Analysis of Clinical Manifestations of Port Wine Stain Patients at the Institute of Dermatology, Thailand: A 5-Year Retrospective Study

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Abstract

Port wine stains (PWS) are progressive capillary vascular malformations that do not resolve spontaneously. Various publications have reported differing results concerning the natural history of PWS, a crucial aspect of its management. The objective of this study was to analyze the clinical manifestations of PWS, encompassing the type of lesions, associated anomalies, and their interrelationships. Data were collected from all PWS patients in the Institute of Dermatology, Thailand database from 2018 to 2023. This retrospective study included 135 patients, with an average age of 27.11 years. The proportion of females (55.6%) slightly exceeded that of males. The face was the most common location (57.8%), with the majority of lesions appeared as red (63.7%) and predominantly flat (68.9%). However, hypertrophic and nodular lesions were present in 20% and 10.4% of cases, respectively. The different age groups between hypertrophic and nodular lesions of PWS were significant (P-value = 0.022). Hypertrophic PWS patients had the highest proportion in the age range of 11-20 years (29.6%) whereas Nodule PWS patients had the highest proportion in the age range of 31-40 years (53.8%). Red and purple lesions were significantly associated with hypertrophic PWS (p-values 0.001 and 0.003, respectively). The V3, upper lip, lower lip, and oral mucosa sublocations exhibited a significant difference in hypertrophic PWS (p-value 0.006, 0.003, 0.015, and <0.001, respectively). Moreover, V1, V2, and upper lip sublocations were significantly related to anomalies in PWS patients (p-values 0.045, 0.009, and 0.014, respectively) encompassing eye, brain, and Sturge-Weber syndrome.

In conclusion, the findings of this study contribute to a better understanding of PWS's natural history, adding value to a more comprehensive approach to its management. However, advancing future research will be essential for obtaining more information.

Keywords**:** *Port Wine Stain, Capillary Vascular Malformation, Hypertrophic Lesion, Nodular Lesion*

1. Introduction

Port wine stains (PWS) are vascular ectasias that can progress in vessel diameter and the thickening of lesions over time (Kelly et al., 2005; Tran et al., 2021; van Raath et al., 2021), which do not heal spontaneously (Ae & Js, 2012; Brightman, Geronemus, & Reddy, 2015; Chang, Kim, & Lee, 2011; Faurschou, Olesen, Leonardi-Bee, & Haedersdal, 2011; Yang et al., 2015). The progressive lesions can develop hypertrophy and nodularity, posing challenges for treatment. PWS commonly affects the head and neck regions, causing significant cosmetic concerns. Moreover, PWS may impair sight, speech, nasal breathing, and hearing as it progresses (Han et al., 2020). Associated anomalies frequently found with PWS include eye, brain, or syndromes such as Sturge-Weber syndrome (SWS).

Several publications with different results have reported on the natural history of PWS, including the age of onset of hypertrophy ranging from 1 to 29 years. Soft tissue hypertrophy typically starts at the age of 9 on average, with the V2/maxillary segment being the most commonly involved location in upper lip hypertrophy. Bony hypertrophy begins at an average age of 15 years, while nodule formation starts at an average age of 22 years (Klapman & Yao, 2001; Lee, Chung, Cerrati, & Waner, 2015). The peak of

hypertrophy occurs between 20 to 39 years. Hypertrophy alone is most often observed as red lesions, while hypertrophy and nodules are most commonly seen as purple lesions. Nodules are associated with all three colors and are least often observed as pink lesions (Klapman, & Yao, 2001). In the current study, the authors aimed to identify the most common location that is significantly related to hypertrophic PWS, which involves cosmetic concern areas as well as the associated anomalies. It is very beneficial to both patients and doctors to pay more attention to the management and prevention of unwanted complications and associated anomalies. Therefore, this retrospective study aimed to analyze the clinical manifestations of PWS patients from the Institute of Dermatology, Thailand.

2. Objectives

To describe the clinical manifestations of PWS patients, including the types of lesions and associated anomalies, as well as their relationships.

3. Materials and Methods

All previously untreated PWS patients who visited the Institute of Dermatology, Thailand, from 2018 to 2023 were included in this retrospective study. Data collection for all subjects commenced after receiving approval from the Institutional Dermatology Human Research Ethics Committee. Patients with insufficient data, such as unclear or missing photographs, were excluded. Demographic information was recorded, including age, sex, skin type, and overall health condition. Clinical manifestations, such as color, type (flat, hypertrophy, nodule), appearance, lesion surface (by using patient's photo to compare with each part of the patient's body, categorized as less than or more than 50%), location, complications (bleeding, ulcer, pyogenic granuloma), and associated symptoms were evaluated through photographs and documented. Statistics analysis was performed using Statistics for Windows, version 26.0 (IBM SPSS Inc., Chicago, IL, USA). Descriptive statistics included mean, standard deviation, frequency, and percentage. For categorical data, the Chi-square test and Fisher's exact test were employed to analyze the variables and examine the relationships within hypertrophic PWS, the color of the lesion, and locations.

4. Results and Discussion

4.1 Results

This study involved 182 previously untreated PWS patients, with 47 participants excluded due to insufficient data. Thus, a total of 135 PWS patients were included, and their average age was 27.11 years (age range: 1 to 66 years). Females constituted 55.6% of the participants, slightly outnumbering males. The most common skin type was type III (48.9%), followed by type IV (28.1%) and type II (12.6%). The mean onset of lesions was 0.11 ± 0.97 years; clinical manifestations are detailed in Table 1. The face was the most common location (57.8%), with 63.7% of patients having a red lesion, followed by purple (33.3%) and pink (3%). The majority of lesions were flat (68.9%), while 20.0% were hypertrophic and 10.4% were nodules. Figure 1 illustrates the different age groups between hypertrophic and nodular lesions of PWS significantly (P-value = 0.022). Hypertrophic PWS patients had the highest proportion in the age range of 11-20 years (29.6%), whereas Nodule PWS patients had the highest proportion in the age range of 31-40 years (53.8%). Approximately 68.9% of lesions covered less than 50% of each part of the patient's body. The most common complications included bleeding (3.7%), ulceration (2.2%), and pyogenic granuloma (1.5%). Table 2 presents the sublocations of lesions among the 135 PWS cases, with a majority of face lesions located in the V2 sublocation (42.6%).

Table 1 Number and percentage of clinical manifestations among 135 PWS patients

Clinical manifestations	**Number**	**%**
Color of the lesions		
Pink	4	3
Red	86	63.7
Purple	45	33.3
Appearance of the lesions		
Homogeneous	93	68.9
Heterogeneous	42	31.1
Symmetry	2	1.5
Asymmetry	133	98.5
Flat	94	68.9
Hypertrophic	27	20
Nodule	14	10.4
Border of the lesion		
well-defined	108	80
Ill-defined	27	20
Lesion surface		
<50% of each location	93	68.9
>50% of each location	42	31.1
Site		
Left	52	38.5
Right	66	48.9
Midline	17	12.6
Complications		
Bleeding	5	3.7
Ulcer	3	2.2
Pyogenic granuloma	2	1.5

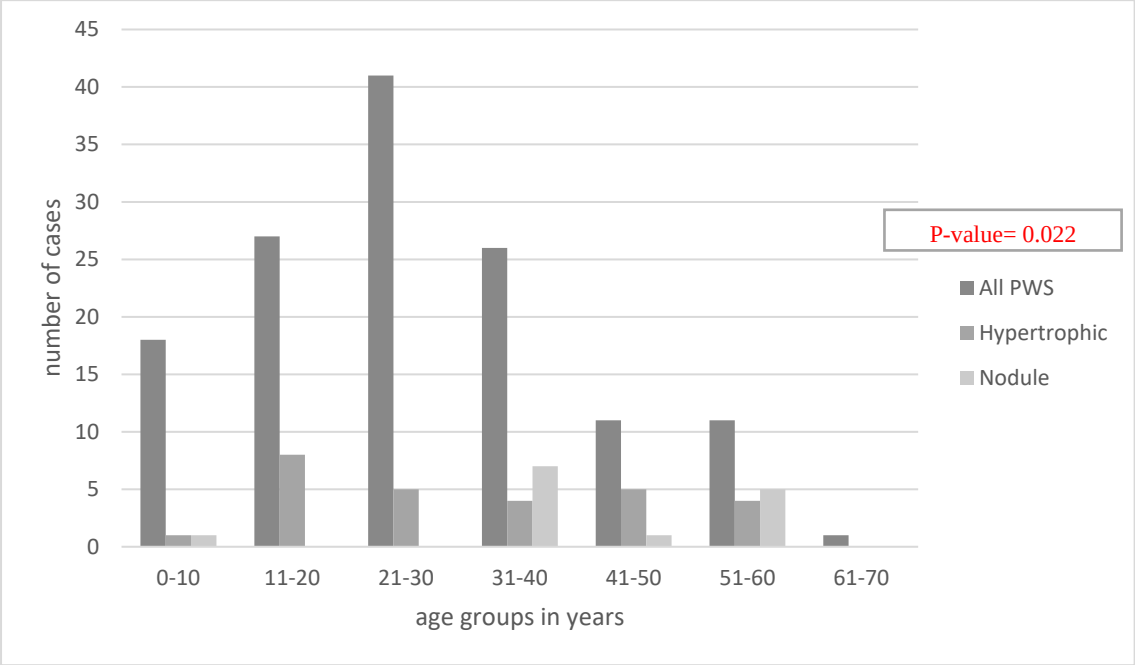

Figure 1 Different age groups of PWS patients and types of PWS

Table 2 Number and percent of the sublocations for lesions among 135 PWS patients

Sublocation	Number	%
Face*	78	57.8
V1	33	32.7
V2	43	42.6
V3	25	24.7
Upper eyelid	24	17.8
Lower eyelid	11	8.1
Upper lip	22	16.3
Lower lip	6	4.4
Oral mucosa	6	4.4
Scalp	10	7.4
Temporal	4	3
Occipital	6	4.4
Neck	23	17
Anterior	5	3.7
Midline	0	0
Lateral	18	13.3
Trunk*	15	11.1
Anterior	12	8.9
Posterior	2	1.5
Midline	4	3
Lateral	11	8.1
Arm*	15	11.1
Proximal	8	5.9
Distal	9	6.7
Forearm*	11	8.1
Proximal	6	4.4
Distal	9	6.7
Thigh*	4	3
Proximal	3	2.2
Distal	1	0.7
Leg*	11	8.1
Proximal	6	4.4
Distal	8	5.9
Hand	3	2.2
Dorsal	2	1.5
Ventral	1	0.7
Foot*	2	1.5
Dorsal	2	1.5
Ventral	1	0.7

*Multiple sublocation involvement for 1 patient

Table 3 illustrates the relationship between hypertrophic PWS, color, and the location or sublocation of the lesions. Red and purple lesions were significantly associated with hypertrophic PWS (p-values of 0.001 and 0.003, respectively). Moreover, individuals with purple lesions had a higher proportion of hypertrophy than those without. Significant differences were observed in hypertrophic PWS concerning V3, upper lip, lower lip, and oral mucosa sublocations (p-values of 0.006, 0.003, 0.015, and <0.001, respectively).

Table 3 Relationship between hypertrophic PWS with color, location, and sublocation of lesions

Factors	Hypertrophic PWS		P-value
	No, n(%)	Yes, n(%)	
Color of the lesion			
Pink	4 (3.7)	0 (0)	0.583[f]
Red	76 (70.4)	10 (37.0)	0.001[c]
Purple	28 (25.9)	17 (63.0)	0.003[c]
Lesion surface			0.780[c]
<50% of each location	75 (69.4)	18 (66.7)	
>50% of each location	33 (30.6)	9 (33.3)	
Face			
V1	26 (24.1)	7 (25.9)	0.841[c]
V2	31 (28.7)	12 (44.4)	0.116[c]
V3	15 (13.9)	10 (37.0)	0.006[c]
Upper eyelid	17 (15.7)	7 (25.9)	0.260[c]
Lower eyelid	8 (7.4)	3 (11.1)	0.460[c]
Upper lip	12 (11.1)	10 (37.0)	0.003[c]
Lower lip	2 (1.9)	4 (14.8)	0.015[c]
Oral mucosa	0 (0)	6 (22.2)	< 0.001[c]
Scalp	10 (9.3)	0 (0)	0.211[f]
Temporal	4 (3.7)	0(0)	0.583[f]
Occipital	6 (5.6)	0 (0)	0.599[f]
Neck	19 (17.6)	4 (14.8)	1.00[f]
Anterior	5 (4.6)	0 (0)	0.583[f]
Lateral	14 (13.0)	4 (14.8)	0.758[f]
Trunk	12 (11.1)	3 (11.1)	1.00[f]
Anterior	10 (9.3)	2 (7.4)	1.00[f]
Posterior	2 (1.9)	0 (0)	1.00[f]
Midline	2 (1.9)	2 (7.4)	0.178[f]
Lateral	10 (9.3)	1 (3.7)	0.693[f]
Arm	13 (12.0)	2 (7.4)	0.735[f]
Proximal	7 (6.5)	1 (3.7)	1.00[f]
Distal	8 (7.4)	1 (3.7)	0.687[f]
Forearm	10 (9.3)	1 (3.7)	0.693[f]
Proximal	6 (5.6)	0 (0)	0.599[f]
Distal	8 (7.4)	1 (3.7)	0.687[f]
Thigh	4 (3.7)	0 (0)	0.583[f]
Proximal	3 (2.8)	0 (0)	1.00[f]
Distal	1 (0.9)	0 (0)	1.00[f]
Leg	9 (8.3)	2 (7.4)	1.00[f]
Proximal	5 (4.6)	1 (3.7)	1.00[f]
Distal	7 (6.5)	1 (3.7)	1.00[f]
Hand	3 (2.8)	0 (0)	1.00[f]
Dorsal	2 (1.9)	0 (0)	1.00[f]
Ventral	1 (0.9)	0 (0)	1.00[f]
Foot	1 (0.9)	1 (3.7)	0.361[f]
Dorsal	1 (0.9)	1 (3.7)	0.361[f]
Ventral	1 (0.9)	0 (0)	1.00[f]

Statistical method used: f = Fisher's exact test, c = Chi-square test

Anomalies or syndromes were identified in 3.7% of the patients, with eye (glaucoma, visual loss) and brain (seizure) anomalies each accounting for 1.5%. Sturge-Weber syndrome (SWS) was the only syndrome identified in this study, as depicted in Table 4. The relationship between locations or sublocations and anomalies or SWS in PWS patients is detailed in Table 5. The V1, V2, and upper lip (categorized in V2) sublocations were significantly associated with anomalies in PWS patients (p-values of 0.045, 0.009, and 0.014, respectively).

Table 4 Number and percent of associated anomalies among 135 PWS patients

Abnormalities or syndrome	Number	%	PWS locations
Eye	2	1.5	
Glaucoma	1	0.7	V1, V2
Visual Loss	1	0.7	V1, V2
Brain (seizure)	2	1.5	(1) V2,V3, (2) V1,V2,V3,Neck
Sturge-Weber syndrome	1	0.7	V1, V2

Table 5 Relationship between locations or sublocations and the anomalies or SWS in PWS patients

Factors	Abnormality		P-value[f]
	No, n(%)	Yes, n(%)	
Lesion surface			0.588
<50% of each location	91 (69.5)	2 (50.0)	
>50% of each location	40 (30.5)	2 (50.0)	
Face			
V1	30 (22.9)	3 (75.0)	0.045
V2	39 (29.8)	4 (100)	0.009
V3	23 (17.6)	2 (50.0)	0.156
Sublocation			
Upper eyelid	23 (17.6)	1 (25.0)	0.547
Lower eyelid	10 (7.6)	1 (25.0)	0.291
Upper lip	19 (14.5)	3 (75.0)	0.014
Lower lip	6 (4.6)	0 (0)	1.00
Oral mucosa	6 (4.6)	0 (0)	1.00
Scalp	10 (7.6)	0 (0)	1.00
Temporal	4 (3.1)	0 (0)	1.00
Occipital	6 (4.6)	0 (0)	1.00

Statistical method used: f = Fisher's exact test

4.2 Discussion

As is well known, PWS undergoes changes over time due to the progression of dilated vessels in the papillary and upper reticular dermis. The proposed pathogenesis of PWS includes neuronal dysregulation, genetic alterations (*GNAQ* gene), and overexpression of vascular endothelial growth factors (VEGF). Lesions may shift in color from pink or red to deep red or purple, and hypertrophy or nodularity may develop, especially in untreated lesions (Barsky, Rosen, Geer, & Noe, 1980; Enzinger & Weiss, 1988). Dynamic changes in lesions and the limitations of laser treatment lead to resistant and recalcitrant PWS due to heterogeneity, as well as deeper, excessively small, or excessively large dilated vessels, and the formation of fibrous tissue (Finley, Noe, Arndt, & Rosen, 1984; Jamjanya, Vejjabhinanta, Tanasombatkul, & Phinyo, 2023). This study analyzed PWS patients across various age groups, including information on advanced lesions, especially hypertrophy, nodules, and complications of the disease. Furthermore, the setting included complicated conditions such as large lesions (more than 50% of each location) and associated anomalies or

syndromes. The face was the most commonly affected location, consistent with other articles reporting higher cosmetic concerns in this area, especially among female patients. This study found hypertrophy and nodules at 20% and 10.4%, respectively. The majority of the hypertrophic and nodular lesions were found in patients older than 11-20 and 31-40 years, respectively. According to Klapman et al., the peak age onset of thickening is 20 to 39 years (Klapman, & Yao, 2001). Drooge et al. also reported a median age of hypertrophy at 12 years and nodularity at 39 years. Although reported age-dependent hypertrophy may differ among various studies due to differences in PWS populations, previous treatments, and other study methodologies, similar results of red and purple PWS increasing the proportion of hypertrophy were found in most studies (Lee et al., 2015; van Drooge et al., 2012). Moreover, This retrospective study showed that the V3, upper lip, lower lip, and oral mucosa sublocations exhibited a significant difference in hypertrophic PWS, consistent with similar results from Drooge et al. and Lee et al., who reported the most common location of hypertrophy ~~as~~ mostly occurred on the face, rarely occurring on extremities.

Anomalies or syndromes were identified in a small percentage of patients, with eye and brain anomalies, including SWS predominantly found in the V1 and V2 sublocations. According to the consensus statement, the best predictor for SWS risks is facial PWS involving any part of the forehead, including the upper eyelid and the midline frontonasal prominence, which follows the embryonal vasculature, akin to the V1 distribution (Sabeti et al., 2021). Advanced lesions, characterized by progressive vascular ectasia, hypertrophy, and nodularity, are prone to complications such as bleeding, ulcers, and pyogenic granulomas, as indicated by the results herein. Less commonly found complications include eczematous changes or infections, which were not found in this report (Higueros, Roe, Granell, & Baselga, 2017).

The major strengths of this study include the variable age and the analysis of advanced lesions in PWS patients. However, several limitations need to be addressed. First, there may be selection bias due to data being obtained from a tertiary medical center and a population seeking treatment, particularly among female patients. Therefore, caution must be exercised in generalizing the results. Additionally, some patients were excluded due to insufficient data for analysis. Second, there may be inaccurate data due to recall bias, such as the onset of the disease. However, this retrospective study is a crucial tool for comprehending the rare and prolonged natural history of PWS. Gaining more insight into the natural course of PWS will contribute to determining appropriate guidelines for management and preventive measures, particularly in advanced lesions like hypertrophy. Further large or multicenter studies and enhanced technologies, especially advanced photographic tools, will provide more valuable data for future research.

5. Conclusion

The complexity of the natural history of PWS is crucial for enhancing the management of individual patients. Understanding the associations between the characteristics of the lesions and their locations could contribute to more targeted interventions and a better comprehension of the natural history of PWS. Further advancement in research is necessary to explore more valuable data.

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7. References

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