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T-cell lymphoma - standard treatment: The Mexican experience

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T-cell lymphomas are uncommon malignancies that represent between 7 to 37 % of all lymphomas; and showed to close relationship with geographic presentation, because are most common in Asia and in some counties of Latin America. The information about this type of lymphomas is rare and specifically in Caribean area is null. In our country, T-cell lymphomas represent less than 10% of all malignant lymphomas, and some subtypes are no diagnosed or reported. Moreover, this information can contain bias because immunophenotyping studies are not available in all oncologic centres. Our Institution have national coverage, with about 58,700,00 around the country and have 108,150 clinics of first contact, 2126 of second level and 25 national centers that include oncologic departaments, but only an tertiary national reference center, that is the Oncology Hospital at National Medical Center. In the last 10 years, a median of 13,956 patients are diagnosed and treated every year. Malignant lymphoma represent the 5ª cause of consult, with a mean of 503 patients every year.We have data of 8210 patients, and seven hundred and twenty-two (9%) are T-cell lymphoma. Table 1 shown the different subtypes, as observed the most frequent is the natural/killer cell lymphona, nasal type; the peripheral T-cell lymphoma, unspecified, represent only the 13% of all T-cell lymphoma.

Natural killer cell lymphoma, nasal type

Table 2 shown the characteristics of this patient. Female predominance, early stage, good performance stage, no B symptoms , high levels of lactic dehidrogenase, and low- and low-intermediate clinical risk according to the International Prognostic Index (IPI) were common. Immunophenotype was performed in all cases and showed the characteristics of NK cell. $CD10^+$, $CD56^+$, $CD57^+$, cytoplasmic $CD3^+$, $CD20^-$, EBV latent membrane protein $(LMP\text{-}1)^+$ (73%).

Therapy

Initially patients were treated with conventional radiation therapy: 45 to 50 Gy in 20 sesions. Complete response (CR) was observed in 61 cases (92%), however, relapse, generally outside the radiation field, was common. Salvage therapy can obtain second relapse in some patients, but at 10 years, only 24 patients (36%) are alive free of disease. Taking in consideration that relapse ocurr outside the radiation field, suggested the presence of micro foci of tumor cells in other sites, we conduct unn pilot study to assess efficacy and toxicity of adjuvant chemotherapy, six courses of conventional CHOP, in patients that achieved CR after radiation. Forty-three patients were included, CR was observed in 41 (95%), and overall survival at 5-years was 86%, thus now we treat all patients with NK/cell lymphoma amd early stage with combined therapy. However, 15% of patients are refractory or relapse and die secondary to tumor progression, thus in 2004, we began an controlled clinical trial to assess if the use of an combined regimen that include methotrexate, etoposide(that have been suggested are more specific to T-cell lymphoma), cyclophosphamide and dexamethasone, compared to CHOP can improve outcome. Until now, we included 34 patients, but results are no mature.

Recently, has been reported that some cases of NK/cell lymphoma, nasal type, are stage III and IV, thus it will be an disseminated disease or well could be considered as distant metastases. Unfortunately, no specific infor-

Table 1. Type of T-cell lymphomas observed in an Mexican population.

	No	*%*
Nodal		
Peripheral T -cell lymphoma, unspecified	99	13
Angioimmunoblastic, T-cell lymphoma	3	< 1
Anaplastic large cell lymphoma	263	36
Extranodal		
Subcutaneous panniculitis T-cell lymphoma	3	< 1
Cutaneous, gamma-delta, T-cell lymphoma	0	
Hepato-splenic gamma-delta, T-cell lymphoma	4	< 1
Extranodal, natural killer cell lymphoma, nasal type	348	48%
Enteropathy, T-cell lymphoma	2	< 1

Table 2. Clinical and laboratory characteristics of NK/cell lymphoma, nasal type.

	No	*%*
Number	348	100
Age (years) median	43.4	
range	23-69	
Sex: male/female	155/193	42/55
Ann Arbor stage:		
I- II	279	79
III-IV	73	20
ECOG performance status:		
0,1	299	85
2,3	49	14
B symptoms, yes	58	16
Bulky disease (tumor mass > 10 cm)	110	31
No. of extranodal sites		
0, 1	275	79
> 2	73	20
LDH level		
Normal	71	20
Higher	277	79
IPI:		
0,1	163	46
2	95	27
3, 4	90	25

Table 3. NK cell lymphoma, nasal type with disseminated disease or distant metastases.

	No	*%*
Number	32	100
Sex: male/female	14/18	43/56
Age (years) median	50.6	
range	40-73	
IPI clinical risk		
high	32	100
Bulky disease (tumor mass > 10 cm)	28	88
ECOG performance status 2,3	3	100
Beta 2 microglobulin (> 5 ug/dL)	32	100
LDH. Higher (> 2 N)	32	100
Nodal involvement	21	68
Extranodal involvement		
skin	18	
lung	17	
gastric	10	
liver	10	
spleen	10	
testicle	7	
bone marrow	3	

mation about this presentation and outcome with treatment, has been reported. In an analysis performed in 108 cases, we detect 10 cases with disseminated disease, all were refractory to treatment and die < 1 year from diagnosis. For this reason, we conduct an prospective , no controlled, clinical trial, employed an probably more specific therapy. Table 3 shown the main characteristics of these cases.

Chemotherapy

Cyclophosphamide, 2 g/m^2, iv, day 1
Etoposide, 400 mg/m^2, IV, days 1 and 2
Methotrexate, 200 mg/m^2, iv, day 1 with leucovorin rescue, 21 mg/m^2, iv , by 12 doses.
Dexamethasone, 20 mg/m^2, po, daily, days 1 to 4 each cycle was administered every 14 days for an number of 6. Granulocyte colony-stimulating factor was employed to ameliorate the possibility of severe granulocytopenia.

Radiotherapy

If the patient achieve CR, 6 weeks later, radiotherapy 50 Gy was administered.
CR was observed in 21 cases (65 %), and actuarial 5-years overall survival is 65 %. We can no compare our results because specific therapy to disseminated disease has not been reported.

Anaplastic large cell lymphoma (ALCL)

Represent the 2º cause of T-cell lymphoma. Table 4 shown the main characteristics of these patients according if ALK is positive or not. We did not have any specific treatment and patients with ALCL are treated with the same regimens

Table 5. Response type in anaplastic large cell lymphoma.

Regimen	*No*	*CR*	*OS **
CHOP	74	87	77
CHOP INTENSIVE	56	85	80
CMED	41	80	70
CHOP DENSE (CHOP-14)	63	92	88 **

**Actuarial at 5 years; **Actuarial at 3 years.*

Table 6. Peripheral T-cell lymphoma, unspecified.

	No	*%*
Number	99	100
Age (years) median	43.8	
range	29-67	
Stage		
I- II	49	48
II-IV	50	51
ECOG performance status		
0,1	68	65
2,3	31	31
IPI:		
0,1	39	38
2	28	27
3	32	32
B symptoms	38	37
Bulky disease (tumor mass > 10 cm)	44	43

employed in diffuse large cell lymphoma (DLCL). Table 5 showed that response and outcome of out patients, no clear differenes could be observed. No differences were observed between AL^+ or ALK^-. The use of dose dense (CHOP 14) appear to have an best outcome, but the follow-up is to short to drawn definitive conclusions. Now, we continue to employed CHOP-14 and adjuvant radiotherapy to sites of bulky nodal disease.

Peripheral T-cell lymphoma, unspecified (PTCLU)

The characteristics of Mexican patients with PTCLu are different to reports from USA and Europe, including a low number of cases. Table 6 shown the principal characteristics of these patients. As ALCL, we did not have any specific therapy and patients are treated with CHOP or CHOP-like regimens, the CR rate and OS are the same that ALCL.

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