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Pigmented Papules and Patches of the Folds: A Case Series of Lichen Planus Pigmentosus Inversus with Review of the Literature

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Abstract

We report nine cases of Lichen Planus Pigmentosus (LPP) inversus in Caucasian patients. They were 5 women and 4 men aged from 29 to 77 years with violaceous hyper pigmented ovalar or annular macules and patches mostly located at axillary folds but also groin, submammary folds, popliteal and genital regions. Histological examinations showed a band-like lymphocytic infiltrate in the upper dermis and melanophages in the papillary dermis. LPP inversus is a rare variant of LPP appearing in non-sun exposed areas. In contrast to LPP which occurs almost exclusively in dark skinned individuals, a comprehensive review of the literature revealed that about half of the cases reported of LPP inversus affects fair skinned individuals including Caucasian patients.

Keywords: Lichen planus pigmentosus; Hyper pigmented; Lymphocytic infiltrate; Papillary dermis

Introduction

Lichen Planus Pigmentosus (LPP) inversus is a rare variant of LPP occurring in flexural regions with asymptomatic to mildly pruritic violaceous and dark-brownish macules and/or patches [1]. Usually mucosae, scalp and palmoplantar area are not affected [2]. LPP is described almost exclusively in dark skinned individuals. We report here nine cases of LPP inversus in nine Caucasian patients, and an accurate review of the literature about the published cases. Including ours, 48 cases of LPP inversus have been reported, a half of which in Caucasian individuals.

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Nine Caucasian patients, five women and four men, with asymptomatic to mildly pruritic, sharply demarcated violaceous and hyperpigmented macules and patches located at different folds, mainly axillae and groins, were included in the study. Clinical and histopathological characteristics are shown on (Table 1). The age of onset of our patients range from 29-77 years, with a mean age of 44.7 years and a female:male ratio of 1.25:1. No association with systemic diseases, viral hepatitis and drug exposure was documented in any case. Lesions appeared from 4-18 months before diagnosis. A 4 mm punch biopsy was performed in all patients except patients 3 and 5. Histological changes were similar in all cases with a slight to moderate inflammatory infiltrate in the upper dermis with a band like pattern. Vacuolar alterations of the basal epidermal layers were observed in all patients, but only in four patients were prominent. Melanophages in the upper dermis were present in all cases. In case n. 8, immunohistochemistry showed the presence of CD8 positive and granzyme positive lymphocytes in close contact with damaged keratinocytes of the basal epidermal layers. Only three patients were treated with topical steroids without any significant improvement except for one that showed a complete resolution. After a follow up of 6-24 months, most patients showed persistent asymptomatic lesions (Figures 1 and 2).

Discussion

LPP is a rare lichenoid dermatitis characterized by the presence of hyper pigmented, dark-brown maculae and patches in sun exposed areas occurring mainly in dark skinned individuals such as those from India and the Middle East [3,4]. In 2001, Pock et al. [1] described seven European Caucasian patients with lesions unrelated to sun exposure arising on intertriginous areas and proposed the term LPP inversus [1]. A comprehensive PubMed search (2001- 30 March 2015) revealed additional 32 cases of LPP inversus described since (Table 2). Including our patients, of all the reported cases of LPP inversus about half (23/48) occurred in Caucasian individuals. The disease appears slightly more common in females (29 females vs 19 males) and the age ranges from 15 to 84 years, with a mean age at diagnosis of 54.2 years. About 80% of patients had lesions at the axillae, usually bilaterally, 50% at the groins and 23% in the submammary folds. One case with lesions in the post auricular sulci was reported [5]. The majority of patients had no or very mild pruritus, a factor that may contribute to a delay in physician consultation, and may cause an underdiagnosis of this disorder. The main differential diagnoses are erythema dyschromicum perstans

Patients	Age	Sex	Location	Pruritus	Duration	Histology	Race
1	46	F	axillae	no	3 months	A,B,D	caucasian
2	29	M	axillae, groin	yes	/	A,C,D	caucasian
3	76	M	axillae,	yes	8 months	/	caucasian
4	75	F	intergluteal fold	no	5 months	A,C	caucasian
5	39	F	submammary, groin,axillae	no	1 year	/	caucasian
6	49	M	axillae, groin	no	>1 year	A,B	caucasian
7	51	M	axollae, groin, popliteal folds	no	4 months	C,D	caucasian
8	37	F	genital area	no	/	A,C	caucasian
9	77	F	axillae, groin	no	4 months	A,B,D	caucasian

A: Incontinence of pigment, B: Slight inflammatory infiltrates with lymphocytes in the upper dermis, C: Moderate inflammatory infiltrates with lymphocytes in the upper dermis, D: hydropic degeneration of the basal layer of epidermis, E: Intensive lichenoid inflammatory reaction.

Table 1. Summary of clinical and histological data in our series of patients with LPP-inversus.

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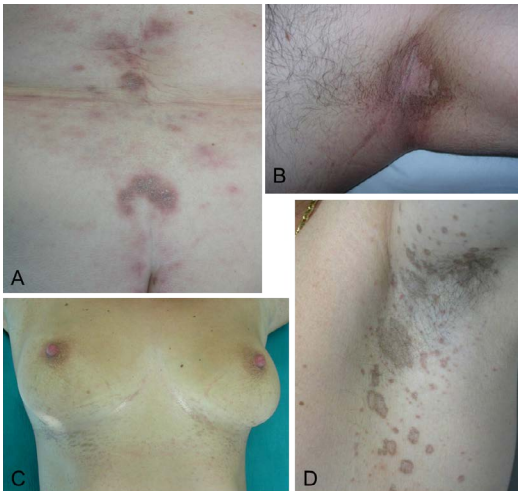

Figure 1: Clinical appearance of Lichen planus pigmentosus inversus: multiple hyperpigmented lesions with smooth surface. (A, B) Early erithemato-violaceous lesions at sacral area (A) and left axillary fold (B), (C) Sub-mammary and (D) axillary fold lesions resulting with the appearance of the late phase (brownish).

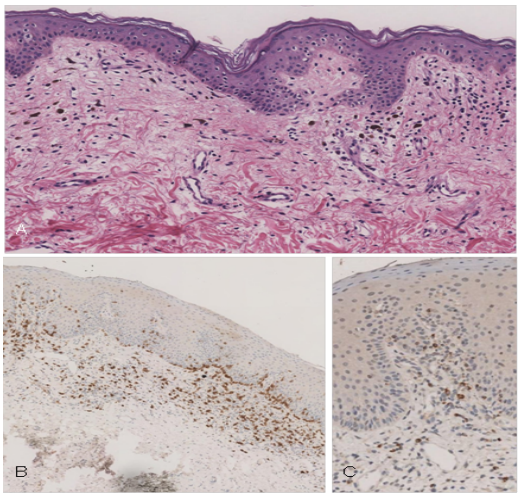

Figure 2: Histologic aspects of lichen planus pigmentosus inversus: basal vacuolar changes, a band like infiltrate of lymphocytes in the upper dermis and incontinence of pigment (A). Numerous CD8+ cells in the basal epidermal layers (B), granzyme +cells in close apposition to damaged basal keratinocytes (C).

References	Age	Sex	Location	Pruritus	Duration	Histology	Race
Pock et al. 2001	66	M	axillae, back	mild	2 months	A,B	caucasian
	54	F	axillae, shins	/	6 months	A,B	caucasian
	68	F	axillae, groin, submammary	/	5 months	A,B	caucasian
	71	F	axillae, groin	/	5 weeks	A,D,E	caucasian
	60	F	axillae, groin	/	1 year	A,C	caucasian
	57	M	axillae, groin, wrists	/	6 months	A,B	caucasian
	46	M	axillae	/	15 years	A,D,E	caucasian
Munoz-Perez at al. 2002	27	M	axillae, abdominal fold, groin, upper limb	no	2 months	A,D,E	hispanic
Kashima et al. 2007	51	F	axillae, popliteal fold	no	2 months	A,C,D	asian
	62	M	axillae, popliteal fold, groin	no	6 months	A,C,D	asian
Bennassar et al. 2009	84	M	axillae, neck	mild	2 months	D,E	caucasian
	72	F	inframammary	no	3 months	A,D,E	caucasian
	59	M	axillae, groin	no	several months	E	caucasian
	54	F	axillae, popliteal fold	no	1 year	A,C	caucasian
Kim et al. 2007	70	M	groin	no	5 months	A,C,D	asian
Kim et al. 2008	49	F	groin	no	several months	A,E	asian
	25	F	axillae	no	1 year	A,D,E	asian
Ohishima et al. 2011	54	F	axillae, groin, submammary, neck, popliteal folds	mild	4 months	A,B	asian
Jung et al. 2011	31	F	axillae ,popliteal folds, antecubital folds	no	5 years	A,B	asian

Gaertner et al. 2012	58	M	groin	no	several weeks	A,C,E	caucasian
Majima et al. 2013	65	M	groin, axillae	no	1 year	A,C	asian
	64	M	groin	mild	2 months	A,D, E	asian
Barros et al. 2013	25	M	axillae, neck, popliteal folds, groin	no	9 months	A,C,D	black
Nijhawan et al. 2013	47	M	axillae, retroauricolar folds, intergluteal fold	mild	3 months	A,E	/
Ghorbel et al. 2014	74	F	neck, axillae, submammary folds, groin	/	15 days	A,B	middle-easten
	60	F	neck, inframammary folds, sacral area	yes	3 years	A, E	middle-easten
	54	F	submammary, groin, genitalia	yes	15 days	E	middle-easten
	60	F	submammary fold and groin	yes	1 year	A,E	middle-easten
	49	F	axillae , groin, vulva	yes	15 days	A,E	middle-easten
	76	F	submammary folds	yes	3 months	A,B	middle-easten
Dizen Namdar et al 2014	40	F	axilla, groin, submammarian, antecubital and popliteal fossae	no	3 months	E,A,D	middle-easten
	45	F	axilla, submammarian	yes	2 months	E,A,D	middle-easten
	61	M	axillae	no	1 month	E,A,D	middle-easten
	67	F	axilla, submammarian, groin	no	1 year	C.A.D	middle-easten
	55	M	axilla, groin	slight	3 months	C,A,D	middle-easten
Murzaku et al. 2014	45	F	axilla	mild	2 years	A,C,D	hispanic
Chen et al. 2015	15	F	abdomen, left neck, axillae, groin, inframammary	no	6 months	B, A	asian
	44	F	abdomen, waist,axillae, groin	no	6 months	C,A	asian
	35	F	axillae,groin,inframammary areas, popliteal folds, antecubital fossae, inner wrists, abdomen	no	10 months	C,A	asian

A: Incontinence of pigment, B: Slight inflammatory infiltrates with lymphocytes in the upper dermis, C: Moderate inflammatory infiltrates with lymphocytes in the upper dermis, D: hydropic degeneration of the basal layer of epidermis, E: Intensive lichenoid inflammatory reaction.

Table 2: Summary of LPP-inversus cases reported in literature.

for those patients with more widespread lesions, post-inflammatory hyperpigmentation, figurate erythema, fixed drug eruption and LPP [2]. The clinical and the histological features are usually sufficient in making the diagnosis. A case report described the dermoscopic features of LPP inversus, with diffuse brown patches containing multiple granular gray-brown dots and an overlying scale [6].

LPP inversus belongs to the lichenoid dermatosis which includes lichen planus, LPP, lichenoid drug eruptions, annular lichenoid dermatitis of youth, graft versus host diseases [7]. LPP inversus microscopically resembles late phase lichen planus lesions, with epidermic atrophy, irregular hydropic degeneration of the basal layer and absence of epidermic hyperplasia. There is an exuberant pigmentary incontinence and a lichenoid inflammatory infiltrate with lymphocytes and histiocytes [2]. The pathogenesis appears to be related to a CD8+ T lymphocyte-mediated cytotoxic activity against basal keratinocytes [2,8] as suggested by immunohistochemical features performed in some patients, including our [3,8,9]. Pock et al. proposed that in LPP inversus the lichenoid reaction occurs within a short period of time with dramatically intensive hydropic degeneration of basal keratinocytes, with no time for compensatory increased proliferation of keratinocytes, as it occurs in typical lichen planus such that the papules transform quickly into brown macules [1,10]. No drugs, infections or systemic co-morbidities have been documented in LPP inversus cases neither in literature nor in our cases. External stimuli, such as friction [Koebner phenomenon], may be a triggering factor [9], but this has been postulated as an explanation for the isolated or exclusive distribution of lesions in intertriginous area [11], and it has not been confirmed.

Treatment of LPP-inversus is not well established. Some cases undergo spontaneous remission within months to years [2]. Topical treatment with high potency corticosteroids [9,12,13] or topical tacrolimus have been used to accelerate the process [12,14], but with minimal improvement. A case report showed only a slight lightening of the lesion after oral deflazacort 45 mg tapered gradually over a period of 2 months [15], and two cases reported improvement of lesions after the discontinuation of wearing tight underclothes [13]. Three of our cases were treated with topical steroids, with no significant improvement except for one that showed a complete resolution, five patients were lost at follow up and the last one had no treatment with spontaneous resolution of pruritus but permanence of pigmentation [16,17].

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