Clinical and Pathological Evaluation of Benign Skin Lesions
(Penilaian Klinikal dan Patologi Lesi Kulit Benigna)

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ABSTRACT

Skin lesions are commonly benign in nature. The present study aims to evaluate the prevalence and clinicopathological characteristics of a large series of benign skin lesions (BSLs) excised in our clinic. Patients with skin lesions who underwent total excisional biopsy at the general surgery clinic between 2012 and 2016 were reviewed. A total of 551 patients with BSLs were included in the study. Of these, 43.7% were females and 56.7% were males. The age range was between 2 and 98 years with a mean of 39.7 years. The most commonly occurring group of BSLs was of the appendageal tumors (33.3%), and this finding was statistically significant. The most common keratinocytic BSL (13.6%) was verruca vulgaris. In the present study, various types of BSLs and their occurrences were evaluated. Benign skin tumors can turn into malignant types. A biopsy should be performed to establish the exact diagnosis. We performed an excisional biopsy to confirm the diagnosis.

Keywords: Benign skin lesions; clinicopathological examination; excisional biopsy

ABSTRAK

Lesi kulit adalah perkara biasa dan kebanyakannya lesi jinak. Tujuan kajian ini adalah untuk menilai kelaziman dan ciri klinikopatologi siri besar lesi kulit benigna yang dikeluarkan di klinik kami. Pesakit yang mengalami lesi kulit dikaji semula, yang menjalani jumlah biopsi ekslusif dalam klinik pembedahan umum antara 2012 dan 2016. Sejumlah 551 pesakit dengan lesi kulit benigna termasuk dalam kajian ini. Daripada pesakit ini, 43.7% adalah wanita dan 56.7% adalah lelaki. Julat umur adalah antara 2 dan 98 tahun dengan purata 39.7 tahun. Kumpulan yang paling biasa (33.3%) lesi kulit jinak adalah tumor lampiran dan penemuan ini secara statistik secara signifikan. Lesi kulit yang paling biasa (13.6%) adalah verruca vulgaris. Dalam kajian ini, pelbagai jenis lesi kulit benigna dan frekuensi relatifnya dinilai. Tumor kulit benigna boleh berubah menjadi jenis malignan. Biopsi perlu diambil untuk menentukan diagnosis yang tepat. Kami melakukan biopsi pengecualian untuk diagnosis.

Kata kunci: Biopsi eksisi; lesi kulit benigna; pemeriksaan klinikopatologi

INTRODUCTION

The vast majority of skin lesions are benign (Nguyen & Zuniga 2013). A benign skin lesion (BSL) does not spread to other parts of the body but continues its growth at the location of its origin (Higgins et al. 2015; Ingraffea 2013). Premalignant skin lesions (PSLs) can transform into malignant tumors at a rate of 10% (Freak 2005; Ingraffea 2013). They are most commonly seen in males (Higgins et al. 2015; Ingraffea 2013). The lifetime risk of skin cancer development has been reported in one out of five people in the United States (Freak 2005; Higgins et al. 2015; Ingraffea 2013).

Skin lesions are usually sporadic; however, they can also be a symptom of a syndrome, or they may be associated with systemic malignancies (Ingraffea 2013; Nguyen & Zuniga 2013). Therefore, clinicians should differentiate benign from malignant lesions and should follow a systematic approach in evaluating these lesions (Gogi & Ramanujam 2013). If there is a clinical suspicion of malignancy, biopsy should definitely be performed (Woon & Serpell 2008).

Along with the reported findings in the literature, the present study aims to review and evaluate the prevalence and clinicopathological features of the BSLs that are surgically excised in our clinic. Patients with skin lesions who underwent total excisional biopsy at the general surgery department between 2012 and 2016 were reviewed. The histopathological diagnoses of these lesions were examined to determine whether they were associated with the tumor size, location, and number and whether they were associated with the age and gender.

MATERIALS AND METHODS

The present study included patients with skin lesions treated in our general surgery clinic between 2012 and 2016. Patients were followed up for recurrence for a mean period of 2 years. The patients' charts showed that a total of 712 patients underwent excisional biopsy due to several types of skin lesions (Edlich et al. 2004). Of these, 27 patients were diagnosed with nonspecific skin lesions and 136 were diagnosed with malignant skin lesions (MSLs).

Ultrasonography, computed tomography, or magnetic resonance imaging was performed for patients with skin lesions before biopsy, depending on physical examination findings of the size and appearance of the lesion. Fine-needle, tru-cut, or excisional biopsy was performed for diagnosis. Patients with nonspecific skin lesions and MSLs were excluded from the study. Of those who were diagnosed with a MSL through pathological examination, nine had been prediagnosed with BSL after the physical examination; however, the excisional biopsy result was reported to confirm malignant lesion.

A total of 551 patients with BSLs were included in the study. Patients with BSLs were evaluated. Patients undergoing follow-up or tru-cut biopsy, those who were not followed up, those without excisional biopsy, and those whose data were not accessible were excluded from the study. Patients undergoing fine-needle biopsy and tru-cut biopsy for the diagnosis of BLS (14 patients) were excluded from the study because of their small number. Patients undergoing excisional biopsy and those whose data were accessible were included in the study.

The lesion size, number of lesions, and morphology were not limited.

The age and gender of patients as well as the number, size in millimeter (mm), anatomical location, and histopathological diagnosis of the skin lesions were evaluated. They were categorized into 0-14, 15-59, and ≥60 age groups based on other scientific studies (Murray et al. 2007).

In the present study, BSLs were categorized and listed according to the World Health Organization histological classification (LeBoit et al. 2006). Accordingly, they were categorized into six main groups and examined. These main groups were keratinocytic, melanocytic, appendageal, hematolymphoid, soft tissue, and neural BSLs. The lesions included in these main groups were examined (Table 1).

STATISTICAL ANALYSES

The data obtained from the present study were analyzed using IBM SPSS Statistics Version 22 package software. Shapiro-Wilk test was performed to determine normal

TABLE 1. Benign skin lesions subtypes

Benign skin lesions		Number of lesions	
		n	%
Keratinocytic	Verruca vulgaris	75	53.19
	Verruca plantaris	29	20.57
	Seborrheic keratosis	27	19.15
	Keratoacanthoma	5	3.55
	Lichen planus-like keratosis	5	3.55
Melanocytic	Melanocytic nevi	55	77.46
	Combined nevus	16	22.54
Appendageal	Hidrocystoma	1	0.54
	Cystic sebaceous tumor	144	78.26
	Chondroid syringoma	2	1.09
	Hidradenoma	2	1.09
	Pilomatricoma	8	4.35
	Trichoblastoma	1	0.54
	Trichilemmoma	24	13.04
	Sebaceoma	2	1.09
Hemato-lymphoid	Lymphomatoid granulomatosis	3	60
	Juvenile xanthogranuloma	2	40
Soft tissue	Dermatofibroma	33	22.76
	Cherry hemangioma	15	10.34
	Pyogenic granuloma	19	13.1
	Cavernous hemangioma	2	1.38
	Arteriovenous hemangioma	3	2.07
	Lymphangioma circumscriptum	2	1.38
	Digital fibrokeratoma	4	2.76
	Dermatomyofibroma	3	2.07
	Lipoma	41	28.28
	Digital mucous cyst	1	0.69
	Keloid scar	17	11.72
	Hypertrophic scar	5	3.45
Neural	Neurothekeoma	3	60
	Neuroma	1	20
	Granular cell tumor	1	20

distribution of the variables. In interpreting the results, if p value was greater than 0.05, it was considered that the variables came from the normal distribution; if p value was less than 0.05, it was considered that the variables did not come from the normal distribution. The Mann–Whitney U and Kruskal–Wallis H tests were used to examine the differences between the groups as the variables were not normally distributed. The Chi-square (χ^2) analysis was used to analyze the associations between the groups of nominal variables. Fisher's exact test was used when the expected values in the cells of the 2 × 2 tables did not achieve a sufficient size. The significance level of 0.05 was used to interpret the results. A p value less than 0.05 indicated a significant association, whereas p values greater than 0.05 indicated that there was no significant association.

RESULTS

The present study included a total of 551 patients. The majority of patients (56.2%, n = 310) were males, and the study population had a female:male ratio of 241/310 (0.77). The age of patients in the study ranged from 2 to 98 years, and the mean age was 39.7 years. The most common (18.8%, n = 104) accompanying disease group were hepatobiliary disorders (fatty liver and gall bladder stone). BSLs were most commonly located in the head and neck region (43.1%, n = 239). The lesions were mostly single (82.5%, n = 455) with a mean diameter of 14.1 mm. The success rate of excisional biopsy diagnosis was 100% (n = 551). The mean follow-up period was 2 years. The rate of local recurrence was 2.3% (n = 13) (Table 2).

A statistically significant difference between the gender and the BSL groups (p = 0.001) was observed. Appendageal BSLs were present in 29.05% (n = 70) of females and in 36.77% (n = 114) of males. Soft tissue BSLs were present in 21.58% (n = 52) of females and in 30% (n = 93) of males. Keratinocytic BSLs were present in 26.14% (n = 63) of females and in 25.16% (n = 78) of males. Melanocytic BSLs were present in 21.58% (n = 52) of females and in 6.13% (n = 18) of males. Hematolymphoid BSLs were present in 1.24% (n = 3) of females and in 0.65% (n=2) of males. Neural BSLs were present in 0.41% (n = 1) of females and in 1.29% (n = 4) of males (Table 3).

In the present study, a statistically significant association between the BSL groups and the age distribution (p = 0.008) was observed. In the 0–14 age group, 2.94% (n = 1) of patients had appendageal BSLs. This was 35.23% (n = 155) in the 15–59 age group, and 36.36% (n = 36) in the 60 and above age group. Soft tissue BSLs were present in 35.29% (n = 12) of patients in the 0-14 age group. Additionally, these types of skin lesions were present in 27.05% (n = 119) in the 15-59 age group and in 18.18% (n = 14) in the 60 and above age group. Keratinocytic BSLs were present in 41.18% (n = 14) of patients in the 0-14 age group, in 22.5% (n = 99) in the 15-59 age group, and in 36.36% (n = 28) in the 60 and above age group. Melanocytic BSLs were present in 14.71% (n = 5) of patients in the 0-14 age group, in 13.41% (n = 59) in the 15-59 age group, and in 9.09% (n = 7) in the 60 and above age group. Hematolymphoid BSLs were present in 2.94% (n = 1) of patients in the 0-14 age group and in 0.91% (n = 4) in the 15-59 age group. Neural BSLs were present in 2.94% (n = 1) of patients in the 0-14 age group and in 0.91% (n = 4) in the 15-59 age group (Table 3).

TABLE 2. Demographic and clinical characteristics of subjects

Demographic and clinical features	Distribution of properties
Gender (Female/Male)	241/310 (0.77)
Age	2–98 (mean 39.7) years
Age distribution	0–14 (6.1%, n = 34) 15–59 (79.8%, n = 440) ≥60 (13.9%, n = 77)
Comorbidities	Hepatobiliary disease (18.8%, n = 104) Renal disease (12.5%, n = 69) Endocrine diseases (7%, n = 39) Vascular disease (6.2%, n = 34) Gynecological disease (2.3%, n = 13)
The main complaint	Painless swelling (90%, n = 496) Color change (32%, n = 176)
Lesion localization	Head and neck (43.4%, n = 239) Trunk (25.9%, n = 143) Upper extremities (13.7%, n = 76) Lower extremities (17.0%, n = 94)
Number of lesions	Single (82.5%, n = 455) Multiple (17.4%, n = 96)
Lesion diameter	1–70 (mean 14.1) mm

There was a statistically significant relationship between the original localization of the tumor and the BSL groups (p = 0.001). Appendageal BSLs comprised 36.55% (n = 87) of the neoplasms originating from the head and neck region, 48.95% (n = 70) of the neoplasms originating from the trunk, 26.32% (n = 20) from tumors of the upper extremities, and 7.45% (n = 7) from tumors of the lower extremities. Soft tissue BSLs comprised 15.55% (n = 37) of the neoplasms originating from the head and neck region, 30.07% (n = 43) from the trunk, 47.37% (n = 36) from the upper extremities, and 30.85% (n = 29) from the lower extremities. Keratinocytic BSLs comprised 21.85% (n = 52) of the neoplasms originating from the head and neck region, 18.42% (n = 20) from the trunk, 18.42% (n = 14) from the upper extremities, and 58.51% (n = 55) from the lower extremities. Melanocytic BSLs comprised 23.95% (n = 57) of the neoplasms originating from the head and neck region, 6.29% (n = 9) from the trunk, 3.95% (n = 3) from the upper extremities, and 2.13% (n = 2) from the lower extremities. Hematolymphoid BSLs comprised 0.42% (n = 1) of the neoplasms originating from the head and neck region, 0.7% (n = 1) from the trunk, and 3.95% (n = 3) from the upper extremities. Neural BSLs comprised 1.68% (n = 4) of the tumors originating from the head and neck region and 1.06% (n=1) of the tumors originating from the lower extremities (Table 3).

There was a statistically significant difference between the number of the lesions and the BSL groups (p = 0.001). Appendageal BSLs comprised 35.82% (n = 163) of the single lesions and 21.88% (n = 21) of the multiple lesions. Soft tissue BSLs comprised 28.13% (n = 128) of the single lesions and 17.71% (n = 17) of the multiple lesions. Keratinocytic BSLs comprised 23.3% (n = 106) of the single lesions and 36.46% (n = 35) of the multiple lesions. Melanocytic BSLs comprised 10.55% (n = 48) of the single lesions and 23.96% (n = 23) of the multiple lesions. Hematolymphoid BSLs comprised 1.1% (n = 5) of the single lesions. A total of 1.1% of the single lesions was considered as neural BSLs.

There were statistically significant differences between BSL groups in terms of the diameters of the lesions (p = 0.001). The mean diameters of the lesions were 17.33 (n = 184) for appendageal BSLs, 15.8 mm (n = 5) for neural BSLs, 15.66 mm (n = 145) for soft tissue BSLs, 11.26 mm (n = 141) for keratinocytic BSLs, 9.2 mm (n = 5) for hematolymphoid BSLs, and 8.73 mm (n = 71) for

TABLE 3. The relationship between gender, age, number of lesions, and localization of benign skin lesions

Benign skin lesions	Gender					Chi-square Test
	Female		Male			
	n	%	n	%		p
Keratinocytic	63	26.14	78	25.16		
Melanocytic	52	21.58	19	6.13		
Appendageal	70	29.05	114	36.77		0.001
Haematolymphoid	3	1.24	2	0.65		
Soft tissue	52	21.58	93	30		
Neural	1	0.41	4	1.29		

	Age groups						Chi-square Test
	0-14 Years		15-59 years		≥60 years		
	n	%	n	%	n	%	p
Keratinocytic	14	41.18	99	22.5	28	36.36	
Melanocytic	5	14.71	59	13.41	7	9.09	
Appendageal	1	2.94	155	35.23	28	36.36	0.008
Haematolymphoid	1	2.94	4	0.91	0	0	
Soft tissue	12	35.29	119	27.05	14	18.18	
Neural	1	2.94	4	0.91	0	0	

	Localization								Chi-square Test
	Head and neck		Trunk		Upper extremity		Lower extremity		
	n	%	n	%	n	%	n	%	p
Keratinocytic	52	21.85	20	13.99	14	18.42	55	58.51	
Melanocytic	57	23.95	9	6.29	3	3.95	2	2.13	
Appendageal	87	36.55	70	48.95	20	26.32	7	7.45	0.001
Haematolymphoid	1	0.42	1	0.7	3	3.95	0	0	
Soft tissue	37	15.55	43	30.07	36	47.37	29	30.85	
Neural	4	1.68	0	0	0	0	1	1.06	

TABLE 4. The relationship between number of lesions and diameter of benign skin lesions

| Benign skin lesions | Number of lesions | | | | Chi-square Test |
| | Single | | Multiple | | |
	n	%	n	%	p
Keratinocytic	106	23.3	35	36.46	
Melanocytic	48	10.55	23	23.96	
Appendageal	163	35.82	21	21.88	0.001
Hematolymphoid	5	1.1	0	0	
Soft tissue	128	28.13	17	17.71	
Neural	5	1.1	0	0	

| | Lesion diameter (mm) | | | | | Kruskal–Wallis Test |
	n	Mean	Min	Max	SD	p
Keratinocytic	141	11.26	1	35	7.19	
Melanocytic	71	8.73	2	50	6.2	
Appendageal	184	17.33	3	55	9.68	0.001
Hematolymphoid	5	9.2	3	16	5.81	
Soft tissue	145	15.66	2	70	13.22	
Neural	5	15.8	6	35	11.92	

neural BSLs. The lesion diameter of the melanocytic BSLs was significantly lower compared with that of the main groups of appendageal and soft tissue BSLs. The lesion diameter of the keratinocytic BSLs and soft tissue BSLs were significantly lower than that of the appendageal BSLs (Table 4).

DISCUSSION

The epidemiological studies on skin diseases have reported the rates of BSL and MSL at 4.5-12% and 1.5-6%, respectively (Bertanha et al. 2006; Furue et al. 2011; Mohammedamin et al. 2006). In general, the ratio of BSLs to the malignant ones is 1.5 or 4.5 (Bertanha et al. 2006; Furue et al. 2011; Kartal et al. 2015; Mohammedamin et al. 2006). Recent studies have reported a tendency of PSLs to increase over the last years, with rates 1.82%-4% found in large-scale epidemiological studies (Bas et al. 2014; Choi et al. 2016; Kim et al. 2010).

In various studies, BSLs were mostly seen in women (53.7%-63.2%) (Bertanha et al. 2016; Sinikumpu et al. 2014). In the present study, 56% (n = 310) of all BSLs were found in males, and 47.7% (n = 241) were found in females. In several epidemiological studies conducted in various countries, the most common type of BSL in females and males is keratinocytic BSLs (Furue et al. 2011; Kartal et al. 2015; Mohammedamin et al. 2006). In the present study, appendageal BSLs was the most common type found in females and males.

In various studies, 55%-60% of BSLs were seen in the 15-59 age group (Furue et al. 2011; Sinikumpu et al. 2014). In the present study, 79.85% (n = 440) of all BSLs were seen in the 15–59 age group. The most common BSL type among children, adolescents, middle-aged, and elderly people has been reported to be keratinocytic BSL based on epidemiological studies on skin diseases (Kyriakis et al.

2012; Sinikumpu et al. 2014). In the present study, the most common types of BSL in the 0-14 and 15-59 age groups are keratinocytic and appendageal BSLs, respectively; overall, keratinocytic and appendageal BSLs are the most common BSL types.

In some studies, BSLs have been reported to be more common in the head and neck regions, and in some studies they have been reported to be more common in the truncal region (Gogi & Ramanujam 2013; Pujani et al. 2016). In the present study, 43.19% (n = 238) of BSLs were localized in the head and neck region. The BSL diameters reported in the studies are usually less than 25 mm (Furue et al. 2011; Pujani et al. 2016). In the present study, the lesion diameter of BSLs was between 1 and 70 mm, and the mean was 14.1 mm. Appendageal BSLs were found to be the largest lesions with a mean diameter of 17.33 mm. BSLs reported in the literature are generally singular (Ferrándiz et al. 2017; Pujani et al. 2016). In the present study, 82.57% (n = 455) of BSLs were single lesions.

BSLs can accompany some systemic diseases (Nguyen & Zuniga 2013). An underlying systemic disease should be investigated especially in the presence of multiple lesions. In the presence of multiple seborrheic keratosis (SK); trichilemmoma; or cystic sebaceous tumors (CSTs), malignancies of the internal organs, such as the stomach, colon, or the pancreas, should be suspected (Gogi & Ramanujam 2013; Kanitakis 2010; Luba et al. 2003). The incidences of CSTs, keratoacanthoma, and sebaceoma increase in Muir–Torre syndrome; the incidences of hemangioma, lipoma, and trichilemmoma increase in Cowden's disease; the incidence of CST increases in Gardner syndrome (Gogi & Ramanujam 2013; Luba et al. 2003). However, we did not observe any of these conditions in the present study.

Several studies have demonstrated that some BSLs may develop into malignant tumors (Lee 2010). It has

been reported that basal cell carcinoma may develop from SK; squamous cell carcinoma may develop from verruca vulgaris or keratoacanthoma lesions; melanoma may develop from melanocytic nevi (Gogi & Ramanujam 2013). None of these conditions were found in the present study. Malignant lesions can be misdiagnosed as benign (Lee 2010). In the present study, although the physical examination findings of nine patients were like BSL, the pathological examination confirmed MSL. These patients accounted for 1.6% of MSL patients. For this reason, biopsy should be taken to confirm the diagnosis (Ferrándiz et al. 2017).

Several studies recommend fine-needle aspiration, core, or excisional biopsy to be performed, allowing for a definite diagnosis to be made so that the tumor structure and histological type can be identified, and its grade can be determined (Ferrándiz et al. 2017; Hwang et al. 2016). Studies report that the core biopsy is superior to the fine-needle aspiration biopsy and excisional biopsy is superior to core biopsy in terms of sensitivity, specificity, predictive value, and accuracy (Wakely & Kneisl 2000; Woon & Serpell 2008). It has been reported that the overall diagnostic accuracy of the excisional biopsy may be as high as 98% (Kasraeian et al. 2010).

In the present study, an excisional biopsy was performed that preserved the healthy margins (>1 mm) for all lesions prediagnosed as BSL. The diagnostic accuracy was found to be 100%. Several studies have reported that there might be recurrences in the lesions after the excisional biopsies at varying rates ranging from 2%–5% (Layfield et al. 2014). The recurrence rate after excisional biopsy was 2.3% in the present study, and surgical excision was repeated in these patients (Kasraeian et al. 2010; Layfield et al. 2014). Excisional biopsy was successful in the diagnosis and treatment of patients.

CONCLUSION

In the present study, we evaluated the clinical profile and different types of BSLs in terms of age, gender, and area distribution. Some BSLs may be associated with systemic diseases or malignancies. BSLs may also develop into a malignant tumor. Therefore, clinicians should follow a systematic approach to BSLs. Sometimes, the diagnosis of skin neoplasias cannot be made based on their clinical characteristics solely. Hence, a pathological examination should be performed. As in the present study, excisional biopsy can be performed successfully for both diagnosis and treatment.

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