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Clinical and Demographical Characteristics of Turkish Patients with Lichen Planus Pigmentosus

Ayşe Akbaş[1*], Fadime Kilinç[1], Sertaç Şener[1], Huban Sibel Orhun[2] and Akin Aktaş[3]

[1]Department of Dermatology, Ministry of Health, Atatürk Training and Research Hospital, Ankara, Turkey.
[2]Department of Pathology, Ministry of Health, Atatürk Training and Research Hospital, Ankara, Turkey.
[3]Department of Dermatology, School of Medicine, Yildirim Beyazit University, Ankara, Turkey.

Authors' contributions

This work was carried out in collaboration between all authors. Authors Ayse Akbas and FK developed the concept and designed the study. Author Ayse Akbas wrote the protocol and wrote the first draft of the manuscript. Authors Ayse Akbas, FK and HSO managed the analyses of the study. Author Ayse Akbas managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Lichen Planus Pigmentosus (LPP) is a disease that is mostly seen in India, Latin America and Far East. It is rarely seen and its etiopathogenesis has not been completely clarified yet. In this study, we aimed to investigate the clinical and demographic characteristics of Turkish paitents diagnosed with LPP.

We retrospectively reviewed medical records of patients with LPP, who had been admitted our outpatient clinic between 2009 and 2015. The following clinical and demographic data were obtained from the records: age of onset, clinical findings, lesion site, laboratory findings, etiological

**Corresponding author: E-mail: ayseakbas62@gmail.com;*

factors, concomitant diseases and drug history. There were 47 LPP patients who were diagnosed clinically and histopathologically. The age average of patients was 51.7. 73% were women and 27% were men. Average age was 52.2 in women and 50.6 in men.
When evaluated in terms of localization, 47% was inverse, 45% was localized and 6% was generalized. One patient was in zosteriform pattern. (2%). Area of involvement was as follows: 10.6% face, 23.4% trunk, 4% legs. 36.7% of patients had more than one body part involved. Axilla was the most common localization site with a ratio of 17%.

Keywords: Intertriginious; lichen planus; lichen planus inversus; lichen planus pigmentosus; pigmentation.

1. INTRODUCTION

Liken planus pigmentosus (LPP) is a rarely seen subtype of lichen planus, which is an autoimmune, chronic disease. The etiological background of the disease has not been clarified yet [1,2].

LPP is a pigmentary disease that was firstly defined in 1974 by Bhutani et al. in India [3]. Actinic, linear, zosteriform and inverse types are defined [1]. Pigmentation is generally diffuse, it can be reticular, spotted, linear or perifollicular [1,2].

Although its etiology is not known, it is considered that sun exposure, drugs, hepatitis C virus, internal malignancies ,henna and hair dyes play important role in its pathogenesis [4,5]. It has been suggested that T-lymphocyte intermediated cytotoxicity is responsible for the pathogenesis [5]. Epidemiology of LPP is still not known [4]. Information about epidemiology is limited and its prevalence varies according to populations [6-9]. Widest study regarding to LPP belongs to Kanwar with 124 disease series [7]. It is a rarely seen disease in our country. The studies regarding to this matter are limited and they are in the form of case reports [10-15]. In this study, it is aimed to evaluate the demographic and clinical characteristics of LPP patients who had been followed at our outpatient clinic.

We retrospectively reviewed medical records of patients with LPP, who had been admitted our outpatient clinic between 2009 and 2015.

2. MATERIALS AND METHODS

In our study, after the local ethical committee approval, the medical records of the patients aged ≥18 and who were clinically and histopathologically diagnosed as LPP between January 2009 and December 2015 are retrospectively evaluated. Punch biopsy was taken from the skin lesions of all patients was evaluated histopathologically. Histopathologically, likenoid reaction, atrophy in epidermis, as vacuolar degeneration in basal layer, lymphocytic band infiltration in dermis, pigment incontinense and melanophages were detected. The patients with LPP diagnosis were included in the study. LPP distinguished from pigmented contact dermatitis by no history of topical application (cosmetics, dyes etc..). Patch test was not performed because there was not any history with contact allergen. Demographic characteristics were evaluated in terms of age of onset, disease period, localization, accompanying symptoms, clinical findings, lesion localization, concomitant skin and non-skin diseases, morphology of the lesions and their distribution, pigmentation of color, family history, topical and/or systemic drug history and cosmetic usage, oral mucosa, hair and nail involvement. Detailed statistical analyses were done.

3. RESULTS

There were 47 LPP patients who were diagnosed clinically and histopathologically. The avarage age of the patients was 51.7. 73% were women and 27% were men. Female/male ratio was 2.6. Age varied between 20 and 76. Average age in women was 52.2 and 50.6 in men. The most common age interval was 50-59.

Demographical and clinical characteristics of the patients are shown in Table 1.

Disease period varied between 1 week to 30 years. 64% of the patients had complaints for 0-6 months, 21% had complaints for 6 months-3 years and 15% had complaints for more than 3 years.

In none of the patients, no skin lesion or inflammatory process was present before the pigmentation.

When evaluated in terms of the symptom presence, the number of patients having rash was only 4 (8,5%). When evaluated in terms of localization, 47% was in the inverse region, (45%) were localized. In 6% of the patients common lesions were observed and one case was in zosteriform (2,1%). Involvement in 23.4% was on the trunk, in 10.6% on the face, in 4% on the legs and in 36.7% more than one area was involved.

Axilla was the most common localization site with a ratio of 17%. In 6,3% involvement was in the inguinal region. In one case, lesions were present on hairy skin and in 2 cases, on eyelids. In 6 patients, hyperpigmentation was present in the form of melasma.

Lesions were mostly diffuse, reticular and spotted and 1 was in the form of zosterifom and 1 was in the form of perifollicular pigmentation. There was not any patient with palmoplantar, oral mucosa and nail involvement. There was not any history of topical drug usage and phototerapy. Only in one patient, large parts of his body surface area was involved. In the history of a patient, likenoid drug reaction diagnosis was detected.

In terms of concomitant diseases, thyroid disease was observed in 16 cases, diabetes mellitus in 11 cases, hypertension in 8 cases and coronary artery disease in 6 cases. Anemia, retinopathy, nephropathy, multiple sclerosis, collagen tissue disease, Discoid Lupus Erithematosus (DLE), Crohn's disease, colon and thyroid carcinoma were less present in patients. Laboratory tests, whole blood count, routine biochemistry, hepatitis B and C serology were recorded. In two cases, liver function tests were slightly higher. However, in none of the patients, hepatitis B and C serology was not positive.

4. DISCUSSION

Although LPP was firstly notified in Indians in 1974 by Bhutani, it can be seen in all races [3,10,12]. Its etiology is not completely known [2,16]. It has been proposed that some of the chemical materials may trigger LPP. Face and neck are the most common places [8], Figs. 1a, 2a. Especially the utilization of some chemical and cosmetic materials such as photosensitive drugs, henna, hair dyes including para-phenylendiamine, perfume, mustard including allyl thiocynate and amla which are used mostly by women may be in relation with the facial localization. Also the systemic drugs(diuretics, tetracyclines, retınoids, hydroquinone...) may cause a photosensitive effect in LPP [3,8,17,18]. In Mahajan study, it is also suggested that hormonal factors may be the cause in women [17,6]. It is mostly seen in the third and fourth decades of life (20-45) and women are affected more than men [17,12], Table 2. In our study, we have observed this disease around the age 50. While the age of onset was 20 in our study, it has decreased to 13 in Indians and prevalence age is earlier when compared to us. The reason can be the geographical location, cultural differences and habits [18].

Although Bhutani, Vega et al. does not indicate any gender difference, Al-mutairi has observed LPP more in men [3,6,9]. In our study women were affected more than men similar to the study of Kanwar and Mahajan [7,17]. Disease period was between 1 week and 30 years. 64% of the patients had applied to our outpatient clinic in the first 6 months. This shows that the disease visually affects people.

Typical lesions are dark brown, purple-gray colored macules and papules. They start as oval lesions slowly expand and may take a diffuse and reticular form [13]. Kanwar et al. has only found uniform pattern in one case [7]. In the studies of Bhutani and Vega, they have defined patients with common pigmentation [3,6]. In our study, common pigmentation was only present in four patients. Other cases were in more localized and reticular forms (Figs. 3, 4). They can be rarely annular, follicular, unilateral forms [13,17]. In recent times, its atypical forms such as linear, inversus, zosteriform has been reported [4,10,11,14,15,17,19-22]. Mahajan had specified 8 atypical variants in their study [17]. In our study, on contrary to the other studies, atypical form was common with a frequency of 51%. We have specified inverse type 1 in twenty two cases, zosteriform in 1 case and perifollicular type LPP in 1 case. In zosteriform dissemination, there was no previous infection or inflammatory condition.

LPP is a chronic disease and lesions may progress by expansion [5]. On the contrary of lichen planus, it is generally asymptomatic and it does not cause any disturbance except its appearance [16,9]. There may be slight itching and burning. Kanwar, Bhutani and Vega have notified rash and burning in one third of the patients [3,6,7]. Pruitus was only present in our 4 cases, who had generalized involvement.

Table 1. Demographical of LPP and concomitant diseases

Patient no	Age	Sex	Localization -distribution	Lesion type	D. period	Symptoms	Concomitant disease	Drug usage	Antihbs
1	20	m	Body	Linear	1-2 months				
2	26	m	Popliteal region, inguinal eyelids	Inverse	3 months			Yes	Positive
3	31	f	Leg		1-2 months				
4	33	f	Axilla	Inverse	15 years		D	Yes	
5	33	f	Abdomen		2 months				
6	35	f	Ingunal ,umbilicus, inframammary	Inverse	3 months	+			
7	36	f	Axilla ,Ingunal	Inverse	1 year		A (iron-vitB12)	Yes	
8	37	f	Inframammary	Inverse	2-3 months				
9	38	f	Body	Common	15 years		RAS ,collagen disease	Yes	
10	38	f	Abdominal,Inguinal	Inverse	1 month		Slight LFT increase		
11	44	f	Inframammary, Inguinal, Axilla	Inverse	16 years		DM, A, thyroid ca, D		
12	44	f	Inframammary axilla	Inverse	2 years				Positive
13	45	f	Body, Axilla	Inverse	4 months	+			
14	46	f	Axilla	Inverse	5-6 months		lichenoid drug reax		
15	48	m	Axilla	Inverse	1-2 months				
16	49	m	Umbilicus		3 months		Urinary bladder dysfunction		
17	50	m	Umbilicus axilla	Inverse	1 month		Insulin resistance		
18	51	m	Body		3-4 months		HT, D	Yes	
19	51	m	Neck eyelids		1-2 months		DM, HT, CAD	Yes	
20	51	m	Axilla	Inverse	1 month		TD, DM, asthma, renal tm op	Yes	Positive
21	51	m	Face		1-2 months		D	Yes	
22	52	f	Body		3 months		TD	Yes	
23	52	f	Face		1 year		MS, TD, DM	Yes	
24	53	f	Body		3-4 months		DM	Yes	
25	54	f	Axilla Inframammary Ingunal	Inverse	5 years	+	DM, HT, CAD, TD	Yes	
26	54	f	Inguinal	Inverse	6 months		Gastric reflux, Chron disease	Yes	
27	55	f	Inguinal	Inverse	5 months		DM, HT, HL	Yes	Positive

Patient no	Age	Sex	Localization -distribution	Lesion type	D. period	Symptoms	Concomitant disease	Drug usage	Antihbs
28	56	f	Axilla	Inverse	5-6 months		TD, A (vit 12)	Yes	
29	56	m	back.arms		6 months		CAD	Yes	
30	57	f	Inframammary	Inverse	5-5 months		HL, TD		
31	57	f	Face, Arm, abdoman		3 months		Migraine	Yes	
32	58	f	Body		6 months		A(Iron-vit12)	Yes	
33	58	m	Hairy skin		1 week				
34	58	f	Face and upper hands		8 years		TD , A (iron)	Yes	Positive
35	58	f	Cheeks, face		3 months		TD, HL	Yes	
36	60	f	Legs, face	Common	30 years	+	DM, HT, A	Yes	Positive
37	61	m	Chin, cheeks		1-5 months		DM, HT, Retinopathy, Nephropathy, HL	Yes	Positive
38	61	f	Body,Legs,	Common	3 months		TD, H		
39	62	f	Body		4 years		TH, Parathormone increase		
40	63	f	Inframammary	Inverse	1-5 months		DM, HT, Pustular psoriasis	Yes	
41	65	m	Inguinal	Inverse	7-8 months				
42	68	f	Neck, Antecubital and Popliteal	Inverse	3-4 months		HT, DM, TH, Neuropathy	Yes	
43	68	f	Legs		1 year		TH, Parathormone increase	Yes	
44	70	f	Side of mouth		2 year		DLE,DM, CAH	Yes	Positive
45	72	f	Axilla	Inverse	1-2 months		TH, HT, DM, lft increase,	Yes	
46	73	m	Back		2-3 months		Colon ca op		
47	76	f	Body, Abdomen	Common	4 months		TH, HT, CAD	Yes	

CAH: Coronary artery disease, DLE: Discoid lupus eritematosus, HL: Hyperlipidemi, HT: Hypertension, TH: Thyroid disease, A: Anemia, D: Depression, DM: Diabetes mellitus, LFT: Liver fonctions tests, Ca: Carsinoma

Table 2. Comparison of our study with other studies

Study characteristics	Our study Turkey 2015	Mahajana India 2013	Al-Mutahari Kuwait 2009	Kanwar India 2003	Vega Mexico 1992
No. of patients	47	76	33	124	11
Female / Male Ratio	2,6/1	2,5/1	1/1,75	1,21/1	1/1,17
Onset age	51,8	37	34	26-34	46
Color	Dark Brown	Dark Brown	Dark Brown	DarkBrown	Dark Brown
Most common lesion type	Reticular	Diffuse	Diffuse (54,5)	Diffuse (77,4)	Reticular
Most common localization	More Than One İnvolvement 36% Inverse, Axilla 17%	Face And Neck	Face And Neck(54.5%)	Face And Neck (88,7%)	Face (72.7%) 46% Common
Presence of symptom rash	4 (8,5)	10%	9 (27,3)	39 (31,5)	7 (62%)
Atypical variant	24 Patients (51)	8 Patients (10,5%)	7 Patients İnversus (21%)		
Mucosal ınvolvement	-		1 (3,03) Oral	4 (3,22%)	-
Hairy skin ınvolvement	1 Perifollicular	3,60%	1 (3%)	-	-
Period	0-6 Months (64%)	3,5 + 1,8	6 Weeks - 3 Years	6 Months - 3 Years	3,5 + 1,8
Hepatitis C serology	-	-	20 Cases	-	-
Hepatitis B serology	Antihbs in 8 Patients +		-	-	-
Other lichen planus findings	1 Lichenoid Drug R.		8 (24.2%)	19 Patients	1 Lichen Planus
Concomitant diseases	16 TD,14DM,8HT,6CAD, 1 pustular Psoriasis	2HT, 3DM, 6 Thyroid Disease	-	-	1 Vitiligo

Third of the patients typical lichen planus lesions may accompany. Al-mutairi et al. have determined lichen planus and LPP findings at a ratio of 24%(n= 8 patients). In our study only 1 patient had previously diagnosed as lichenoid drug reaction [7,9].

Rarely preauricular region and chin may be involved [11]. In our study, 5 patients had pigmentation form on their face. Interestingly, the involvement of the eyelids in 2 patients and the perifollicular involvement in one patient were detected.

Besides the face and neck, upper extremities and upper body can also be involved. Intertriginous lesions are less common [2,8]. It is notified that lesions are mostly symmetrically located [3,6,7]. In our study, inversely involved ones are generally symmetrical ones. Pock et al. have called the type of lichen planus showing invers involvement as the LPP inversus [23]. Flexural locations uncommonly involved. In the study of Kanwar et al., lesions are observed in axilla with a ratio of 8,9%, in the rubbed areas of the skin at 6,5% and in inguinal region at 3,2% and they have notified that popliteal region is frequently affected [7]. Barros had specified axillar involvement in inversus type [4]. In our research, we have specified 47% inverse symmetric involvement. Lesions are mostly axillary located. 17% axillar involvement, 6% inguinal involvement and 36,7% more than one involvement are determined. The lesions at intertriginous areas can be caused by the increase of the contact and absorption of the materials of the colored painted clothes due to sweating at the intertriginous areas.

In LPP cases, generally no involvement occurs in oral and genital mucosa, nail and hair. Kanwar et al. have observed mucosal involvement in 4 cases and Al-mutairi in 1 case [7,9]. In this study mucosal and nail involvement was not present in any of the patients.

LPP is known as an uncommon disease. In this study, we have observed that this disease is not such a rare disease. Inconsistency of the pre diagnosis and histopathologic diagnosis may be the cause. Histopathologically, lichenoid reaction is observed that is characterized as atrophy in epidermis, as vacuolar degeneration in basal layer, rare lymphocytic band infiltration in dermis. Pigment incontinense and melanophages are typical [5,9,17,23] (Figs. 1b, 2b). In our research, diagnosis is histopathologically supported in all of the patients.

The relationship of LPP with viral hepatitis, drugs, autoimmune diseases or infections was investigated. Some autoimmune diseases such as hepatitis can be present together with LPP. Especially Hepatitis C accompanying to oral lichen planus was more frequently observed as positive in 60,6% of LPP patients [4,5]. Vachiramon has shown the concomitant appearence of LPP and hepatitis C [24]. Hepatitis C and B were not detected in any of our patients. Only AntiHbs antibodies of 8 cases were positive. As in the cases of Uyar et al., we do not encounter any triggering or accompanying infections [15]. In most of our patients, thyroid disease, diabetes mellitus and hypertension were present that necessitated to use drugs due to their advanced ages. In the study of Muzio et al., 14,3% thyroid disease is observed. It is considered that thyroid antibodies trigger the specific autoimmune response to the organ and caused lichen planus lesions [25]. This may also be valid for other autoimmune originated diseases [5] Some diseases such as rheumatoid arthritis, Myasthenia gravis, systemic lupus erythematosus, autoimmune thyroiditis may accompany lichen planus [14,15]. In our study, we have detected other autoimmune diseases such as discoid lupus erythematosus, Crohn's disease, multiple sclerosis, connective tissue disease, vitamin B12 anemia. In some of the studies, thyroiditis in erosive lichen planus, alopecia areata, celiac disease are found to be significant [5,25,26]. Ebrahimi et al. have found an association in 33 of 120 lichen planus patients (28%) regarding to at least one autoimmune disease [27].

We have specified colon and thyroid cancer history in two patients.

It is considered that some of the antihypertensives and antidiabetic drugs can cause lichen planus [5]. Hypertension and diabetes mellitus in half of our LPP patients can explain this. In our study, the most frequently accompanying diseases were thyroid disease, hypertension, diabetes mellitus and coronary artery disease.Drug usage is also discussed regarding to these diseases. These drugs may have a triggering role on LPP. Rieder et al. have suspected captopril, which is an antihypertensive drug, as a causative factor in one LPP patient [13].

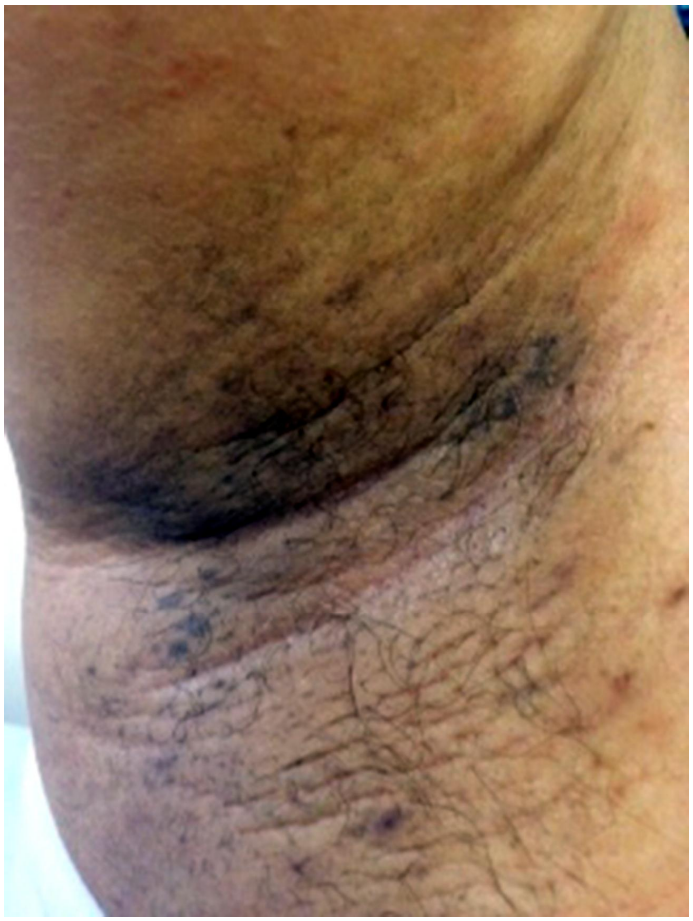

Fig. 1a. Multiple small dark spots on the axilla

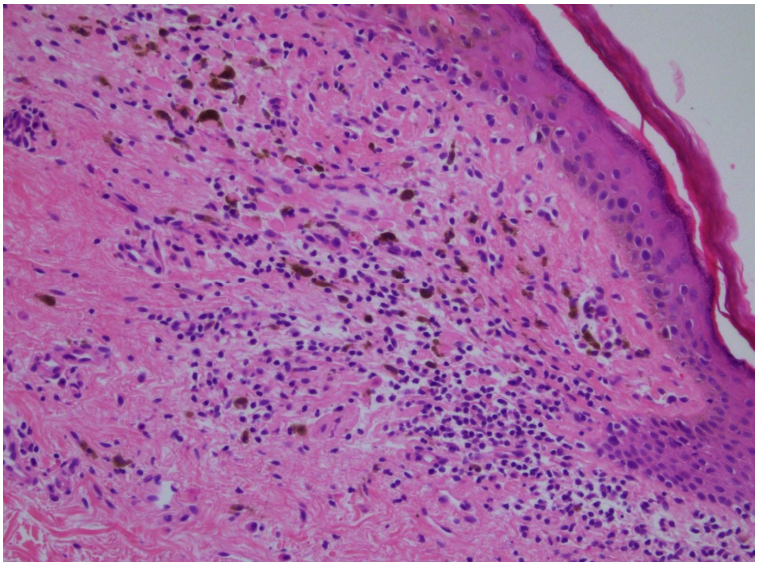

Fig. 1b. Histopathological appearance of the patient (H&E X200)

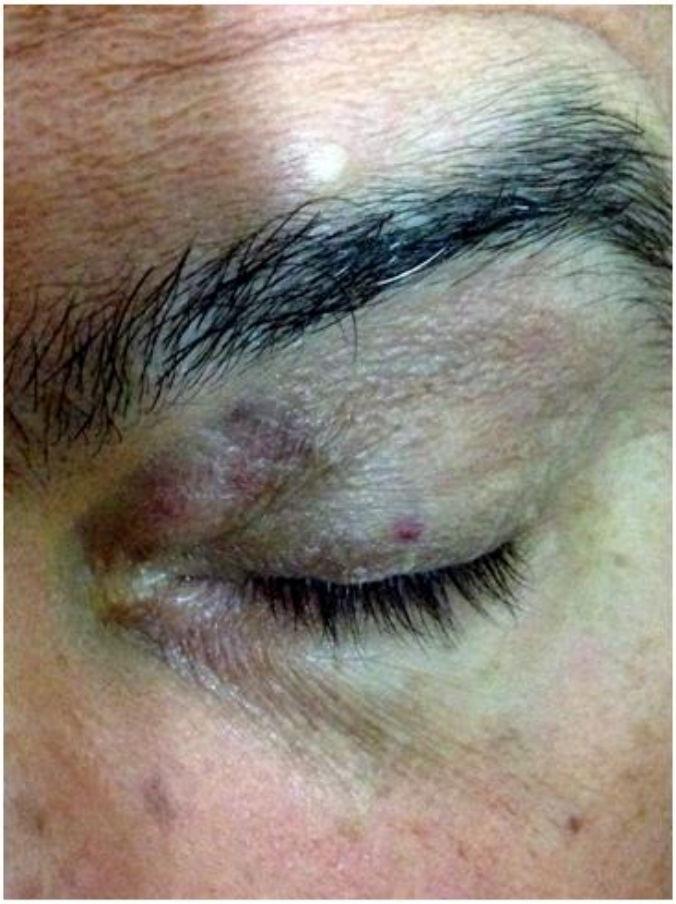

Fig. 2a. Brownish-black spots located on periorbital area

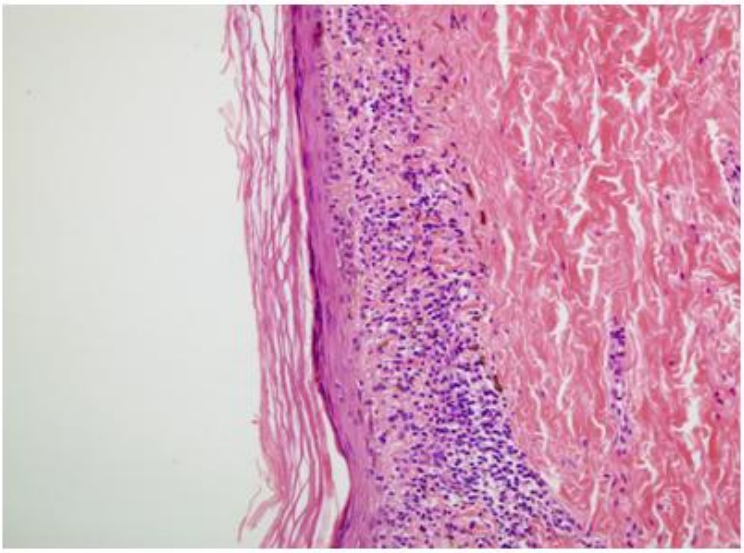

Fig. 2b. Histopathological appearance of the patient (H&E X200)

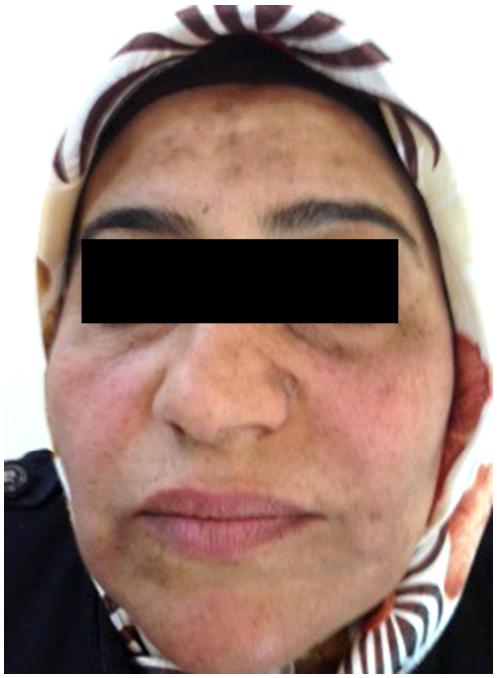

Fig. 3. Hyperpigmented macules and patches located on face (melasma like hyper pigmentation)

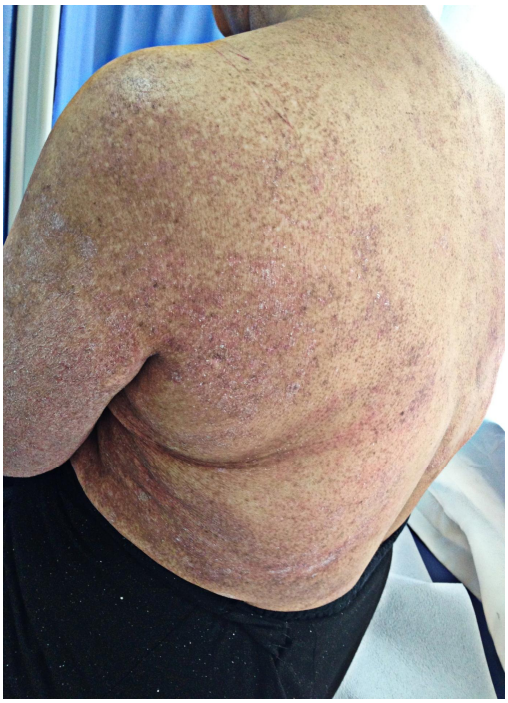

Fig. 4. Multiple dark-brown macules and patches widely distributed on the entire body surface (face, neck, body)

This disease that is assumed to be rare can be neglected due to the consideration of different diagnosis and thus it may delay the primary diagnosis. Hyperpigmentation is difficult to diagnosis. A lot of reason about skin pigmentation. The diseases that are seen with hyperpigmentation such as photosensitization, Ashy dermatosis, pigmented contact dermatitis, pellegra, drug eruptions, postinflammatory hyperpigmentation, actinic lichen planus should be considered in the differential diagnosis [13,4]. In inverse involvement; Duhring disease, Degos disease, acanthosis nigricans should be considered [11,16,17]. LPP distinguished from pigmented contact dermatitis by no history of topical application (cosmetics, dyes etc..). Patch test was not performed because there was not any history with contact allergen. Ashy dermatosis is usually localized on the trunk. There is an early inflammatory phase which described with erythema of the lesions. The pigmentation is annular pattern with central clearing. An erythematous halo arounds the macular pigmentation. There was no erythematous phase in our patients [28]. Our diagnosis are based on the histopathologic algoritm. One of them is epidermal clues (thinning, acanthosis, basal vacuoler degeneration, granular layer changes, apoptosis, spongiosis). The others are dermal inflammatory response.

A little bit differences between LPP and Ashy dermatosis which are lichenoid infiltrate and basal vacuoler dejeneration. LPP is a lichenoid dermatitis which consist of melanofage with lympohyctiocyte mononucleer cells and epidermal changes such as vacuoler degeneration and atrophy is more pronounced. Ashy dermatosis has got perivascular mononuclear inflamation and mild vacuoler degeneration. Colloid bodies much less seen than LPP. Another finding was seen melonofage in the dermis not only seen upper dermis also seen deep dermis. Pigmented contact dermatitis is a different group inflammatory dermatosis which is spongiotic dermatitis. Epidermal changes are more pronounced than LPP and Ashy dermatosis. Akantosis, parakeratozis, spongiosis, hypogranulosis are seen. There is a perivascular inflammation consist of lympohyctiocyte sometimes with eosinophil. Apoptosis could be seen all layers in the epidermis, it is another clue of pigmented contact dermatitis. Apoptosis are also seen LPP but is different epidermal

layer localization which only seen at the basal layer in the epidermis.

In our cases, the histopathologic clues in LPP were lichenoid mononucleer inflamation with melanofage in the dermis and basal vacuoler degeneration of the basal layer in the epidermis seen in %100 of cases. Another finding was apoptosis at the basal layer in the epidermis seen in %90 of cases [29].

Treatment of LPP is not satisfactory. Mostly topical corticosteroids and topical calcineurin inhibitors are used [1,9,13,17]. In our research, these topicals were also applied. However, as the treatment responses were not recorded in detail, we do not discuss treatment of LPP.

5. CONCLUSION

Demographic and clinical characteristics of 47 LPP patients who are diagnosed at our outpatient clinic were reviewed retrospectively. Although the etiology of LPP is not exactly known, there is significant advances in understanding of the disease. We can encounter LPP patients with various clinical manifestations. Because the symptoms and findings constitute a basis for the diagnosis of LPP, it is important to know the clinical characteristics of the patients. Its differential diagnosis with other pigmentary diseases should be done. Also we should be more careful in terms of the triggering roles of the concomitant diseases.

CONSENT

As per international standard or university standard, patient's written consent has been collected and preserved by the authors.

ETHICAL APPROVAL

As per international standard or university standard, written approval of Yildirim Beyazit University Ethics committee has been collected and preserved by the author(s). LPP IRB; Ins tutions rewiev board number) 11.02.2015 date no: 66.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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