

Profile of Clinical, Dermoscopic, Histopathological Feature Seborrheic Keratosis in Sanglah General Hospital Period January 2016-December 2017

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Abstract: Seborrheic Keratosis (SK) is one of the most common epidermal tumor on the skin. The clinical presentation can be quite variable. Even though SK is presently one of the most common cosmetic skin problem, there is lack data relating its clinical, dermoscopic, and histopathologic correlation. The aim of this study to provide useful information about the clinical profile, dermoscopic, histopathological feature of SK. This retrospective study obtained data from medical record patients SK at out-patient clinic Sanglah General Hospital during January 2016 until December 2017. The new SK cases on in January 2016 until December 2017 were 53 cases. There were 21 male and 32 female. SK most commonly occurs at the age over 60 years old (35%). SK lesion commonly found on the sun exposed area like face (47%) and neck (50%). SK most commonly occurred on patients had history of sun exposure more than 2 hours/day (45%). Positive family history was found on 37 cases (69%). The most common SK subtype was dermatosis papulo nigra (56%), followed by melanoacanthoma or pigmented SK in 10 subjects (18,8%), common SK in 9 subjects (16,9%), and irritated SK in 4 subjects (7,54%). In this study only 2 subtype SK done dermoscopic and histopathological examination (melanoacanthoma and irritated SK). The most common dermoscopic finding seen in melanoacanthoma SK were millia like cyst in 10 subjects (90%), comedo like opening in 10 subjects (90%), gyri and sulci in 10 subject (90%). The most common dermoscopic finding seen in irritated SK were millia like cyst in 3 subjects (100%), comedo like opening in 3 subjects (100%), gyri & sulci in 3 subject (100%), and also haipin vessel in 1 subject (33,3%). There was correlation between dermoscopy and histopatology finding in these report.

1 INTRODUCTION

SK is one of the most common epidermal tumor of the skin that affects both sexes and usually arises in individual older than 50 years. It present as sharply demarcated, slightly raised brownish patches or plaques, usually on sun-exposed surface of the skin. Many individual with SK have a positive family history. SK demonstrated irregularities in the expression of the apoptosis markers of p53 and Bcl-2, though no genetic locul or chromosomal imbalance has been detected to date (Thomas, Swanson, and Lee, 2008; Roh *et al.*, 2016). Family history of SKs should be sought if there are multiple SKs and if associated with an early age of onset.³ The other possible risk factor for SK is viral infection like human papilloma virus (HPV) based on clinical

similarities to warts (Thomas, Swanson, and Lee, 2008; Roh *et al.*, 2016).

Based on the clinical and histopathological SK can be divided into six mayor subtype: common SK, reticulated (adenoid) SK, stucco SK, pigmented (melanoacanthoma) SK, dermatosis papula nigra SK, clonal SK, and irritated SK (Thomas, Swanson, and Lee, 2008). Despite the diagnosis is most often clinically straight-forward, some SK cases also need dermoscopic and histopathology examination because the tumor can mimic the other premalignant or malignant lesion (Park, Park, and Cho, 2011; Kim *et al.*, 2013). Dermoscopic examination reveal specific criteria according to the particular histological architecture.

This study describes the clinical, typical dermoscopic features of Sk along with their histopathological correlations of SK.

2 METHOD

This retrospective study obtained data from medical record patients SK at out-patient clinic Sanglah General Hospital during January 2016 until December 2017. Data got from medical record patients consists with clinical diagnose of SK, description of dermoscopic and histopathological images in these patients. All patients who diagnosed with SK were subjected to get information from medical record about the age, gender, history of sun exposure a day (outdoor occupations and hobbies), family history of SK, clinical evaluation of the SK regarding the site and the subtype SK (common SK, reticulated or adenoid SK, stucco SK, pigmented or melanoacanthoma SK, dermatosis papula nigra SK, clonal SK, and irritated SK). Evaluation the specific dermoscopic features of SK such as fissure and ridges or gyri and sulci, hairpin vessels, comedo-like opening, milia-like cyst. Evaluation histopathological features of SK such as papillomatous surface of the epidermis, hyperkeratosis or parakeratosis, epidermal cysts, horn cyst, enlarged capillaries of dermal papillae, increased melanin number, squamous edies and keratin filled invagination. Photographic documentation of clinical type, dermoscopic and histopathological features were got from case reports of SK patients in that period.

The subjects demographic data (ie gender, age range, location, subtype of SK, family history of SK, and history sun exposure) were presented as number and percentage. Statistical significance the frequency of dermoscopic and histopathologic feature in SK was assessed using chi-squared. The cutoff for statistical significance was set at $p < 0,001$. Analyzed using the SPSS version 21.0 for windows

3 RESULTS

The new SK cases on in January 2016 until December 2017 were 53 cases. There were 21 male and 32 female. The age range from 19-76 years, the mean age 49,75. SK most commonly occurs at the age over 60 years in 19 subjects (35%). SK lesion commonly found on the sun exposed area like face in 25 subjects (47%) and neck in 27 subjects (50%). The other location were on the back in 13 subjects (24,5%), on the chest in 7 subjects (13,2%), on the upper extremities in 6 subjects (11,3%), on the lower extremities 4 subjects (7,5%), and there were only 1 subject (1,88%) on each location like abdomen, symphysis, inguinal and labia majora. The most

common SK subtype was dermatosis papulo nigra in 30 subjects (56%) followed by melanoacanthoma or pigmented SK in 10 subjects (18,8%), common SK in 9 subjects (16,9%), and irritated SK in 4 subjects (7,54%). Positive family history was found on 37 subjects (69,8%). SK cases most commonly occurred on patients had history of sun exposure more than 2 hours/day in 24 subjects (45,2%). Table 1. Demonstrate the demographic data of subjects.

In this study only 2 subtype SK done dermoscopic and histopathological examination (melanoacanthoma and irritated SK). The most common dermoscopic finding seen in 11 subjects melanoacanthoma SK were millia like cyst in 10 subjects (90%), comedo like opening in 10 subjects (90%), and also gyr & sulci in 11 subject (100%). Only 2 cases of melanoacanthoma SK done histopathology examination. The most common histopathology finding seen in melanoacanthoma SK were epidermal cyst or keratin filled invagination in 2 subjects (100%), horn cyst in 2 subjects (100%), hyperkeratosis, parakerosis, akantosis and papillomatosis in 2 subjects (100%), and increase of melanin number in 1 subject (50%). The presence of millia like cyst was statistically significant with epidermal cyst, presence of comedo like opening was statistically significant with horn cyst, presence of gyri & sulcus was statistically significant with hyperkeratosis, parakerosis, akantosis and papillomatosis ($p < 0,001$). The most common dermoscopic finding seen in 3 subjects irritated SK were millia like cyst in 3 subjects (100%), comedo like opening in 3 subjects (100%), gyri & sulci in 3 subject (100%), and also hairpin vessel in 1 subject (33,3%). All of the 3 subjects irritated SK done histopathology examination. The most common histopathology finding seen in irritated SK were epidermal cyst or keratin filled invagination in 3 subject (100%), horn cyst in 3 subject (100%), hyperkeratosis, parakerosis, akantosis and papillomatosis in 3 subject (100%), enlarge capillaries in 1 subject (33,3%), inflammation infiltrate lymphocyte and neutrophil in 1 subject (33,3%), and squamous edies in 2 subjects (66,6%). The presence of millia like cyst was statistically significant with epidermal cyst, presence of comedo like opening was statistically significant with horn cyst, presence of gyri & sulcus was statistically significant with hyperkeratosis, parakerosis, akantosis and papillomatosis, presence of hairpin vessel was statistically significant with enlarge capillaries ($p < 0,001$). Table 2 Demonstrate the crosstabulation frequency dermoscopic and histopathologic feature

seen in melanoacanthoma and irritated SK using chi-squared test.

Table 1: Demographic Data of Subjects.

Variable	Subject (n)	Percentage
Gender		
Male	21	39,6%
Female	32	60,3%
Age Range (years)		
10-20 years	2	3,7%
21-30 years	1	1,8%
31-40 years	15	28,3%
41-50 years	8	15,1%
51-60 years	8	15,1%
>60 years	19	35,8%

Location		
Face	25	47,1%
Neck	27	50,9%
Back	7	13,2%
Chest	13	24,5%
Abdoment	1	1,8%
Upper extremities	6	11,3%
Lower extremities	4	7,5%
Symphisis	1	1,8%
Inguinal	1	1,8%
Labia majora	1	1,8%
Subtype SK		
Dermatosis papulo nigra	30	56,6%
Irritated	4	7,5%
Melanoacanthoma or pigmented Common	10	18,8%
	9	16,9%
Family History of SK		
Positive		
Negative	37	69,8%
	16	30,1%
History of Sun Exposure		
<1 hour/day	10	18,8%
1-2 hours/day	19	35,8%
>2 hours/day	24	45,2%

Table 2: Crosstabulation Frequency Dermoscopic*Histopathologic Feature in Melanoacanthoma & Irritated SK using Chi-Squared Test.

Dermoscopic Melanoacanthom SK (2 subjects)	Histopathologic Melanoacanthoma SK (2 subjects)				p-value	Dermoscopic Irritated SK (3 subjects)	Histopathologic Irritated SK (3 subjects)				p-value
	EC	HC	HP	EC			EC	HC	HP	EC	
ML	2	0	0	0	<0.001	ML	3	0	0	0	<0.001
CL	0	2	0	0	<0.001	CL	0	3	0	0	<0.001
GS	0	0	2	0	<0.001	GS	0	0	3	0	<0.001
HV	0	0	0	0		HV	0	0	0	1	<0.001
Total	2	2	2	0		Total	3	3	3	1	

ML : Millia Like Cyst, CL : Comedo Like Opening, GS: Gyri & Sulcus, HV: Hairpin Vessel, EC: Epidermal Cyst, HC: Horn Cyst, HP: Hyperkeratosis, Papilomatosis, EC: Enlarge Capillaries

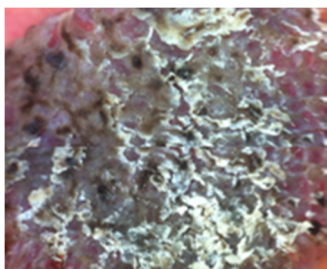


Figure 1: Dermoscopic image of irritated SK presenting milia like cysts, hyperkeratosis, comedo like openings, fissures, ridges, gyri and sulcus.

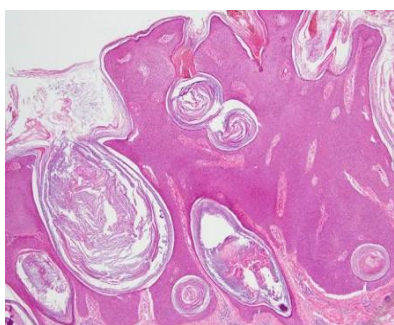


Figure 2: Histopatologic image of irritated SK presenting keratin filled invagination or epidermal cyst, horn cyst, and squamous eddies.

4 DISCUSSION

A study conducted by Alapatt et al on 50 participants reported the peak incidence of SK was 31-50 years (Alpatt, Sukumar, and Bhat, 2016). A Korean study by Kwon et al, has reported that 88,1% of Korean male aged 40-70 years had at least one lesion (Kwon *et al.*, 2003). SK in this study mostly occur in middle-aged individuals, the peak incidence in this study was over 60 years.

Gender distribution of SK in this study more common in female than male with ratio 1.5:1. In some study slight female preponderance of SK was seen. A study conducted by Alapatt et al show that female preponderance of 76% SK cases (Alapatt, Sukumar, and Bhat, 2016). This condition could be due to the fact that women usually seek dermatological advice due to cosmetic concern more than man.

There are many risk factors have been implicated in the etiology of SK. Many individual of SKs have a positive family for the condition. SKs demonstrate irregularities in the expressions in the apoptosis markers p53 and Bcl-2, though no genetic locus or chromosomal imbalance has been detected (Thomas, Swanson, and Lee, 2008). Family history associated

with multiple seborrheic keratoses on early age of onset. Genetic predisposition inherited SK associated with an autosomal dominant trait. Activating mutations in FGFR3 which provide proliferative signals to keratinocytes, increased expression of Bcl2 and Ki-67, increased DNp63a expression and activating PIK3CA mutations has been noted in the pathogenesis of SK. Increased expression of keratinocyte derived Endothelin I mediated by TNF α and Endothelin Converting Enzyme 1 α (ECE 1 α) is linked to pigmentation seen in SK (Shariff, Balamurugan, and Saravanan, 2017). In this study positive family history was found on 37 cases (69%). From 37 cases who had positive family history only 2 subjects (5,4%) occurred on early age onset at age range 10-20 years, 7 subjects (18,9%) occurred at age range 31-40 years, and the other occurred at age more than 40 years.

Sunlight and *Human Papilloma Virus (HPV)* has been implicated in the risk factors of seborrheic keratosis (Shariff, Balamurugan, and Saravanan, 2017). Hafner et al, reported that UV-light-induced mutations of the gene encoding FGFR3 may contribute to formation of SK (Roh *et al.*, 2016). In this study only investigate the risk factor of sun exposure. The most common location of SK lesion in this study on the sun exposed area like face (47%) and neck (50%). SK cases most commonly occurred on patients had history of sun exposure more than 2 hours/day (45%). This result similar with study conducted on Korea males by Kwon et al on 303 volunteers aged 40-70 years, which showed cumulative sunlight exposure to be a contributing factor (Alapatt, Sukumar, and Bhat, 2016).

Our study showed the highest incidence of SK was dermatosis papulo nigra (56%), followed by melanoacanthoma or pigmented SK in 10 subjects (18,8%), common SK in 9 subjects (16,9%), and irritated SK in 4 subjects (7,54%). In this study only 2 subtype SK done dermoscopic and histopathological examination (melanoacanthoma and irritated SK) because this type of SK usually mimic the other pigmented lesion like nevocellular nevus and melanoma.

Melanoacanthoma is a heavily pigmented variant of SK, histopathologically characterized by increased large, dendritic, melanin-rich melanocyte throughout the tumor. The heavy pigmentation of melanoacanthoma masks dermoscopic finding, rendering it almost impossible to differentiate this condition from melanoma and other pigmented skin lesions like melanoma (Minagawa, 2017). The most common dermoscopic finding seen in melanoacanthoma SK were milium like cyst in 10

subjects (90%), comedo like opening in 10 subjects (90%), and also gyr & sulci in 10 subject (90%). Only 2 cases of melanoacanthoma SK done histopathology examination. The most common histopathology finding seen in melanoacanthoma SK were epidermal cyst or keratin filled invagination in 2 subjects (100%), horn cyst in 2 subjects (100%), hyperkeratosis, parakerosis, akantosis and papillomatosis in 2 subjects (100%), and increase of melanin number in 1 subject (50%). The presence of millia like cyst was statistically significant with epidermal cyst (100%), presence of comedo like opening was statistically significant with horn cyst (100%), presence of gyri & sulcus was statistically significant with hyperkeratosis, parakerosis, akantosis and papillomatosis (100%) with $p < 0,001$. These finding simillar with the previous study by Alapatt et al showed that milia like cysts in dermoscopy corespond to epidermal cyst (100%), presence of gyri & sulcus corespond to papillomatosis (89%), and the other features of histopathologic were horn cyst in 32,30% of the cases, pigmentation in 74,20% of the cases, acanthosis in 18% of the cases, and hyperkeratosis in 58,10% of cases (Alapatt, Sukumar, and Bhat, 2016).

The most common dermoscopic finding seen in irritated SK in this study were millia like cyst in 3 subjects (100%), comedo like opening in 3 subjects (100%), gyri & sulci in 3 subject (100%), and also haipin vessel in 1 subject (33,3%). The most common histopathology finding seen in irritated SK in this study were epidermal cyst or keratin filled invagination in 3 subject (100%), horn cyst in 3 subject (100%), hyperkeratosis, parakerosis, akantosis and papillomatosis in 3 subject (100%), enlarge capillaries in 1 subject (33,3%), inflammation infiltrate lymphocyte and neutrophil in 1 subject (33,3%), and squamous edies in 2 subjects (66,6%). The presence of millia like cyst was statistically significant with epidermal cyst (100%), presence of comedo like opening was statistically significant with horn cyst (100%), presence of gyri & sulcus was statistically significant with hyperkeratosis, parakerosis, akantosis and papillomatosis (100%), presence of hairpin vessel was statistically significant with enlarge capillaries (100%) with $p < 0,001$. Irritated SK have two histopathological characteristic, numerous squamous eddies and downward ploriferation of the epidermis. Dermoscopic finding of irritated SK usually not only typical demoscopic image like the other type SK but also can found pinkish structures on white background (Minagawa, 2017).

5 CONCLUSIONS

Clinical profile SK in this study most commonly occured on age over 60 years, female subjects, location on sun exposed area like face and neck, in subjects who had history of sun exposed more than 2 hous/day. Highest incidence of SK was dermatosis papulo nigra (56%), followed by melanoacanthoma or pigmented SK in 10 subjects (18,8%), common SK in 9 subjects (16,9%), and irritated SK in 4 subjects (7,54%). There was correlation between dermoscopy and histopatology finding of SK in these study.

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