Lichen Planus Pigmentosus: A study for association of Thyroid Dysfunction

Karn D, KC S, Timalsina M

Department of Dermatology

Dhulikhel Hospital, Kathmandu University Hospital

Dhulikhel, Kavre, Nepal.

Corresponding Author

Dharmendra Karn

Department of Dermatology

Dhulikhel Hospital, Kathmandu University Hospital

Dhulikhel, Kavre, Nepal.

E-mail: dddkarn@gmail.com

Citation

Karn D, KC S, Timalsina M. Lichen Planus Pigmentosus: A study for association of thyroid dysfunction. *Kathmandu Univ Med J* 2016;53(1):36-40.

ABSTRACT

Background

Lichen planus pigmentosus (LPP) is considered a chronic and progressive variant of lichen planus. Although pigmentation occurs in the sun exposed areas, the etiology remains unknown and there are no appropriate treatment guidelines. Association with thyroid disorder has been described in various disorders of pigmentation.

Objective

The objective of this study was to find the association between LPP and thyroid dysfunction.

Method

A total of 54 clinically diagnosed cases of LPP and 54 age and sex matched healthy control volunteers were included in this case control study. Thyroid function test and thyroid peroxidase antibody were analysed to determine the probable association between thyroid diseases and LPP.

Result

Seventeen (31.7%) patients had biochemical evidence of hypothyroidism and 3 had hyperthyroidism among the diseased group. Among the control group two persons were tested positive for hypothyroidism ($\chi^2 = 0.34$; $p < 0.05$). Similarly, the levels of thyroid peroxidase antibody in the LPP patients were found to be significantly higher than those of controls ($p<0.05$).

Conclusion

Thyroid disorder was found to be an associated factor in LPP. Hence, we recommend routine thyroid function tests in patients with LPP. Further research is warranted among large number of patients to elucidate the exact association.

KEY WORDS

Lichen planus pigmentosus, thyroid disorders

INTRODUCTION

Lichen planus pigmentosus (LPP) is characterized by gradual onset slate gray to brown macular hyperpigmentation predominantly over the sun exposed areas of face and neck.[1-3] It tends to affect middle-aged and darkly pigmented individuals and is usually been reported from India, the Middle East and Latin America. Though considered to be an uncommon variant of lichen planus it does not involve skin appendages or mucosal surfaces. It is generally asymptomatic, but some patients describe mild pruritus. Various patterns of pigmentation have been described including diffuse, reticulate, blotchy, linear, band-like, zosteriform and perifollicular.[1,4,5] Flexural involvement of axilla, submammary areas and groin have been reported with similar clinical and histopathological findings and have been termed as LPP-inversus.[6]

The key histopathological features in the epidermis include minimal epidermal atrophy, apoptotic keratinocytes and vacuolar degeneration of the basal layer. The dermal layers show band like perivascular lympho-histiocytic inflammatory infiltrate, scattered melanophages and pigment incontinence.[6,7] Unlike erythema dyschromicum perstans, lesions of LPP lack the characteristic inflammatory erythema and the melanin deposition is in the superficial dermis rather than the deeper dermis. Pattern resembling lichenoid reaction and presence of colloid bodies are more distinct in LPP than erythema dyschromicum perstans. Other differential diagnosis includes lichenoid drug eruption, pigmented contact dermatitis, post inflammatory hyperpigmentation and acanthosis nigricans. Defining prognosis of the disease is often difficult and endures a chronic and resistant course.

The exact etiology remains to be uncertain. However ultraviolet rays, hepatitis C and the use of henna, hair dye, mustard oil or Indian gooseberry (amla) oil have been suggested as the probable associated factors. Very few studies that have tried to elucidate the etiological factors related to LPP. Hence this study aims to analyse the probable association between LPP and thyroid disorders.

METHODS

Fifty four clinically diagnosed cases of LPP were subjected for measurement of free triiodothyronine (fT3), free thyroxine (fT4), thyroid stimulating hormone (TSH) and detection of anti-thyroid peroxidase antibody (TPO-Ab). Hepatitis C serology was also done for all subjects. Diagnosis was made clinically based on the characteristic morphology, colour and distribution of lesions. Clinical history and examination were taken in all subjects, including patients' age, age at onset, duration of disease, associated diseases, history of thyroid disorder, use of hair dye, henna or body oils. Fifty four age and sex matched healthy volunteers (mean age 48.0 ± 7.2) consisted the control group. Patients with clinical evidence of thyroid disorder, past history of thyroid surgery and patients taking replacement therapy or anti-thyroid drugs were excluded from the study. Cases with evidence of thyroid dysfunction were referred to the endocrine department for its needful management. The study was conducted from July 2010 till December 2013. Informed consent was taken from each participant and the study was approved by the institutional ethical review committee.

Serum levels of fT3 (normal range: 2.2-4.2 pg/mL), fT4 (normal range: 0.8-1.7 ng/dL), TSH (normal range: 0.3-3.6 µIU/mL) and TPO-Ab (threshold value: <16 IU/ml) were measured by using enzyme linked immunosorbent assay.

Statistical analysis

Quantitative variables expressed as mean ± SD were analyzed using Statistical Package for Social Sciences (SPSS) version 16. Chi-square test (χ^2) with cross tabulation was used to associate two quantitative variables and Pearson correlation coefficient (ρ) was used to compare different variables against each other. A p-value of <0.05 was considered to be significant.

RESULTS

There were 43 female and 11 male patients (mean age 49.4 ± 7.4 years) with clinical evidence of LPP. Relevant patient profile was recorded (Table 1). Photographs of various patterns of LPP were recorded (Fig. 1/2). Dermoscopic examination revealed diffuse brownish and structureless patches in diffuse LPP and fine to course granular dots in blotchy LPP (Fig. 3). Minimally atrophic epidermis with scattered apoptotic bodies, vacuolar degeneration of the basal layer, perifollicular lymphohistiocytic infiltration and scattered melanophages in the upper dermis was appreciated in the histopathology (Fig. 4).

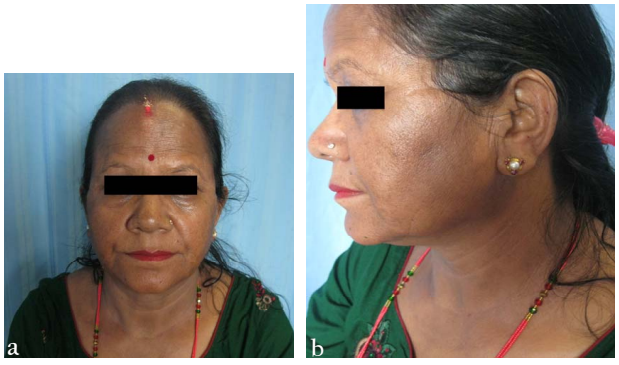

Figure 1. Characteristic slate gray pigmentation of diffuse lichen planus pigmentosus on: (a) face, and (b) neck region.

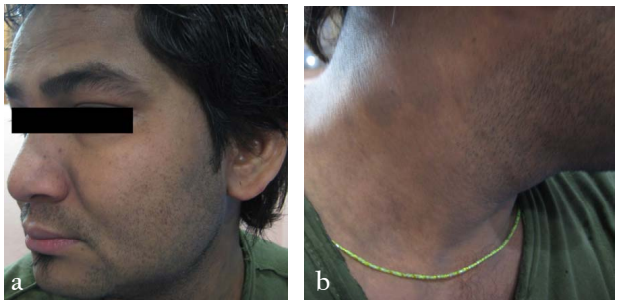

Figure 2. Characteristic slate gray pigmentation of blotchy lichen planus pigmentosus on: (a) face, and (b) neck region.

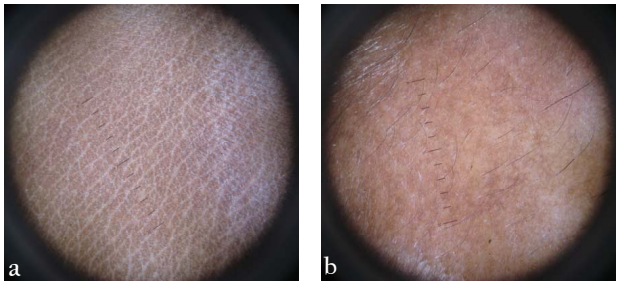

Figure 3. Dermoscopic appearance of the lesions: (a) diffuse brownish and structureless patches in diffuse LPP, and (b) fine to course granular dots in blotchy LPP.

Table 1. Characteristics of 54 patients with lichen planus pigmentosus

Age (years)	49.42 ± 7.4
Duration of disease (years)	1.16 ± 3.37 (range: 2 months- 7 years)
Frequent use of	
• Henna	11 (20.37%)
• Hair dye	7 (13%)
• Both Henna and Hair dye	13 (24%)
• Mustard oil	3 (5.6%)
• Indian gooseberry (amla) oil	5 (9.3%)
• None of above	15 (27.8%)
Location	
• Face and Neck	44 (81.48%)
• Trunk	7 (12.96%)
• Upper limbs	3 (5.56)
Pattern of Pigmentation	
• Diffuse	39 (72.22%)
• Blotchy	10 (18.52%)
• Reticular	5 (9.26%)
Pruritus	19 (35.19%)
Concomitant lichen planus	0
Associated LPP-inversus	1
Positive hepatitis C serology	0
Associated diffuse hair fall	33 (61.1%)

LPP, lichen planus pigmentosus.

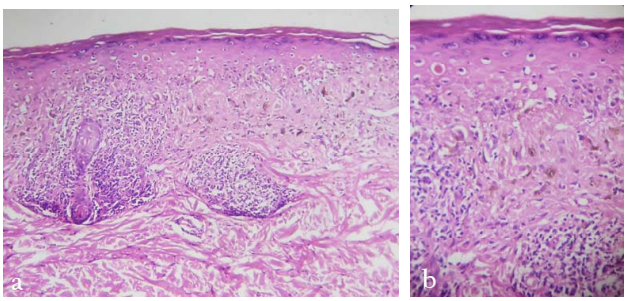

Figure 4. Histopathological findings in the case: mild epidermal atrophy, apoptotic keratinocytes, vacuolar degeneration of the basal layer, perifollicular lymphohistiocytic infiltrate and scattered melanophages. (Hematoxylin and eosin stain; [a] X10, [b] X40)

Biochemical parameters suggestive of hypothyroidism was detected among 17 (31.48%) patients of LPP group and two (3.7%) in the control group. Similarly, there were three (5.55%) patients with evidence of hyperthyroidism in the LPP group and none in the control. (χ^2 = 0.34 (df =1); p <0.05). Among the hypothyroid patients, 8 (47%) patients with obvious clinical features of thyroid dysfunction were considered as overt hypothyroidism and the rest as subclinical hypothyroidism. All three patients with hyperthyroidism had overt clinical manifestations.

TSH, fT3 and fT4 levels were compared (Table 2). It shows a significant difference between mean values of the parameters between cases and control. Similarly TPO-Ab showed significant difference in chi square test between cases and control (Table 3).

Table 2. Comparison of mean ± standard deviation for thyroid stimulating hormone (TSH), free T3 and free T4 levels among cases and control

	Case (N=54) ($\bar{x}$ ± SD)	Control (N=54) ($\bar{x}$ ± SD)	p-value
TSH (µIU/L)	4.46 ± 5.11	2.49 ± 1.17	0.006
Free T3 (pg/ml)	2.36 ± 1.30	3.11 ± 0.76	0.0004
Free T4(ng/dl)	1.23 ± 0.72	1.51 ± 0.47	0.01

Table 3. Comparison of thyroid peroxidase antibody (TPO-Ab) among cases and control

TPO-Ab	Case (N=54)	Control (N=54)	χ^2	p-value
Positive	11	2	7.08	0.007
Negative	43	52		

DISCUSSION

The overall prevalence and etiology of LPP is not known. The present study is a compilation of 54 clinically diagnosed cases of LPP over a period of 30 months. The subjects were compared with 54 healthy volunteers for their thyroid

function test results. Significant association between thyroid disorders and the pigmentation has been observed.

LPP was initially reported from India by Bhutani et al.[8] This rare variant of lichen planus is considered a common pigmentary disorder among skin phototypes III-IV among middle aged people from India, Latin America and the Middle East.[9] Although being a common entity there are limited studies of LPP and much of them are case reports. Very few of them have tried to assess its probable etiology. Till date little is known about the causative agent. Use of henna, hair dye, mustard oil or amla oil and hepatitis C have been seen to be associated but it lacks conclusive evidence.[1,9] The disease has been reported to have slight preponderance among females as in our study. This might be because of the frequent use of hair henna, hair dye, mustard oil or Indian gooseberry oil. Application of such agents for cosmetic purpose or as an emollient is a common practice. Mustard oil contains a compound allylthiocynate, which is a potential photosensitizer and may provoke the disease. Further, hyperpigmentation of LPP may be an outcome of allergic or irritant contact dermatitis to above reported agents. Among LPP patients, positive patch test results with various antigens was documented to be 36% by Tienthavorn et al.[10]

LPP is most commonly described on sun-exposed areas such as the face and neck. In this study majority of the LPP lesions were found in the sun exposed area. Ultraviolet light exposure may be a significant stimulus for its causation. As described in lichen planus actinicus, ultraviolet radiation might have caused expression of self-antigens on the basal keratinocytes causing recruitment of cytotoxic T-cells and resulting characteristic histopathological changes.[11] However cases with involvement of the scalp, trunk, abdomen and predominance of intertriginous folds have been described which opposes the theory of ultraviolet radiation.[12] Linear LPP along the blaschko's line have also been described.[13] Involvement of the disease in these various patterns really challenges the etiology and indicates a probable systemic etiology.

Coexistent classical lichen planus has been described in nearly 20% patients with LPP.[9] But no coexistence of classical lichen planus with LPP was observed among any of our subjects. Cell-mediated immunity seems to play a role in triggering lichen planus.[14] But no conclusive study has yet documented the likely trigger and causation of LPP. Unlike mentioned by other studies, our cases had no mucosal pigmentation.[1,7] Mucosal presentation is not considered a characteristic feature of LPP. An unusual presentation of lichen planus in the oral mucosa with histopathologic resemblance to LPP has been described.[15]

In the present study, diffuse variant was the commonest presentation and none of the cases had involvement of the lower extremities. As in the classic lichen planus, association between hepatitis C and LPP has been a matter of controversy in LPP as well. There are varying reports of strong to poor correlation.[2,14] Replication of the virus within the lesions of oral lichen planus has been found using reverse transcriptase polymerase chain reaction and has suggested as a trigger. But none of our 54 patients showed a positive serology to hepatitis C. Further, wide geographical variation of the virus has been suggested for such varying association. Comparative study among general population might help to clarify this association.

Generalized or localized hyperpigmentation may result from a variety of systemic causes. In search of a probable cause we have found high prevalence of thyroid disorder among patients with LPP. To our knowledge this seems to be a very first study of its kind. The generalized pigmentation in hyperthyroid state has been attributed to the increased adrenocorticotrophic hormone (ACTH) as compensation to cortisol degradation.[16] Both localized and generalized forms of pigmentation similar to that of Addison disease has been described in patients with thyrotoxicosis. A case of melanonychia involving all 10 fingernails has been described in association hyperthyroidism and acute liver injury.[17] Similarly, a high prevalence of thyroid disorders have been described among individuals with vitiligo.[18] High levels of circulating autoantibodies against thyroid hormones has also been described suggesting a probable autoimmune link.[19]

In the present study, majority of the LPP patients (61.1%) had associated diffuse hair fall which might be a clinical manifestation of thyroid disorder. Treatment with thyroxine (T4) to animals has shown alteration in hair growth and pigmentation.[20] But no definite explanation has been found relating pigmentation with decreased circulating thyroid hormone levels. A probable explanation may be because of the increased adrenocorticotropic hormone (ACTH) secretion by the same basophilic cells of the pituitary which is responsible for secreting thyroid stimulating hormone (TSH) as a result of positive feedback mechanism. Animal studies have demonstrated increase in ACTH and α-melanocyte-stimulating hormone after injections of thyrotropin-releasing hormone (TRH).[21] Recently, TRH has been found to stimulate melanogenesis significantly in organ-cultured human hair follicles.[22] TRH stimulates melanin synthesis, intrafollicular tyrosinase mRNA and enzyme activity, melanosome formation and increases melanocyte dendricity. However, the authors did not find stimulation of human epidermal melanogenesis in situ with TRH. This finding may contradict our findings, where a majority of patients with hypothyroidism had pigmentation. Hence, there may be a possibility of stimulation of human epidermal melanogenesis in vivo which needs further confirmation.

CONCLUSION

In conclusion, a significant association was seen among patients with LPP and thyroid Disorder. Hence, routine

assessment of thyroid function test is advised. Future research is warranted among large number of LPP patients to elucidate the definite concept.

Thyroid disorder has been found to be significant among patients with lichen planus pigmentosus in this preliminary study. We recommend routine thyroid function test in patients with lichen planus pigmentosus.

REFERENCES

1. Kanwar AJ, Dogra S, Handa S, Parsad D, Radotra BD. A study of 124 Indian patients with lichen planus pigmentosus. *Clin Exp Dermatol* 2003;28:481-85.
2. Al-Mutairi N, El-Khalawany M. Clinicopathological characteristics of lichen planus pigmentosus and its response to tacrolimus ointment: an open label, non-randomized, prospective study. *J Eur Acad Dermatol Venereol* 2010;24:535-40.
3. Rieder E, Kaplan J, Kamino H, Sanchez M, Pomeranz MK. Lichen planus pigmentosus. *Dermatol Online J* 2013;19:20713.
4. Kumar YH, Babu AR. Segmental lichen planus pigmentosus: An unusual presentation. *Indian Dermatol Online J* 2014;5:157-9.
5. Cho S, Whang KK. Lichen planus pigmentosus presenting in zosteriform pattern. *J Dermatol* 1997;24:193-97.
6. Pock L, Jelinkova L, Drlik L, Abrhamova S, Vojtechovska S, Sezemska D, et al. Lichen planus pigmentosus-inversus. *J Eur Acad Dermatol Venereol*. 2001;15:452–54.
7. Vega ME, Waxtein L, Arenas R, Hojyo T, Dominquez-Soto L. Ashy dermatosis and lichen planus pigmentosus: a clinicopathologic study of 31 cases. *Int J Dermatol* 1992;31:90-94.
8. Bhutani LK, Bedi TR, Pandhi RK, Nayak NC. Lichen planus pigmentosus. Dermatologica 1974;149:43-50.
9. Chang MW. Disorders of hyperpigmentation. In: Dermatology (Bolognia JL, Jorizzo JL, Schaffer JV, eds), 3rd ed. Elsevier Saunders, 2012:1049–74.
10. Tienthavorn T, Tresukosol P, Sudtikoonaseth P. Patch testing and histopathology in Thai patients with hyperpigmentation due to Erythema dyschromicumperstans, Lichen planus pigmentosus, and pigmented contact dermatitis. *Asian Pac J Allergy Immunol* 2014;32:185-192.
11. Kim GH, Mikkilineni R. Lichen planus actinicus. *Dermatol Online J* 2007;13:13.
12. Ozden MG, Yildiz L, Aydin F, Senturk N, Canturk T, Turanli AY. Lichen planus pigmentosus presenting as generalized reticulate pigmentation with scalp involvement. *Clin Exp Dermatol.* 2009;34:636-7.
13. Hong S, Shin JH, Kang HY. Two cases of lichen planus pigmentosus presenting with a linear pattern. *J Korean Med Sci.* 2004;19:152-4.
14. Shai A, Halevy S. Lichen planus and lichen planus-like eruptions: pathogenesis and associated diseases. *Int J Dermatol* 1992;31: 379-84.
15. Laskaris GC, Papavasiliou SS, Bovopoulou OD, Nicolis GD. Lichen planus pigmentosus of the oral mucosa: a rare clinical variety. *Dermatologica* 1981;162 61–3.
16. Diven DG, Gwinup G, Newton RC. The thyroid. *Dermatol Clin* 1989;7:547–57.
17. Accordino RE, Langs-Barlow A, Phelps RG, Hammond B, Mercer SE. Transient, transverse melanonychia associated with Graves disease and acute hepatitis. *Pediatr Dermatol* 2012;29:220-2.
18. Sheth VM, Guo Y, Qureshi AA. Comorbidities associated with vitiligo: a ten-year retrospective study. *Dermatology* 2013;227:311-5.
19. Colucci R, Lotti F, Dragoni F, Arunachalam M, Lotti T, Benvenga S, et al. High prevalence of circulating autoantibodies against thyroid hormones in vitiligo and correlation with clinical and historical parameters of patients. *Br J Dermatol* 2014;171:786-98.
20. Berman A. Peripheral effects of L-thyroxine on hair growth and coloration in cattle. *J Endocrinol* 1960;20:288–92.
21. Beech J, McFarlane D, Lindborg S, Sojka JE, Boston RC. α-Melanocyte--stimulating hormone and adrenocorticotropin concentrations in response to thyrotropin-releasing hormone and comparison with adrenocorticotropin concentration after domperidone administration in healthy horses and horses with pituitary pars intermedia dysfunction. *J Am Vet Med Assoc* 2011;238:1305-15.
22. Gáspár E, Nguyen-Thi KT, Hardenbicker C, Tiede S, Plate C, Bodo E, et al. Thyrotropin-releasing hormone selectively stimulates human hair follicle pigmentation. *J Invest Dermatol.* 2011;131:2368-77.