CD30(+)-lymphoproliferative disorders. Report of a 26-case-series and literature review

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ABSTRACT

Background. CD30(+)-lymphoproliferative disorders (CD30(+)-LPD) constitute a heterogeneous group of neoplasms with different therapeutic approaches and outcomes. They can be primary cutaneous, including lymphomatoid papulosis (LyP), primary cutaneous anaplastic large cell lymphoma (PC-ALCL) and borderline cases, which have good prognoses. A second group is secondary to another lymphoma, such as anaplastic large cell lymphoma (ALCL) occurring after mycosis fungoides (MF-T), Sezary's syndrome, LyP, and Hodgkin's disease. Another different group of disorders showing CD30(+) expression, not belonging to the groups above mentioned, must be kept in mind in order to perform a differential diagnosis, including rare primary lymphomas, such as adult T-cell leukemia/lymphoma, or angiocentric cutaneous T-cell lymphoma of childhood (hydroa-like lymphoma), and secondary skin involvement due to systemic ALCL. As differential diagnosis among them is virtually impossible if based on histological features alone, data on the clinical presentation and evolution are crucial to establish a correct diagnosis.

Objectives. The aim of this study is to review the clinicopathologic characteristics and to evaluate the prognosis of patients with confirmed CD30(+)-LPD evaluated and treated at the Department of Dermatology, Hospital General de Agudos "Dr. Cosme Argerich", and to review the literature.

Methods. We performed a retrospective analysis of the database from our Department. All patients meeting the clinicopathologic criteria of CD30(+)-LPD from November 1995 to September 2010 were included. A review of the clinical data was performed to assess the following parameters: diagnosis, sex, age at diagnosis, stage of disease, evolution time, response to treatment and survival.

Results. A total of 26 patients with diagnosis of CD30+ LPD were included. Nineteen (73%) were primary CD30(+)-LPD: 11 (58%) were LyP (4 associated to MF), 3 (16 %) were borderline cases, and 5 (26%) were PC-ALCL. Mean age at diagnosis was 56 years (range 27-84 years), 13 (68%) were male. Mean follow-up time was 52 months. Among patients who received systemic treatment (n=19), remission was considered complete in 7 (37%), partial in 9 (47%) patients, and 3/19 patients showed spontaneous resolution. Two patients died (10%), both belonging to the PC-ALCL group. Seven patients (27%) were secondary CD30(+)-LPD, all of them related to MF-T, while 6 (86%) were male. Mean age at transformation was 57 years, and mean follow-up time was 71 months. All patients required polychemotherapy. Death occurred in 4 patients (57%), and in 3 patients delay between initial diagnosis to transformation was less than 2 years. Overall survival between both groups was statistically significant (p=0.028).

Conclusions. Primary cutaneous CD30(+)-LPD have good prognosis and spontaneous resolution has been observed in some patients. Even though in our report PC-ALCL had an unusually high mortality rate (40%), we have reasons to believe those deaths were not directly related to the lymphomas. Contrary to what is observed in primary CD30(+)-LPD, secondary disorders show a more aggressive course with much lower survival rates. In our series mortality rate was higher than 50%, and every patient required systemic polychemotherapy (Dermatol. Argent., 2011, 17(4): 284-293).

Keywords

lymphomas, CD30+, lymphomatoid papulosis, primary cutaneous anaplastic large cell lymphoma, borderline, transformed mycosis fungoides.

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Introduction

The CD30+-lymphoproliferative syndromes (LPS) spectrum is the second most frequent type of primary cutaneous T-cell lymphomas (CTCL) and about 25-30% of diagnosed cases after mycosis fungoides (MF)[1-2].
It constitutes a heterogeneous group of entities consisting of primary and secondary conditions. Among the former are the primary cutaneous CD 30+ anaplastic large cell lymphoma (PC-ALCL), lymphomatoid papulosis (LyP) and borderline cases. All these entities have overlapping clinical and histological features, which in many cases are difficult to differentiate, and are at present considered to be within the spectrum of the same disease. They generally have a benign course, with low mortality rates and recurrent clinical conditions with spontaneous regression of the lesions in some cases[3].
Unlike primary conditions, there are entities in which CD30+ large cells are also present but evolve much more aggressively. They are transformations into CD30+ anaplastic large cell lymphoma (ALCL) from a previous lymphoma such as MF, LyP, Sézary's syndrome (SS) and Hodgkin's disease (HD). They are known as secondary ALCL. Besides, the CD30+ large cell infiltrates may be the consequence of a manifestation of a systemic primary ALCL of nodal origin with secondary cutaneous involvement. The differentiation between both entities is important because they have different biological behaviors, which implies a more aggressive therapeutic approach for the latter group of entities than for the primary cutaneous conditions.
It is also important to take into account that the CD30+ expression may be present in many other types of lymphomas, such as adult T-cell leukemia/lymphoma, pagetoid reticulosis, angiocentric cutaneous T-cell lymphoma of childhood (hydroa-like lymphoma) and Hodgkin's lymphoma[4]. It is evident that it is virtually impossible to differentiate these entities only on the basis of histological findings. Therefore, the clinical presentation data and even the evolution at times are crucial to establish a final diagnosis.
The objective of this paper is to describe the clinical and histological features, the therapeutic response and evolution of all the CD30+ LPS evaluated at our hospital throughout a period of 15 years.

Materials and methods

A retrospective study was carried out of all the patients attended to at the Dermatology Department at Hospital General de Agudos Dr Cosme Argerich between November 1995 and September 2010. The lymphomas were classified (WHO-EORTC) and re-staged (ISCL-EORTC) according to the latest international recommendations for cutaneous lymphomas[5-7]. The MF transformation (MF-T) was defined according to previously published criteria[8].
In all patients the following data was collected: age, sex, disease evolution time, therapeutic response, survival and follow-up time. We considered: complete response (CP) as the disappearance of all clinical and laboratory signs and symptoms of active disease for at least 12 weeks; partial response (PR) as the reduction in the size of lesions of over 25% for at least 12 weeks; progressive disease (PD) as the objectifiable increase in size of any of the measurable lesions of over 25% or the appearance of new lesions or extracutaneous disease.
All the patients were examined at intervals of 3 to 6 months during treatment, once a year if they were disease free or at any time when they evidenced changes. Blood count with smears, renal and liver function tests were carried out in all patients both at baseline and at each stage change. Besides, LDH and beta 2 microglobulin tests and thorax, abdomen and pelvis tomographies with and without contrast were performed on patients with PC-ALCL and secondary CD30+ LPS in search of extracutaneous involvement. When adenopathies were found

ABBREVIATIONS

LPS: lymphoproliferative syndromes
CTCL: primary cutaneous T-cell lymphomas
CD30+ LPS-PC: CD30+ primary cutaneous lymphoproliferative syndromes
CD30+ LPS-SC: CD30+ secondary cutaneous lymphoproliferative syndromes
WHO: World Health Organization
EORTC: European Organization for Research and Treatment of Cancer
ISCL: International Society of Cutaneous Lymphomas
MF: mycosis fungoides
PC-ALCL: primary cutaneous CD30+ anaplastic large cell lymphoma
ALCL: CD30+ anaplastic large cell lymphoma
LyP: lymphomatoid papulosis
HD: Hodgkin's disease
SS: Sézary's syndrome
MF-T: mycosis fungoides transformation
CR: complete response
PR: partial response
PD: progressive disease
PUVA: Psoralen Ultra-Violet A Phototherapy
IFN: interferon
TNF: tumoral necrosis factor
LDH: lactic dehydrogenase

during the physical examination, a surgical biopsy followed by histopathological and immunohistochemical study was performed. Bone marrow biopsies were performed on all the patients presenting secondary CD30+ conditions. On the patients with PC-ALCL, bone marrow biopsies were performed in some initial cases, but this practice was challenged according to the new international recommendations and it is no longer a routine practice for low grade lymphomas at our department[5-7,9]. The histopathological studies were carried out on 10% formalin-fixed tissue samples with hematoxilin and eosin and conventional immunohistochemistry techniques using dextran polymer as the detection system. The antibodies used were anti CD3 (Polyclonal Dako®), CD4, CD8, CD20 and CD30 (Monoclonal Leica® ex-Novocastra®) in all the cases. The results were expressed as proportions. To compare the overall survival between LPS-PC and LPS-SC the time elapsed between diagnosis and death dates was calculated through Kaplan-Meier's technique.

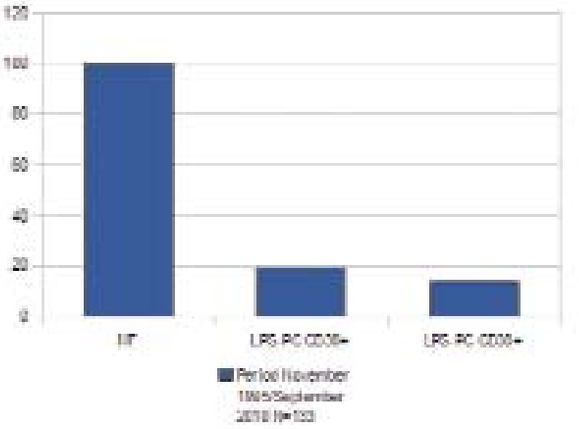
Results

Between November 1995 and September 2010, 138 primary cutaneous lymphoma cases were evaluated at our department. The majority of these cases (133) were diagnosed with CTCL, of which 100 were MF and 19 were primary cutaneous CD30+ LPS. Within the MF group, 7 patients suffered a transformation into CD30+ anaplastic lymphoma and were considered secondary cutaneous CD30+ LPS, making up the 26-patient sample with CD30+ LPS (Graph 1).

Within the primary cutaneous CD30+ LPS group (CD30+ LPS-PC), we found 11 LyP, 5 PC-ALCL and 3 borderline cases (Graph 2). Mean age of this group was 56 years and the sex distribution was 13:6 male:female. The overall survival of the group was 89%, with a mean follow-up time of 52 months.

Among the PC-ALCL patients, the mean age at onset of the disease was 63 years (range 33-84), with a 4:1 male:female ratio. Mean follow-up time was 72 months. Staging at onset of the disease was: T1a, T1b, T2a and T2c in 2 cases (Table 1). Three out of 5 patients received interferon (IFN) and two received polychemotherapy. Treatment response was: CR I 2/5 and PD in 2/5. One case self-resolved. The mortality rate was 40% but both deaths were classified as unrelated to the disease even if in both cases the patients presented PR with further PD and required polychemotherapy. One of the patients suffered from severe heart disease and death occurred due to an acute myocardial infarction and the other patient was an elderly man whose cause of death was generalized deterioration due to old age. The mortality rate in this group

GRAPH 1: Relative CTCL frequency



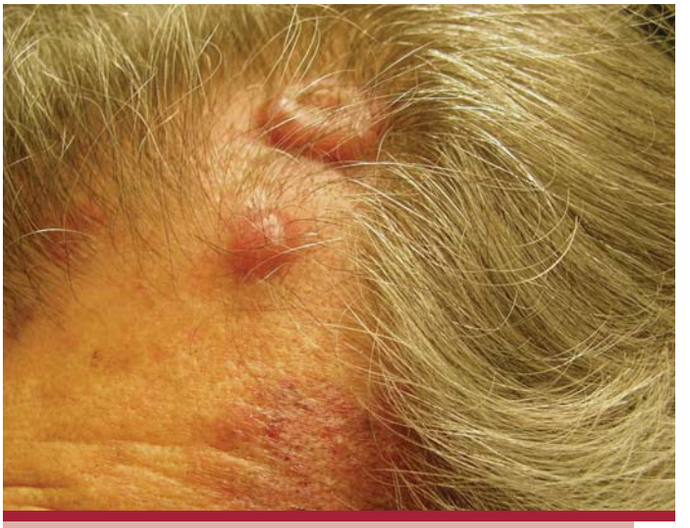


Photo 1: PC-ALCL - Erythematous tumoral lesions on forehead area.

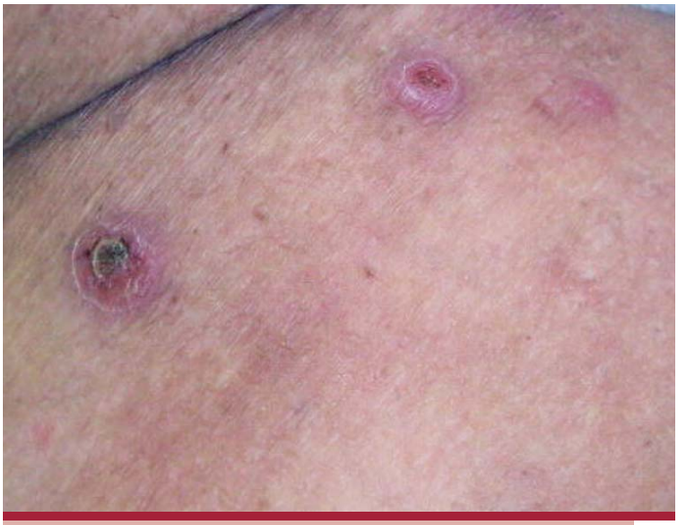


Photo 2: LyP - Multiple ulcerated papules on inguinal region.

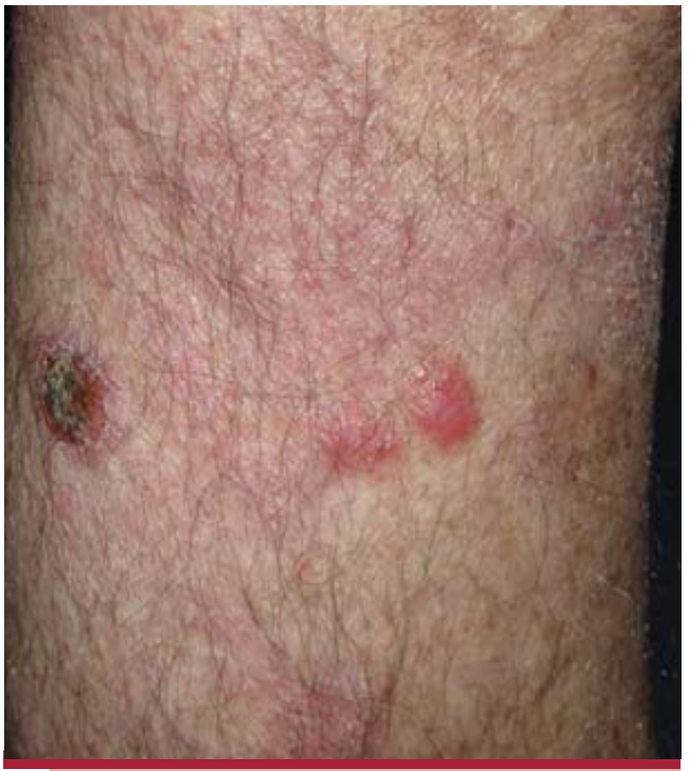


Photo 3: MF + LyP - Erythematous papules adjacent to erythematosquamous macules.

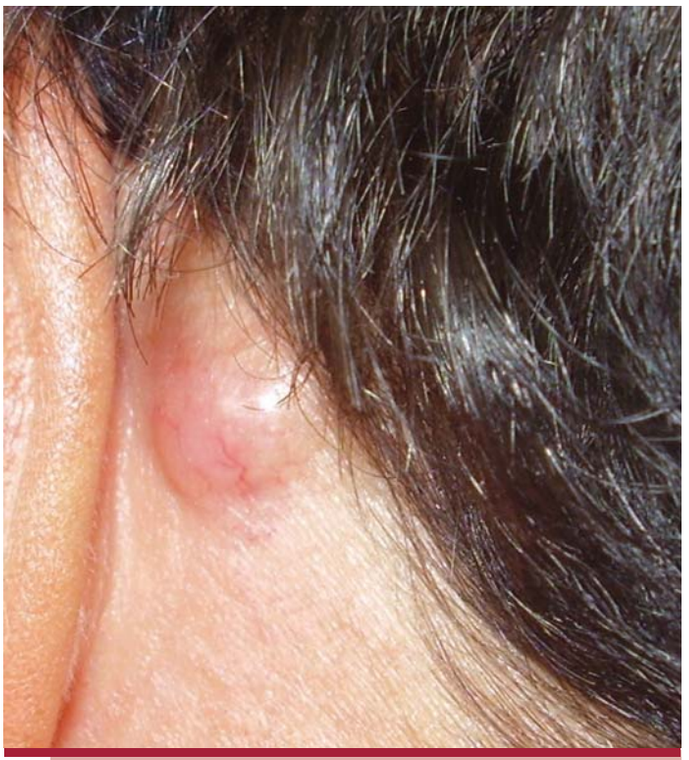


Photo 4: Borderline - Slightly erythematous tumoral lesion with telangiectasias on back of left ear.

corresponds to 100% of cases with fatal outcome in this CD30+ LPS-PC.

In the LyP group (11/19 patients), the mean age at the onset of the disease was 56 years and there was a male/female ratio of 8:3. Four/11 patients presented LyP preceded by MF, with a mean time of 12 months between both diagnoses. All the patients were male and the mean age at the onset of the disease was 64 years (55-75 years). All four cases presented stage IB MF and stage T3b LyP. Histopathology in all of them corresponded to LyP type A. All patients received PUVA combined with alpha IFN and the response was CR in two patients and PR in the other two. Survival rate of this group was 100%. In 7/11 patients with LyP not associated to MF the male:female ratio was 4:3 and the onset mean age was 49 years. Histopathology showed: 2 type A cases, 2 type B and 3 type C. The stages at the onset of disease were: T3b in 3 patients, T2a in 2, T2b and T2c in the rest of them. As regards treatment, two patients presented self-remission and all the others were treated with PUVA. Two CR and three PR were observed of which one patient also received systemic corticosteroids and two, alpha INF. Survival rate of this group was 100%.

The cases classified as CD30+ LPS-PC borderline (3/19) presented a mean age of 48 years (range 45-52) at diagnosis. Two cases were female and one male. They were staged at T1b, T2b and T3b. Mean follow up was 30 months. One patient received IFN monotherapy and showed CR. The other two patients presented PR and required PUVA associated to alpha IFN or metotrexato. In one of them, as CP was not achieved , polychemotherapy was indicated with PR. This group's survival was 100%.

In the secondary CD30+ LPS group, (CD30+ LPS-SC), only MF-T cases were observed. 7 patients with a 6:1 male:female ratio and a mean follow-up of 71 months were evaluated. Mean age at transformation diagnosis was 57 years (range 44-70), with a mean delay of 48 months between diagnosis and transformation. Staging at the time of MF diagnosis was: 4/7 IIB, 2 stage II and 1 IB, and they all presented tumoral disease at transformation. Four patients presented classic MF, 2 follicular MF and 1 bullous MF. One patient showed CR after treatment with radiotherapy, IFN and polychemotherapy. A case of PR was observed after polychemotherapy treatment. Five/7 patients received treatment with polychemotherapy due to PD after treatment with radiotherapy, PUVA or bexarotene and four died in spite of the treatment. In these four patients, mean age at the onset of transformation was 53 years, in 3/4 patients the stage was IIB and 1 IVA2, and the mean time between MF diagnosis and trasformation was 22 months. The MF-T group's mortality rate was 57%. Survival in this group against the PC-LPS was significantly lower (a=0,028) (Graph 3) (Table 2).

Discussion

The CD30+ LPS-PC make up a well defined group of lymphomas which share the CD30+ expression on the surface of the infiltrating large cells. This set of diseases represents the second most frequent type of primary cutaneous lymphomas, only outnumbered by MF[2,4-5]. However, the spectrum of diseases which may express CD30 is wide (Table 3) and their clinical manifestations and prognoses may be quite different, which has therapeutic implications. To be able to classify and analyze the present series of cases adequately, we have decided to divide them into primary and secondary conditions.

The CD30+ LPS-PC represent approximately 25 to 30% of cutaneous lymphomas5. It is a group of rare diseases whose diagnosis is difficult and requires a thorough clinico-histological correlation. Even so, diagnosis is many times confirmed according to the course of the disease, which frequently presents spontaneous resolution of the lesions and in some cases recurrence[10]. At the most benign end of this spectrum of diseases is LyP and at the opposite end is PC-ALCL.

All these conditions share the CD30+ expression, a transmembrane glycoprotein belonging to the TNF receptors family. Since its discovery, the CD30+ expression has been considered a reliable marker to identify this group of lymphomas due to the fact that it is absent in normal tissue except in some isolated lymphoblasts located around the B-cells follicles. It is highly expressed in HD and Reed-Sternberg cells and fosters cell activation, proliferation, differentiation and death phenomena[11].

PC-ALCL represent approximately 9% of cutaneous lymphomas. They affect mainly adults in their 60's and they rarely occur in children[12-13]. Clinically, they manifest as single or very few lesions grouped in a certain body area, but multifocal involvement may occur in 20% of patients (Photo 1)[14]. Up to 10% may present extracutaneous manifestations, usually with regional ganglionar involvement. They have a very good prognosis, with a survival time of 5 years in over 90% of cases and the lesions may even resolve spontaneously without any treatment[15-16]. However,. Woo et al[17] described a form in which there is extensive involvement on limbs which evolves with extracutaneous involvement, and systemic involvement has even been demonstrated in very few cases. Therefore, different studies have attempted to find predictive factors of unfavorable prognosis and molecular markers which allow a more precise differentiation between PC-ALCL and LyP and MF-T. Different markers such as TRAF1, MUM1, BCL2 and CD15 have been used but no significantly conclusive differences have been found in the expressions of these molecules in the different entities[18-19].

In our study PC-ALCL patients evidenced similar features to the ones described in other studies: mean age (63 years) and male sex predominance (4:1). 5-year survival occurred in 90% of cases, which significantly differs from the studies carried out in Europe and the United States. The only 2 patients who died evidenced severe comorbidities, were older than 70 years old, and even if the cause of death did not seem to have any direct relationship to their underlying disease, they were the only ones who presented extracutaneous progression of the disease and required treatment with systemic chemotherapy. Given the low number of cases, it is not possible to establish whether there is a random relationship, as the mortality rate of these patients and the extracutaneous progression (40% in both cases) is much higher than the one previously described, i.e.

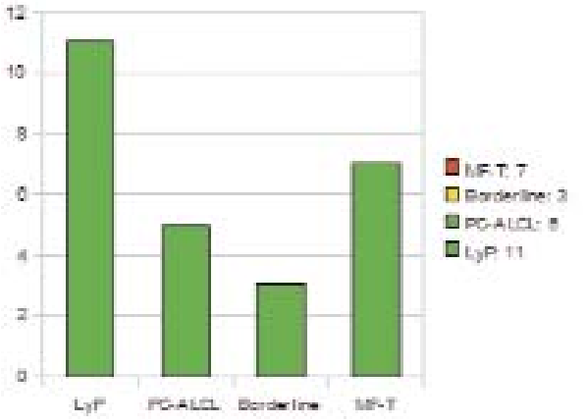
5-year survival in over 90% and extracutaneous involvement in 10% of the cases[14].

LyP is a lymphoproliferative disease first described in 1968 by Macaulay[20]. Even if it was initially considered an inflammatory disease, it is nowadays classified as a low grade cutaneous lymphoma. It is an infrequent disease (incidence: 0.1-0.2 cases/100,000 inhabitants), which affects mainly adults in their 50's, though a few occurrences in children have been described[21]. It is predominant in males with a male:female relationship of 2:1 and its course is benign in almost all cases, even if it is occasionally associated with other cutaneous or systemic lymphomas[10,22]. Clinically, it is characterized by the appearance of

TABLE 1: TNM classification for non-MF, non-SS CTLC. Kim Y. et al7.

T1	**Solitary cutaneous involvement**
	T1a: solitary lesion <5 cm diameter
	T1a: solitary lesion >5cm diameter
T2	**Regional cutaneous involvement: multiple lesions cir cumscribed to one body area or two adjoining areas**
	T2a: the whole disease circumscribed to a circular area <15cm diameter
	T2b: the whole disease circumscribed to a circular area >15cm and <30cm diameter
	T2c: the whole disease circumscribed to a circular area >30cm diameter
T3	**Generalized cutaneous involvement**
	T3a: multiple lesions involving two non-adjoining areas
	T3b: multiple lesions involving ? three areas
N0	**No clinical or pathological LG involvement**
N1	**Involvement of a peripheral lymphatic region which drains a current or previous cutaneous involvement area**
N2	**Involvement of two or more peripheral lymphatic regions or involvement of any lymphatic region which does not drain a current or previous cutaneous involvement area**
N3	**Central LG involvement**
M0	**No evidence of non-lymphatic extracutaneous disease**
M1	**Presence of non-lymphatic extracutaneous disease**

GRAPH 2: Relative frequency of CD30+ LPS



Y= number of cases
X= type of lymphomas

GRAPH 3: Kaplan-Meier Curve. Differences between survival probabilities of primary and secondary CD30+ lymphoproliferative syndromes (p=0.028)

Y= survival probability (%)
X= time (months)

Group:

_____ CD30+ LPS-PC

---------- CD30+ LPS-SC

asymptomatic papules, at times ulcerated, which frequently involve limbs and follow a self-limiting course (Photo 2). Its associations with other hematological malignancies is variable, but they have been described in 10 to 61% of cases[22]. The most frequently associated disease is MF (Photo 3), and such entities may occur simultaneously or consecutively. Some authors suggest that patients with MF which is associated to LyP should present a less aggressive course of the disease[23-24]. The evolution of LyP is benign, with spontaneous resolution between 10 and 20 years after onset and the 5-year survival rate is 100%[5]. This is the reason why it is very important to differentiate it form the other CD30+ lymphoproliferative processes to avoid unnecessarily aggressive treatments. Of three histological types called A, B and C, type A is the most frequent. Type B is similar to MF and it can even present epidermotropism and no CD 30 expression, which may render differential diagnosis between the two entities really troublesome. Type C is similar to ALCL so it is also very important to differentiate it so as to establish prognosis and treatment[25]. (Table 4)

The mean age of the 11 patients with LyP diagnosis was 56 years at the onset of the disease, like it was previously described. 36% (4/11) of the cases was associated with MF, which preceded all of them. These two groups presented no differences as regards onset age or survival. The mean follow-up time in the cases associated with MF (n=4) was 33 months and we had 2 PR and 2 CR cases. The group's survival rate was 100% and the MF, which were diagnosed to be at stage IB in all cases, did not evidence stage progression. Other studies showed a better evolution of the MF associated with LyP[23,24-26]. In the cases without other associations (7/11), the survival rate was also 100%, with a mean follow-up time of 72 months. All the patients with LyP were treated with PUVA except for the cases which evidenced spontaneous resolution (n=2).

TABLE 2: Comparative table between the four CD30+ LPS-PC and LPS-SC groups

	LPS-PC					LPS-SC	
	PC-ALCL	LyP	LyP + MF	*Borderline*		MF-T	p
N	5	7	4	3	19	7	
Mean Age (years)	63	49	63	48	56	57	
Males	4	4	4	1	13	6	
Females	1	3	0	2	6	1	
Survival (%)	60	100	100	100	89	43	0.03
Follow-up time (months)	72	72	33	30	52	71	

The cases which were associated with MF received alpha IFN as well. This analysis should allow us to confirm the benign nature of the disease, even in the cases associated with another cutaneous lymphoma in this series.

The diagnosis of CD30+ LPS-PC may be quite challenging as there is significant overlapping between the clinical and histological characteristics of LyP and PC-ALC, especially with LyP type C. The term borderline is exclusively used for the cases which cannot be classified as PC-ALCL ot LyP[27].

The three cases classified as borderline in the present series were recurrent and presented histopathologies compatible with LyP or PC-ALCL at different times in their courses. The manifestations were isolated, recurrent, at times self-resolving, not ulcerated nodules on different areas (Photo 4). The onset in one of the patients consisted in multiple lesions, ulceration and recurrences on a certain area and extension to other non-adjacent areas, for which he received polychemotherapy and relapsed three months after discontinuation. Even if it is too small a number to reach any conclusions, we consider these patients should be thoroughly monitored throughout the course of the disease and the first option should be the most conservative treatment.

MF-T is histopathologically defined by the presence of large cell which exceed 25% of lymphocyte population or forms microscopic nodules. The size of these lymphocytes is at least four times larger than normal (Photo 5). The incidence of transformation varies from one series to another but it corresponds to around 11 to 23% of MF cases[28].

MF, at its initial stages, is a chronic disease which tends to follow an indolent course and a very low 5-year mortality rate. However, the prognosis for patients who suffer large cell transformation is usually worse, with a reduced five-year survival compared to the other patients with MF. In a study carried out by Diamandidou et al[29], mean survival time since diagnosis of MF/SS in patients with transformation was 37 months, against 163 months on the total population with MF/SS. In this study, the mortality rate of MF-T was 62%.

The majority of patients suffer clinical manifestations of progression of the disease at the time of transformation (Photo 6) and the cases in which it is diagnosed first because of histological alterations are very few. While the advanced stage (T3) implies a bad prognosis, the large cell transformation worsens the course even more[30]. Many studies have been aimed at finding predicting factors of bad prognosis at the time of diagnosis of the disease. It was observed that age over 60 years old and advanced stage (over IV) identified a group of patients with a higher mortality rate[29]. Another case series also evidenced a worse course of disease in patients at advanced stage (stage II) and in patients whose transformation occurred within the first two years after MF diagnosis[31]. Regardless of these variables, this group of patients has a higher mortality rate and thus requires a more aggressive treatment. It is therefore very important to differentiate it form other entities which express CD30 and from other variants of MF which also have a significant large cell population. Such is the case of granulomatous MF, whose prognosis is better than MF-T and presents a considerable population of histiocytes. Without adequate histological evaluation, with CD30 and CD68 expression, a wrong diagnosis could be reached which would lead to unnecessary polychemotherapy treatment[31].

Within the study period, 100 patients with MF were evaluated. 7% presented large cell transformation. Mean age

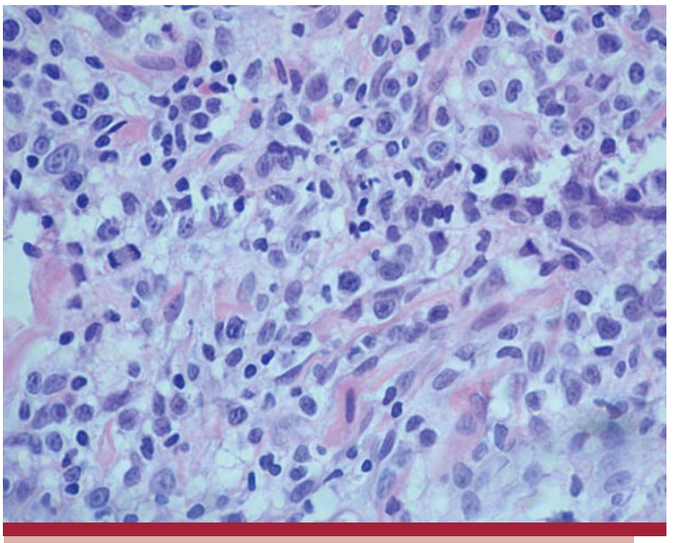


Photo 5: MF-T - Histopathology (HyE) - Dermis diffusely infiltrated by small and large lymphocytes; mitotic figures can be identified.

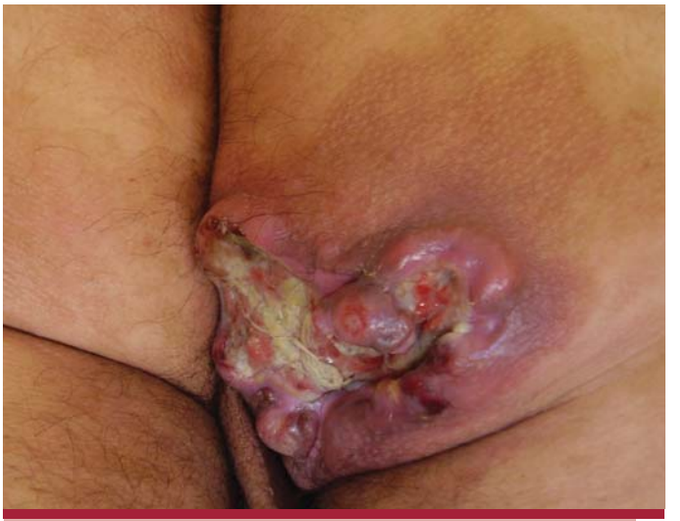


Photo 6: MF-T - Tumors with ulcerated and necrosis areas on buttock over MF erythematosquamous plaque.

TABLE 3: Lymphomas with CD30 expression. Modified by Kempf W.4
Primary cutaneous CD30+ lymphoproliferative syndromes
Lymphomatoid papulosis
Primary cutaneous anaplastic large cell lymphoma
Borderline CD30+ lymphoproliferative syndromes
Other types of cutaneous and systemic lymphomas
Mycosis fungoides/Sézary's syndrome with large cell transformation
Pagetoid reticulosis
Adult T-cell leukemia/lymphoma
Hodgkin's lymphoma
Primary systemic anaplastic large cell lymphoma
Secondary cutaneous infiltrate to primary systemic anaplastic large cell lymphoma
Childhood angiocentric T-cell cutaneous hydroa-like lymphoma
Cutaneous reactions to atypical CD30+ T-cells associated with lymphomas and leukemias

at transformation was 57 years and the time between MF diagnosis and transformation was 48 months. 6 patients were at stage IIB and one IVA2. Even if this coincides with the data given in other publications, all our patients were diagnosed by their clinical progression, so we did not observe any transformation cases at early stages of the disease. All patients received polychemotherapy, one had CR, another one PR, and out of the 5 patients who presented PD, 4 died, which represents a 57% mortality rate. The mean age at transformation diagnosis of the patients who died was 53 years, unlike previous studies, which observed a poorer course in patients over 60. The mean time between diagnosis of MF and transformation was 22 months, which does coincide with data from other case series which point out that patients presenting a rapid large cell transformation (under 24 months) followed a poorer course. However, only in one case in this group the lapse between both diseases was over 2 years (80 months). If this patient is excluded from the analysis, the mean delay between MF and transformation would be 3 months, which leads us to conclude that the mortality rate in our group of patients was associated to a very short period of time between both diseases and it is possible that these patients should receive aggressive treatment earlier.

Conclusions

To conclude, we have observed that in this series the CD30+ LPS population represents the second group of cutaneous lymphomas. Most of the diagnosed cases corresponded to CD30+ LPS-PC, which had a much less aggressive course than the secondary ones. The high mortality rate observed in the PC-ALCL group could be accidental, as they were 2 elderly patients with significant comorbidities. Given the high mortality rate in the MF-T group, it is essential to establish a correct clinicopathologic correlation, as the different conditions may bear great similarities. Age at transformation diagnosis (under 60) and the delay between MF diagnosis and transformation (under two years) characterized the MF-T group with a poorer course.

Accurate, early diagnosis of these entities is essential to make early, adequate therapeutic decisions or to avoid unnecessarily aggressive interventions.

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TABLE 4: LyP histopathological types

	Type A	Type B	Type C
Infiltrate	Superficial and deep. Perivascular and interstitial	Superficial	Deep, without or with scarce subcutaneous cell involvement
Architecture	Cuneiform	In strips	Nodular or diffuse
Number of large cells	Few	Absent or few	Over 75% and with cell atypia
Other cells in the infiltrate	Small lymphocytes, neutrophils, eosinophils	Small and medium lymphocytes with scarce epidermotropism. Less frequently neutrophils and eosinophils	Few small lymphocytes, neutrophils, eosinophils
IHQ	CD2, 3, 5, 45Ro+ CD4, CD30++ CD8- CD15, EMA-	CD30+ CD4+, CD30-/+ CD8-	CD2, 3, 5, 45Ro+ CD4, CD30++ CD8- CD15, EMA-
			Requires clinicopathologic correlation for correct diagnosis

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