

Systematic Review

Oral manifestation of lymphomatoid papulosis: systematic review

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Abstract – Introduction: Lymphomatoid Papulosis (LyP) is a lymphoproliferative disorder with typical histopathological criteria and a spontaneous regression. Only few cases of oral involvement have been reported. We wondered about their clinical characteristics and their association with lymphoma. **Method:** This systematic review is conducted according to the PRISMA statement. The Oxford Centre for Evidence Based Medicine table (OCEBM) and the scoring from the National Agency for Accreditation and Assessment in Health (ANAES) was assigned to each study. **Results:** We have included 16 references. LyP can occur at any age with a female predilection. Oral lesions were unique ulcer and tongue was mostly affected. Histological types A, and C were dominant and LyP resolved spontaneously. 1 case was associated with a lymphoma. **Discussion:** Cutaneous LyP more affects men and are mostly classified as type A while those orals are type A or C. Oral LyP is probably a progressive lesion whose evolution is not illustrated by the histological aspect which often reflects only the initial acute period. **Conclusion:** Our literature review has shown that the epidemiological aspects between oral and cutaneous LyP are not the same. LyP may be associated with an increased risk of developing systemic lymphoproliferative disorders.

Introduction

Lymphomatoid Papulosis (LyP) was first described by Macaulay in 1968 [1] as a chronic cutaneous lesion. Introduced in 2005 [2], consensus classification of primary cutaneous lymphomas of the World Health Organization and the European Organization for Research and Treatment of Cancer (WHO-EORTC) was revised in 2016 [3] and an updated version was published in September 2018 [4]. LyP was classified like a primary CD30+ cutaneous LymphoProliferative Disorder (CD30+LPD).

LyP's etiology is unknown and the mechanisms involved in the spontaneous regression of lesions have also not yet been identified. It is a rare lymphoproliferative disorder with an estimated incidence of 1.2 to 1.9 cases/1,000,000 people. There is a slight male predominance (ratio of 1.3–1.4:1) and LyP can occur at any age, even in childhood, with a peak incidence at the 5th decade [5,6].

The LyPs' clinical characteristics are a chronic course of recurrence, self-healing papulonecrotic or nodular skin lesions, usually with a maximum diameter of 1 to 2 cm [7]. These lesions are mainly found on the trunk and limbs, but they can also occur on the face, scalp, palms, and soles. Few cases with oral or anogenital involvement have been reported [8,9].

Diagnosis is based on its typical clinical presentation with spontaneous lesion regression within weeks or months, as well as typical histopathological criteria which include infiltration pattern, morphology and lymphoid cells phenotype. Initially 3 histological subtypes (A, B and C) were described in the 2005 WHO classification [2]. Since 2010, 2 other different histological subtypes and one subtype with chromosomal rearrangements involving the DUSP-IRF4 locus on 6p25.3 have been characterized and listed in the updated WHO-EORTC classification of 2018 [4]. Table I gives the characteristics of LyPs' different types. Type A LyP is the most common histological manifestation, accounting for 80% of all biopsies characterized. The less common type B (<5% of cases) presents an epidermotropic infiltrate in the form of a band of atypical small and medium lymphocytes. Clusters or leaflets of large CD30+ tumor cells with relatively few inflammatory cells characterizes Type C (10% of cases) [10]. Type D (<5% of cases) involves the pagetoid infiltration of atypical CD8+ and

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Table I. LyP = Histological subtypes, predominant phenotype.

Type*	Histological aspect	Predominant phenotype
A (>80%)	Dermal infiltration of large atypical CD30 + lymphocytes dispersed in clusters, with an inflammation of eosinophils, neutrophils and histiocytes.	CD4+, CD8-
B (<5%)	Small to medium-sized epidermotropic lymphocyte infiltrate with variable expression of CD30 (0-77%)	CD4+, CD8-
C (10%)	Cohesive nodular infiltrate of large atypical CD30 + lymphocytes. Few inflammatory cells (some eosinophils and neutrophils)	CD4+, CD8-
D (<5%)	Epidermotropic infiltrate of atypical CD8 + CD30 + lymphocytes	CD4-, CD8+
E (<5%)	Angioinvasive infiltrate of atypical CD30 + lymphocytes	CD4-, CD8+
With DUSP22-IRF4 rearrangement	Small to medium-sized CD30 + epidermotropic infiltrate and dermal infiltrate of large CD30 + large blast cells	CD4-, CD8+ ou CD4-, CD8-

CD30 + [11]. Type E represents less than 1% of cases and presents an infiltration mainly of pleomorphic CD8 + CD30 + lymphocytes [12]. Finally, LyP with 6p25.3 rearrangement is characterized by an epidermotropic infiltrate of weakly CD30 + with cerebriform nuclei and larger strongly CD30 + blast cells in the dermis. Histologically, this latter subtype also appears to be quite aggressive [13]. Therefore, atypical lymphocytes express CD30 in all types of LyPs except for type B where the expression of CD30 is variable. Most often, CD30 + cells express CD4 (types A, B and C), however CD8 + CD4- phenotype is predominant in E-type LyP and is still seen in D-type LyP [4]. Other rare histopathological variants have been reported such as follicular LyP with folliculotropism of atypical CD30 + lymphocytes [14,15] or syringotropic, granulomatous LyP [16]. Thus, we can expect soon that new types will be included in the classification.

A multidisciplinary group of experts made up of the European Organization for Research and Treatment of Cancer (EORTC – European Organization for Research and Treatment of Cancer), the International Society for Cutaneous Lymphoma (ISCL) and the United States Cutaneous Lymphoma Consortium (USCLC) developed in 2011 consensus recommendations for the management of Lpy skin disorders (CD30 + LPD). The “abstention and surveillance” strategy appears to be a legitimate first-line approach, especially in patients with a limited number of lesions. Initiation of treatment is indicated for patients with diffuse and symptomatic lesions or patients with significant scars or pigmentary changes leading to aesthetic damage [17]. LyP is characterized by an excellent prognosis with a survival rate of 100% at 5 years. However, it is associated with an increased lifelong risk of developing systemic lymphoma or

Table II. Included studies. Scientific evidence: scoring from the National Agency for Accreditation and Assessment in Health (ANAES); OCEBM : Oxford Centre for Evidence Based Medicine table.

Reference	Date	Type of paper	Scientific evidence	OCEBM score	Number of patients (ntot=28)
Kato et al.	1998	Case report	C	4	1
Sciubba et al.	2000	Case report	C	4	1
Chimenti et al.	2001	Case report	C	4	1
Pujol et al.	2003	Literature review and case report	C	4	2
Serra-Guillén et al.	2007	Case report	C	4	1
Agarwal et al.	2008	Case report	C	4	2
Allabert et al.	2008	Literature review and case report	C	4	4
Fernandez-de-Misa et al.	2009	Case report	C	4	1
Saggini et al.	2010	Case report	C	4	1
Kempf et al.	2013	Case report	C	4	3
Booken et al.	2013	Case report	C	4	1
Benslama et al.	2015	Case report	C	4	2
Schwartz et al.	2017	Literature review and case report	C	4	5
Bresztajn et al.	2019	Literature review and case report	C	4	1
Machan et al.	2020	Case report	C	4	1
Narahara et al.	2021	Case report	C	4	1

other lymphoproliferative disorders. These lymphomas can occur before, simultaneously with or after the initial manifestation of LyP not especially around the same site. The prevalence of lymphomas associated with LyP reported in literature varies widely, reports indicate that between 15.5% [18] and 52% [6] of patients are affected, with some people developing several lymphomas.

Because of these findings concerning cutaneous lymphomatoid papulosis and given that only a few cases of mucosal involvement have been reported [8], we wondered about the clinical characteristics of oral LyP and their rate of association with malignant lymphoid pathologies. We therefore performed a systematic literature review on the subject. The primary aim of this systematic review was to do a knowledge synthesis of clinical and histological oral LyP aspects. The secondary aim was to determine their association rate with malignant lymphomas like is reported for cutaneous lymphomatoid papulosis.

Methods

Protocol

The Cochrane Handbook [19] and the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines were used as a guide for planning and performing this systematic review [20].

Information sources and search

Electronic general, open access, regional and grey literature databases were systematically searched up without date limitation. The databases used were Medline, PubMed and Google Scholar. MESH terms and relative keywords were used accordingly for each electronic database. The reference lists of included articles and relevant reviews were manually searched. Grey literature was searched through appropriate databases and registers.

Keywords and data bases

The two concepts of our research equation were "lymphomatoid papulosis" and "oral" which were used with the Boolean operator "AND". Each term was defined by his MESH descriptor and his synonyms separated by Boolean operator "OR". To find articles not indexed in MEDLINE, the terms were also searched in the "Title and Abstract" fields.

Management of bibliographic sources and references was carried out using Zotero software.

Eligibility criteria

Inclusion criteria were:

- Articles answering the research question by reading the title, then the abstract.
- Description of the main clinical signs and oral lesions linked to LyP.
- Case reports, literature reviews, retrospective, or prospective studies on oral manifestations of LyP.
- Diagnosis of oral LyP made and established based on a clinical and immunohistological examination according to the classification of the World Health Organization-European Organization for Research and Treatment of Cancer (WHO-EORTC).
- Therapeutic used mentioned.
- No publication date limit.

Non-inclusion criteria

- Paediatric oral LyP cases.
- Articles not written in French, English, or Spanish.

Study Selection

A study was judged as eligible, when one of the inclusion criteria were fulfilled. After removal of duplicates, articles were screened on their title, and after on their abstract, and finally on their full text. One author (SNP), who screened the titles and/or abstracts of retrieved studies, initially conducted study selection. Subsequently, two authors screened the full texts of eligible studies independently. Differences between the two authors were settled by discussion and agreement between them. To assess the level of evidence, the Oxford Centre for Evidence Based Medicine table (OCEBM Levels of Evidence Working Group, 'The Oxford Levels of Evidence 2') and the scoring from the National Agency for Accreditation and Assessment in Health (ANAES) was assigned to each study.

Data collection process and data items

This systematic review aimed to locate and synthesize the quantitative data from the research literature available in January 2021 about oral LyP. Data extraction was performed independently by the same two review authors and has been listed in a predefined data analysis table that included: authors, year of publication, patients' age and gender location, clinical aspect, histopathological type, treatment used and outcomes (Tab. III).

Risk of bias

To avoid dependencies, we made sure that the samples of included studies were independent, *i.e.* that there was no overlap between clinical cases presented [21,22]. As these were only clinical case reports, this meta-analysis did not require a headcount or analysis of the distributions' degree of variation.

This study presents a publication bias because only cases validated by oral pathology are published. In addition, the clinical and histological descriptions depend on the authors and practitioners.

Results

Studies selection

The search process of our systematic review is presented in the PRISMA flow chart (Fig. 1). Through these searches, as of the latest date of January 2021, 56 references were identified (35 results on Pubmed, 21 on Google Scholar, and 10 on scopus being only duplicates of articles previously found on the 2 other databases), 2 additional articles were selected from the bibliographic references of the articles selected by this search. Articles were selected first by title ($n = 33$) and then by reading the abstract and methodology to rule out articles that were less relevant and did not answer the question. We have selected 29 papers for full read and 13 of them were excluded because of the inclusion and non-inclusion criteria. Thus 16 references were included in our study from these two databases (Tab. II).

Study characteristics

All these articles correspond to grade C of the recommendations and providing an OCEBM score of 4 representing a low level of scientific proof. We therefore note that no high-level evidence has been published to date on this subject.

The included studies characteristics are shown in Table III. We have finally included 16 references in our study, allowing to report 28 clinical cases of oral LyP. The maximum patients sample number was $n = 5$ in a clinical case series.

Clinical aspects and location

Both genders are affected. There is a female predominance: women represent 64% of oral LyP cases (Fig. 2A) with a sex ratio F: M of 1.8: 1, and patients are between 19 and 85 years old (average: 50 years). There is a higher number of cases between 30 and 40 years old (32% of cases) which mainly concerns women (7 women *i.e.* 25% of cases against 2 men), and another peak between 60 and 70 years (25% of cases) with an almost equal sexes repartition with 4 women and 3 men (Fig. 2B).

The clinical appearance of oral LyP lesions is variable: "ulceration" for 34%, "ulcerated red papule" for 10%, or an "inflammatory nodular lesion with an ulcerated center" for 56% (Fig. 3A). Oral lesions can be multiple and therefore affect several sites at the same time. For 28 patients, 37 oral mucosal sites were affected. The lingual location is the most frequent, with 17 out of 28 cases (*i.e.* 61% of cases), mainly on the tongue's dorsal surface. Labial involvement is also observed in 12 patients (43%), from the lip commissure to the mucosal side of the lips. The cheek (3 cases; 11%) may also be concerned. The soft palate (1 case, *i.e.* 3.5%) and maxillary tuberosity (1 case; *i.e.* 3.5%) are more rarely affected (Fig. 3B). While some articles accurately described the site of oral lesions,

Table III. Data collected on the 28 clinical cases reported in the literature.

Author	Date	N°	Sex	Age	Oral site	Type	Therapeutic	Relapse
Kato and al.	1998	1	H	34	Tongue	B	CT + IFN α -2a	Yes
Sciubba and al.	2000	2	F	60	Tongue	NP	No treatment	Yes
Chimenti et al.	2001	3	F	38	Corner of the Lip	A	No treatment	No after 2 years
Pujol and al.	2003	4	F	52	Corner of the Lip and tongue	NP	MTX + corticosteroids	Un
		5	H	33	Tongue	NP	MTX	Yes
Serra-Guillén and al.	2007	6	H	67	Tongue	NP	Corticosteroids	Yes
Agarwal and al.	2008	7	F	46	Tongue	NP	No treatment	Yes
		8	F	36	Cheek	NP	No treatment	Yes
Allabert and al.	2008	9	F	37	Lip	C	No treatment	No after 14 month
		10	F	71	Lip and tongue	C	Corticosteroids	Yes
		11	F	38	Lip and tongue	A	Corticosteroids	Yes
		12	H	66	Lip	A	MTX	Yes
Fernandez-de-Misa and al.	2009	13	H	72	Tongue	NP	No treatment	Yes
Saggini and al.	2010	14	F	19	Tongue	D	No treatment	No after 3 years
Kempf and al.	2013	15	H	74	Oral mlucosa	E	Corticosteroids	Yes
		16	H	62	Lip	E	Surgery	Yes
		17	F	66	Lip and tongue	E	No treatment	Un
Booken and al.	2013	18	H	85	Tongue and oral mucosa	A	No treatment	Yes
Benslama and al.	2015	19	F	63	Tuberosity	A	No treatment	Un
		20	F	32	Cheek	A	No treatment	Un
Schwartz and al.	2017	21	H	42	Tongue	C	No treatment	Yes
		22	F	71	Lip and tongue	C	Corticosteroids	Yes
		23	F	34	Tongue and cheek	C	Chemotherapy	Yes
		24	F	54	Tongue	C	No treatment	Yes
		25	F	62	Lip	C	No treatment	Yes
Bresztajn et al.	2019	26	F	39	Tongue and palate	A	No treatment	Yes
Machan and al.	2020	27	H	21	Corner of the lip	A	MTX + corticosteroids	Yes
Narahara and al.	2021	28	F	25	Lip	A	Corticosteroids	No after 10 month

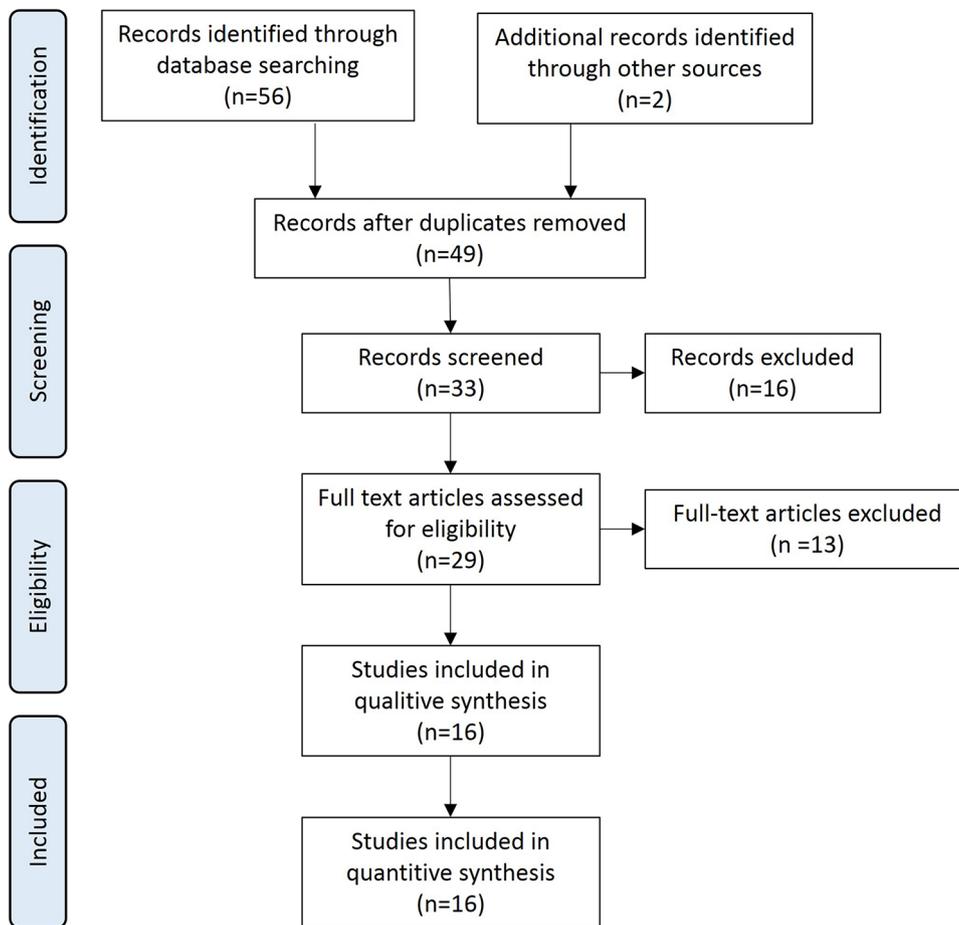


Fig. 1. Search process.

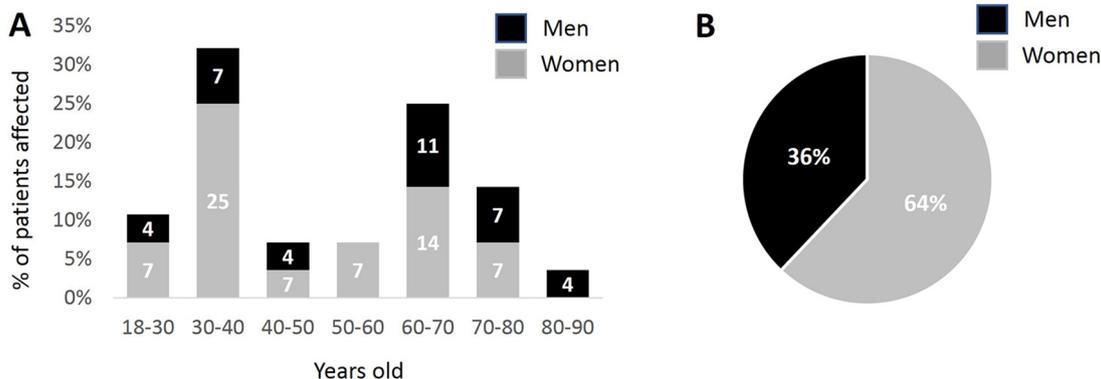


Fig. 2. Epidemiological aspect of oral LyP cases reported in the literature according to sex and age groups.

others used general terms such as “oral mucosa” or “oral cavity”. Simultaneously with the occurrence of lesions of the oral cavity, vulvar genital location of LyP is observed in 2 cases (*i.e.* 7%), and damage to the nasal mucosa in one case.

Histological sub types

Two histological types of LyP are more frequently found, which are types A (9 cases, 32%) and C (7 cases, 24%). There are 3 cases (11%) of type E, 1 case of type B and 1 case of type D. The histological

type is not specified for the last 7 cases (25%) (Fig. 3C). In 5 patients (cases n° 3, 21–24), or 18% of cases, the histopathological results were initially interpreted as high-grade lymphoma.

In the series of 5 cases of oral LyP reported by Schwartz and al. in 2017 [31], before recognizing the diagnosis of type C LyP, the oral lesions biopsied from 4 patients, *i.e.* 80% of the cases in this series (14% of all cases) were wrongly identified as aggressive intraoral peripheral T cell lymphoma. Further analysis, together with spontaneous regression and recurrence of lesions, led to the correct diagnosis of oral LyP.

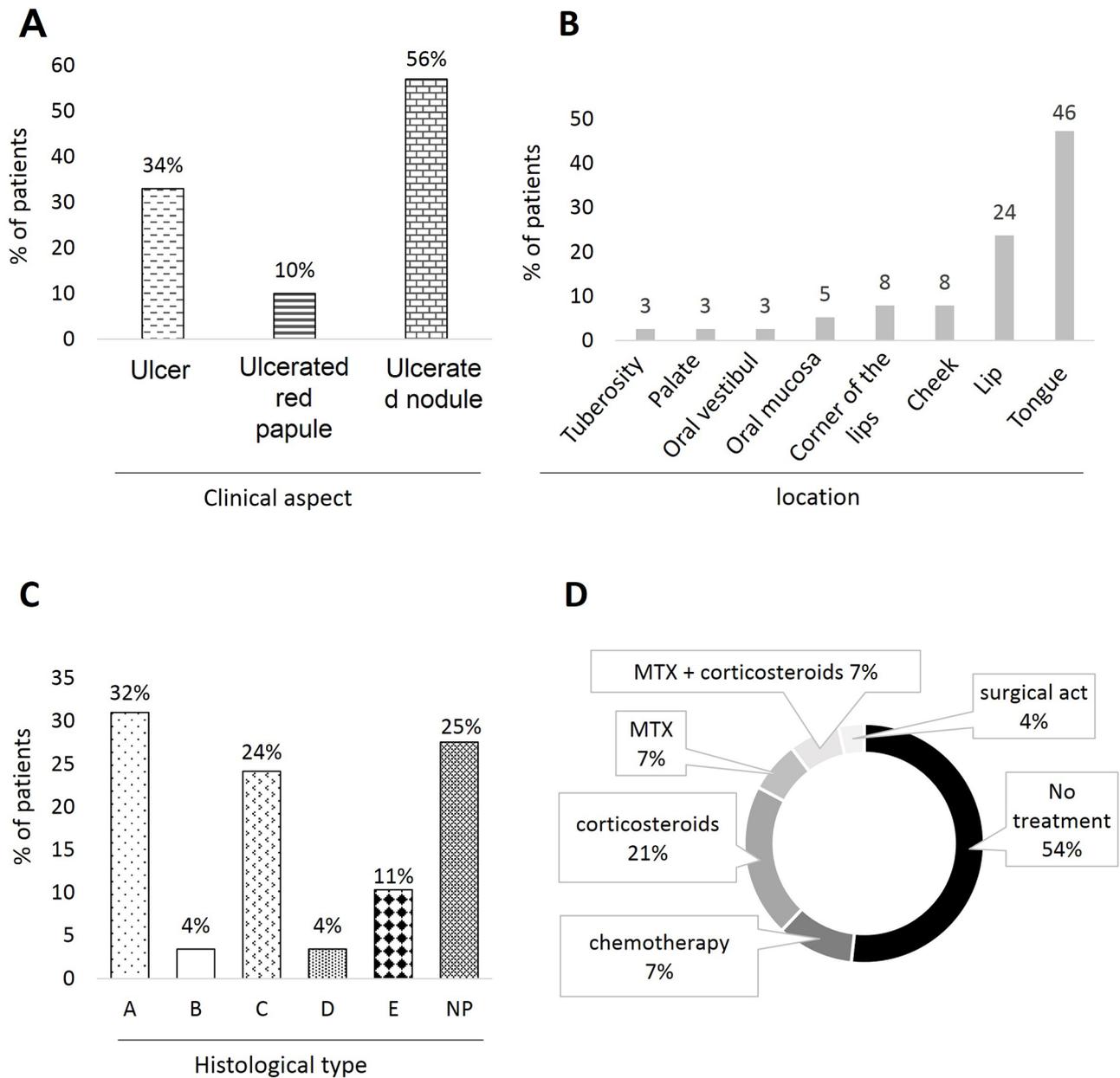


Fig. 3. Clinical and histological characteristics of oral LyP cases reported in the literature. (A) lesion type; (B) oral site concerned; (C) histological sub-type; (D) therapeutic used.

Certain lesions were not listed in these studies because biopsied late, their histological appearance did not allow a diagnosis of LyP to be concluded.

Therapeutic

For 15 cases (54%), no treatment was initiated, and the regression of oral LyP lesions was observed within a period ranging from 15 days to 8 weeks (average = 33 days). Two cases (7%) were treated with chemotherapy due to a misdiagnosis of aggressive lymphoma, 4 patients received methotrexate, with topical corticosteroid for 2 of them, 6 patients (21%) were

treated with corticosteroid therapy alone and in one patient, the lip lesion was surgically removed (Fig. 3D). In all patients who received drug treatment (12 cases, 43%), complete healing of the lesions was observed. If for 4 of them the lesions regression time is not specified, for the 9 other clinical cases (i.e. 75% of cases treated), lesions regression is noted in a maximum of 4 weeks (average = 20 days).

In our study, we can observe 2 groups of patients with a different clinical aspect. In the first group (12 cases, i.e. 43% of cases) the patients are asymptomatic with isolated lesions associated with not or few and spaced recurrences; in the second group (12 cases or 43% of cases) patients present

chronical lesions in the form of flare-ups. Patients with recurrent lesions received drug treatment in 75% of cases, while patients with isolated mucosal manifestations that had little recurrence did not receive treatment in 75% of cases.

Following and evolution

The different treatments, (chemotherapy, radiotherapy, corticosteroids, or surgical excision), did not prevent skin and/or mucosal membrane recurrences in any cases. During the weeks, months or years that followed, in the 13 cases treated, (for 1 of them follow-up is not detailed), 11 patients (*i.e.* 85% of the treated cases) experienced recurrent skin and/or mucous membrane lesions. Those recurrences are therefore observed in the majority of cases (20 out of 28 cases, *i.e.* 71% of cases). Concerning patients treated with methotrexate, two of them (cases n°5 and 12) were reported to have skin recurrences at each attempt to reduce the dosage (<5 g/week for case n°5, <7.5 g/week for case n°12).

Among the 28 cases, only one was associated with malignant lymphoma (case n° 24). In fact, 11 years after the initial presentation of mucosal LyP type C, erythematous plaques located at the abdomen, back and buttocks level were diagnosed as mycosis fungoides.

Discussion

The literature contains few references about LyP's oral manifestations with low-quality studies, retrospective, non-randomized case control series with variable outcomes. The first case of oral LyP was described in 1997, and since then only 27 other cases have been reported in literature. Therefore, our review focused on an adult population of 28 patients with oral LyP.

Publication bias

There is publication bias in this study because it has been shown that studies with positive and significant results are more likely to be submitted and published than studies with negative or no results [37–40]. In fact, concerning our point, in accordance with the 2016 WHO classifications, only oral LyP whose histopathological analysis enabled their characterization are published under this term. It is therefore possible that cases of oral LyP that have not been biopsied or without LyPs' immunohistochemical specific staining will not be reported. However, this lack of staining may be due to poor storage or poor packaging of the sample, or to a variation in the date of sampling of the lesions in relation to the date of the first symptoms.

Oral LyP differs from cutaneous LyP

The results of our literature review on oral LyP were compared with known data on skin localization LyP (Tab. IV). LyP affects both sexes with a female predominance for oral LyP.

There is a difference of age (mean and median) at diagnosis according to sex with a higher incidence in young women between 30 and 40 years, and in both gender between 60 and 70 years for oral LyP while the average age of cutaneous LyP is 45 years with a single peak incidence between 40 and 50 years.

Like oral LyP, cutaneous lesions tend to resolve spontaneously within 3 to 8 weeks and the predominant histological types identified are type A followed by type C. The histologic differences are in B and E types: E type is often found in oral lesions and no in cutaneous, while is the inverse for the B type.

Oral type A LyP: a false majority?

Generally, for cutaneous and oral LyP, type A is the most frequent with 80% of cases. However, we have a lot of missing data: for 28% of cases, the histological type is not specified, which is a significant bias in our analysis. This lack of information may also be due to recent arrival of the classification which recognizes 5 distinct histological types. In fact, the articles without histological type were produced at dates prior to the new classification. While the 2005 classification describes types A, B and C, it was in 2016 that it recognized 5 histological types. Thus, knowledge of the histopathological aspects of LyP was not as clearly conceptualized as it is today, leading in our study to cases of oral LyP whose typing are not clearly explicit, or are badly typed with possibly an overestimation of histological type A. The recently described histological type D and E will probably be more often represented than before. In addition, many cases of oral LyP are not biopsied, resolving spontaneously, sometimes just in 3 weeks.

However, until now, the therapeutic attitude and the medical follow-up do not depend on the histological type. This may be due to the fact that only small patient samples have been analyzed so far. More in-depth studies may be able to highlight differences in clinical course or therapeutic response.

Oral LyP are progressive lesions

The cutaneous involvement of LyP is clinically staged with papular and nodular lesions of small size beginning erythematous, which progress to an ulcerated phase then crusty or even necrotic afterwards, ending in a scarring stage [41]. For the oral lesion, the clinical course is often not described and/or little iconographed. The clinical appearance of an ulcerated nodule is the one most often found in the oral cavity, but some authors have also described an ulcerated papule or an ulcer with infiltrated edges. Therefore, this diversity of oral lesions is perhaps just only one pathology at different stages of development. Moura and al. recognized four different stages of LyP: from an ulcer or erythematous ulcerated papule to a nodule stage, following by a necrotic and a scarring stage. It's the same consideration for Histological aspects and its clinical correspondence. The existence of these clinical stages could explain the histopathological differences that exist in some

Table IV. Synthesis and comparison of clinical and histological data of mucous LyP versus cutaneous LyP.

	Cutaneous LyP	Oral LyP
Sex	Men > Women (1,4:1)	Women > Men (1,8: 1)
Age	Average : 45 yo (4-88 yo); incidence peaking : 40-50 ans	Average : 50 ans (19-85 ans) ; Double incidence peaking: - 30-40 yo for women - 60-70 yo for both sex
Location	Peripheral limbs > trunk > Head and neck	Tongue > Lip
Type of lésions	Papules (68%) > Papules et nodules (22%) > Nodules (7%) > Plates (3%)	Ulcerated nodule (55%) > Ulcer (34%) > Ulcerated papule (10%)
Number of lesions	<12 lésions (50%), Between 12 and 50 lesions (27%), >50 lesions (22%)	Unique lesion unique > multiple lesions
Histological Types	A (47-82%) > C (7-22%) > B (4-17%) > D (≈8%) > E (≈1%)	A (43%) > C (33%) > E (14%) > D-B (5%)
Evolution	Spontaneous regression between 3 and 8 weeks	54% of cases: spontaneous regression in 15 days to 8 weeks
Treatment	Localized Ply: monitoring, topical corticosteroid therapy, phototherapy Disseminated Ply: monitoring, Corticosteroid therapy, Phototherapy, MTX, Systemic retinoids	No treatment > Topic corticosteroid > MTX > Surgery
Follow	Relapse: 40% to 78% after active first-line treatment	71% of relapses occurring on the skin and / or mucous membranes
Lymphoid pathology associated	15.5% to 52%: associated malignant lymphoma before, after or concomitant with Ply	1 case of lymphoid pathology associated with oral Ply-C 11 years

cases. Indeed, it could be conceivable that only the beginner LyP present the histopathological characteristics of LyP while the lesions taken later would present necrotic or scarring histological characteristics (with abundant presence of neutrophils and decrease in lymphocytic infiltrates).

What about treatment?

In our review of the literature, the management of oral LyP lesions has mainly been with no treatment, but topical steroids (35%), methotrexate (20%) and phototherapy (14%) are still commonly prescribed in first-line treatments [36]. The initiation of drug treatment with corticosteroid therapy and/or MTX seems to accelerate the lesions regression, since complete healing is obtained in a maximum of 4 weeks. The therapeutic choice here seems to be partly guided by the difference in the disease's clinical course. Allabert *et al.* in 2008 [2] maintains that the recurrences of LyP lesions are more spaced with corticosteroid therapy (cases n° 10 and 11) and the other authors who have started treatment with MTX say that, at sufficient dosage, a more rapid regression of the lesions with an improvement in frequency is obtained. Regarding treatment with chemotherapy, it has been prescribed in case of erroneous diagnosis. It seems consistent, in view of its predictable toxicity, to avoid it for oral LyP.

With or without treatment, recurrences are frequent. In our study, half of the cases presented relatively few and widely spaced recurrences of isolated lesions while the other half had a chronic course with the regular appearance and disappearance of numerous oral lesions. The potential side effects, long-term complications of active treatment must be weighed against the prognosis of the disease before choosing a treatment strategy.

About associated lymphomas

The prevalence of lymphomas associated with LyP reported in the literature varies widely. Reports indicate that between 15.5% [18] and 52% [7] of patients are affected, with some people developing several lymphomas. The most common secondary lymphoma associated with LyP is fungoid mycosis (MF) (61% of cases), followed by anaplastic cutaneous large cell lymphoma (PC-ALCL) (26% of cases) [7]. Other secondary lymphomas associated with LyP include Hodgkin's lymphoma, myeloid and B cell leukemias. Note, however, that the most common secondary lymphomas associated with LyP are also differential diagnoses of it. Some factors have been reported as unfavorable prognostic indicators for the development of lymphomas associated with LyP such as older age, histological types B and C [7], LyP lesions localized on the head, more frequent high recurrence [42], the detection of a T cell clone in LyP lesions [35,43] and the expression of fascin by large CD30+ cells [44].

But, regarding oral LyP, our study revealed only one case of associated lymphoma, developed 11 years after the presence of oral LyP. Concerning cutaneous LyP, no treatments has been shown to be significantly effective in preventing LyP associated

lymphomas [7]. Due to the risk of a second lymphoid neoplasm, patients with LyP should be monitored throughout their lives so that potentially fatal lymphomas can be detected and treated early [17].

Conclusion

Our literature review has shown that the epidemiological aspects between oral and cutaneous LyP are not the same. Isolated cutaneous damage more affects men and older patients compared to oral locations which seem to mainly affect patients who are women between 30 and 40 years old. Moreover, the histological types found do not seem to be expressed in the same proportions, depending on the affected site. In fact, 80% of skin lesions are classified as type A while those mucous membranes are of type A or C each representing 1/3 of patients. Finally, whereas cutaneous LyP may be associated with an increased risk of developing systemic lymphomas or lymphoproliferative disorders, it does not appear to be clearly the case for oral locations. However, monitoring the development of a "lymphoma" does indeed seem to advise patients with oral LyP pathology, as well as regular oral monitoring. It could be interesting to confirm these data with a larger study, allowing the pooling of a larger number of clinical cases to statistically highlight the histological and clinical differences of oral LyP with cutaneous ones.

Conflict of interest

The authors declare that there is no conflict of interest.

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Ethical approval

Ethical approval was not required.

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