary lesions	5	(2.4)
Panniculitis	4	(1.9)
Degenerative diseases	2	(1.0)
Metabolic diseases	2	(1.0)
Miscellaneous	43	(20.8)
Total	**207**	**(100.0)**

Table 2 - Frequency and percentages of neoplastic skin diseases

Neoplastic skin diseases	n	(%)
Benign melanocytic tumors	29	(19.0)
Malignant melanoma	2	(1.3)
Benign non-melanocytic tumors	91	(59.5)
Malignant non-melanocytic tumors	31	(20.2)
Total	**153**	**(100)**

Table 3 - Pattern of non-neoplastic skin diseases in different age groups.

Non-neoplastic skin diseases	Age group					
	0-15	16-30	31-45	≥46	n	%
Vesiculobullous skin disease	6	8	13	19	46	(22.2)
Dermatitis	2	7	6	15	30	(14.5)
Infection	3	7	4	7	21	(10.1)
Vascular diseases	4	5	2	10	21	(10.1)
Connective tissue diseases	0	6	4	4	14	(6.8)
Non-infectious granulomas	1	3	1	5	10	(4.8)
Drugs	0	0	1	8	9	(4.3)
Pigmentary lesions	1	3	1	0	5	(2.4)
Panniculitis	1	1	0	2	4	(1.9)
Degenerative diseases	0	0	0	2	2	(1.0)
Metabolic diseases	2	0	0	0	2	(1.0)
Miscellaneous	5	13	9	16	43	(20.8)
Total	**25**	**53**	**41**	**88**	**207**	**(100)**

Table 4 - Pattern of neoplastic skin diseases in different age groups.

Neoplastic skin diseases	Age group				Total	
	0-15	16-30	31-45	≥46	n	%
Benign melanocytic neoplasms	1	7	16	5	29	(19.0)
Malignant melanoma	1	0	0	1	2	(1.3)
Benign non-melanocytic neoplasms	12	22	19	38	91	(59.5)
Malignant non-melanocytic neoplasms	1	2	6	22	31	(20.2)
Total	15	31	41	66	153	(100.0)

metabolic , drug or degenerative diseases were identified in this age group. Thirteen cases (24.5%) were in the miscellaneous subcategory.

In the age group of 31-45, the most common non-neoplastic skin disease identified was vesiculobullous diseases. This is followed by dermatitis, infection and connective tissue disease each, vascular diseases, pigmentary diseases and non-infectious granulomas and drug reactions each. No degenerative or metabolic diseases and no panniculitis were identified in this age group. Nine cases (21.9%) were in the miscellaneous subcategory. The most common non-neoplastic skin disease in the age group of ≥46 was vesiculobullous diseases followed by dermatitis. The remaining diagnostic categories in descending order were vascular diseases, drugs, infection, non-infectious granuloma, connective tissue diseases, and finally panniculitis and degenerative diseases each (**Table 3**). No metabolic or pigmentary diseases were identified in this age group. Sixteen cases (18.2%) were in the miscellaneous subcategory.

When the neoplastic category was classified according to different age groups, benign non-melanocytic tumors were the most common diagnostic category in all age groups (80%, 85%, 54.6% and 44%). In the age group of 0-15, the remaining 3 diagnostic subcategories were equally distributed (each one case). In the age group of 16-30, benign melanocytic and malignant non-melanocytic categories were equally distributed (one case) while no cases of malignant melanomas were identified. The second most common neoplastic subcategory after benign non-melanocytic lesions in the age group of 31-45 years were benign melanocytic lesions (n=22, 34%) while malignant non-melanocytic lesions (n=22, 25.5%) were the second most common category in age 46 years and above (**Table 4**).

Discussion. Skin biopsy is the golden method for diagnosis of skin diseases. It is considered a very important investigation in assisting dermatologists in their management of skin diseases. In addition, review of the pathological findings in these skin biopsies encourage proper clinicopathologic correlation and allows better understanding of the general pattern of skin diseases.[8] The current study is the first to describe the histopathological pattern of skin diseases in the western region of Saudi Arabia, based on the examination of skin biopsies reported in King Abdulaziz University Hospital. King Abdulaziz University Hospital is one of the largest governmental hospitals in Jeddah region catering for Saudi and non-Saudi residents. The hospital offers secondary and tertiary care, and is equipped with modern and sophisticated facilities. The Pathology Department in King Abdulaziz University Hospital receives skin biopsies from all hospital departments and clinics as well as referred cases and cases from the private sector. Although this study was based only on skin biopsies received by the Pathology Department in King Abdulaziz University Hospital, we believe that it roughly represents the pathological pattern of such diseases in the western region of Saudi Arabia. This is based on the fact that the hospital receives patients from all regions of the country, Saudi and non-Saudi, all ages and from varied socioeconomic backgrounds.

In the present study, skin diseases in general were more common in females (n=203, 56.4%) than in males (n=157, 43.6%). This is similar to several local and international previously published data,[3-6] where it was explained by the greater health awareness experienced by females in comparison to males. Studies from some other regions of Saudi Arabia[9-12] showed a different pattern and skin diseases were more common among male patients. In the study by Al Shobaili from AlQasim region,[12] male patients attended dermatology clinics more frequently. The higher prevalence of male patients in these studies may be attributed to under-representation of females at Saudi clinics due to cultural barriers.

Additionally, the present study shows that non-neoplastic skin diseases are more common than the neoplastic ones. The prevalence of various non-neoplastic skin diseases varies according to geographical area and is related to racial, environmental, and socioeconomic factors of the population. Eczema and dermatitis are the most prevalent skin disorders reported from developed countries[1] whereas skin infections are predominant in developing African and Asian countries.[13,14] Contact dermatitis or eczema is a polymorphic inflammation of the skin. It occurs at the site of contact with irritating or antigenic substances. Eczematous lesions are characterized by a mono-nuclear infiltrate consisting mainly of T cells in the dermis and epidermis, together with an intercellular epidermal edema or spongiosis.[15]

Our data showed that vesiculobullous skin diseases are the most common skin diseases and together with dermatitis and infection are the 3 most common non-neoplastic skin diseases been diagnosed in our department. With the exception of connective tissue diseases and pigmentary lesions, which were mostly diagnosed in the age group of 16-30, all these non-neoplastic skin diseases are most commonly seen in older age groups especially in the age group of 46 years and above. As a matter of fact, vesiculobullous skin diseases were the most common skin diagnosis in all age

groups from childhood to elderly. As mentioned before, scanty data is available on the pattern of skin diseases on skin biopsy. In one study by Yap from Sarawak,[8] benign tumors (n=71, 17.7%) were the most common pathology identified in skin biopsies examined. This was followed by drug-related dermatoses (n=59, 14.7%) infections (n=56, 14%), and eczema (n=37, 9.2%).

Since no previous histopathological study was available from within Saudi Arabia, we compared our data with the local previously published clinical studies from different regions of Saudi Arabia[3,6,12] as well as studies from United States,[1] Mediterranean Islands,[5] Iran,[6] Jordan,[13] and Tunis.[14] In the previously mentioned study by Al Shobaili,[12] the main volume of patients (71%) presented between ages 5 and 35 years. The most common disease categories occurring in that age group were eczema/dermatitis, pilosebaceous disorders, and viral infections. In the clinical study by Al-Zoman et al,[3] the incidence of skin diseases was higher in females (58.4%) than males (41.6%). The largest number of patients was in the age group of 41-50 years. The most common skin diseases in this study were dermatitis/eczemas (21.3%) followed by diseases of the hair (11.9%) and acne (11.9%). Skin infections due to viruses were seen in 9.7%, bacteria 3%, and fungi 4.5%. Shelleh and Hatitti study[16] from Najran indicated that 37% of their patients had dermatitis or eczema, 12.75% had acne, 7% had vitiligo, 5.9% had viral infections, 5.6% had superficial mycoses, 5% had bacterial infections, 1.5% had psoriasis, and 1.1% had lichen planus. When the results of their study were compared to other local studies, the authors concluded that the incidence of eczema, acne, and vitiligo were slightly higher in Najran area compared to other regions such as Asir, Hail, Al-Jouf, and Jeddah, most likely due to the genetic disposition of Najran community to these diseases.

In the United States,[17] an estimated 60 million of the US population age 1-74 years, had some skin pathology. The prevalence of significant skin pathology increased rapidly with age due to increases in such diagnoses as psoriasis and vitiligo, actinic and seborrheic keratoses as well as malignant and benign tumors. In the mentioned study, the most common skin diseases were of sebaceous glands, dermatophytosis, tumors (malignant and benign), seborrheic dermatitis, atopic dermatitis/eczema, contact dermatitis, and ichthyosis/keratoses. The most common neoplastic subcategory diagnosed in all age groups in the present study was benign non-melanocytic skin neoplasms (n=91, 59.5%). This category was most common in the age group of 46 years and older. Malignant non-melanocytic neoplasms (n=31) were more common than the melanocytic ones (n=2). The most common non-melanocytic malignant neoplasms was squamous cell carcinoma (n=11, 35.4%) followed by basal cell carcinoma (n=11, 35.4%) and skin lymphoma (n=9, 29%). This concurs with other studies from the same region,[18-20] and internationally[8] where basal cell carcinoma followed by squamous cell carcinoma were the most common non-melanocytic skin lesions identified. In the study by Jones et al [21] from USA, 1215 skin biopsies were reviewed and reported 1004 benign, 89 premalignant, and 122 malignant skin lesions. The 5 most frequent biopsy diagnoses were nevi, seborrheic keratoses, actinic keratoses, cysts, and dermatofibromas. The authors concluded that 82.6% of the pathologically examined biopsies were benign, 7.3% were premalignant, while 10% were malignant. In the study from Sarawak,[8] a different pattern of distribution of neoplastic skin diseases was seen with a high proportion of cutaneous lymphoma.

As mentioned before, the differences in the prevalence of various skin diseases in various countries may be attributed to differences in several epidemiological and socioeconomic factors. However, it also could be due to the variation in the methods of diagnosis by pathologists and to the difference in inclusion or exclusion criteria. This variation in diagnostic criteria between pathologists as well as the small number of patients studied may be the 2 limitations in this study. Despite this, it is hoped that the present study may stimulate further larger national studies based on histopathological data.

In conclusion, vesiculobullous diseases, dermatitis, and infections are the 3 most common non-neoplastic skin diseases identified by examination of skin biopsies, and benign non-melanocytic neoplasms are the most common neoplastic. The prevalence of neoplastic and non-neoplastic skin diseases increases with increasing age. Larger multicenter histopathological studies are needed to help assess the pattern of skin diseases based on pathological examination in order to develop public health strategies and to have better clinicopathological correlation.

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