



# Immunologic Biomarkers in Stromal and Tumoral Areas of Extranodal Natural Killer/T-Cell Lymphoma



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## Background

Extranodal natural killer/T-cell lymphoma (ENKTL) is an uncommon malignancy with poor prognosis. There is limited knowledge about the ENKTL immunophenotypic profile.

## Objectives

To investigate the clinicopathological features of ENKTL and evaluate the immunophenotypic expression of CD4, CD8, CD30, CD38, and FOXP3 in malignant and stromal cells.

## Materials & Methods

Retrospective case series carry out at National Cancer Institute, in Lima Peru from 2001 to 2016. We evaluated patients diagnosed with Extranodal natural killer/T-cell lymphoma who received Radiotherapy; etoposide, ifosfamide, cisplatin, and dexamethasone (VIPD); and CHOP. Clinicopathological characteristics, response rates, immunophenotypic expression, and survival were analyzed from medical records.

The positive expression levels of CD4, CD8, FOXP3, CD30, and CD38 were quantified by the percentage of positive cells and classified into 3 categories: strong (>20%), weak (1%–20%), and negative (0%).

## Results

We included 26 cases of ENKTL. The median age of patients was 44 years (range: 11–86); 54% were males, 57.7% were clinical stage IE. All cases were of nasal or nasopharyngeal location. 50% received chemotherapy, and 92.3% received radiotherapy. The chemotherapy regimen was CHOP in 5 cases (38%), cisplatin plus radiotherapy followed by VIPD in 8 cases (62%). In tumoral cells, CD4 and FOXP3 were not expressed in any case, and the expression of CD8, CD30, and CD38 was weak in 57.6%, 84.6%, and 85.7% of cases, respectively. In the stromal area, the expression of CD4, FOXP3, CD30, and CD38 was weak in 90.7%, 91.7%, 92.3%, and 95.3% of cases, respectively. The stromal expression of CD8 was strong in 58% of cases. The median follow-up time was 20 months (range: 0–196 months). For the whole cohort, the 3- and 5-year OS rates were 44% and 38%, respectively. The 3-year OS for stromal CD 30 was as follows: strong 0%, weak 52.9%, and negative 0% with p<0.01. The 3-year OS for clinical stage I was 65.2%, and for clinical stage II and IV were 0%, p<0.01.

## Results

**Table 1.** Clinical and pathological features of patients with extranodal NK/T cell lymphoma.

| Features                        | Frequency (%) | 3y OS | 5y OS | p value |
|---------------------------------|---------------|-------|-------|---------|
| <b>CD30<sup>†</sup></b>         |               |       |       | 0.9     |
| Strong                          | 11 (42.3)     | 36.4  | 36.4  |         |
| Weak                            | 11 (42.3)     | 51.9  | 51.9  |         |
| Negative                        | 4 (15.4)      | 50    | 25    |         |
| <b>CD38<sup>†</sup> (n=21)</b>  |               |       |       | 0.5     |
| Weak                            | 18 (85.7)     | 48.1  | 40.1  |         |
| Negative                        | 3 (14.3)      | 66.7  | 66.7  |         |
| <b>FOXP3<sup>†</sup> (n=24)</b> |               |       |       | -       |
| Negative                        | 24 (100.0)    | 47.6  | 41.7  |         |
| <b>CD4<sup>‡</sup> (n=22)</b>   |               |       |       | 0.3     |
| Strong                          | 4 (18.2)      | 50    | 50    |         |
| Weak                            | 16 (72.7)     | 36.5  | 29.2  |         |
| Negative                        | 2 (9.1)       | 100   | 100   |         |
| <b>CD8<sup>‡</sup></b>          |               |       |       | 0.6     |
| Strong                          | 15 (57.7)     | 46.7  | 35    |         |
| Weak                            | 10 (38.5)     | 35    | 35    |         |
| Negative                        | 1 (3.8)       | 100   | 100   |         |
| <b>CD30<sup>‡</sup></b>         |               |       |       | <0.001  |
| Strong                          | 2 (7.7)       | 0     | 0     |         |
| Weak                            | 22 (84.6)     | 52.9  | 46.3  |         |
| Negative                        | 2 (7.7)       | 0     | 0     |         |
| <b>CD38<sup>‡</sup> (n=21)</b>  |               |       |       | 0.5     |
| Strong                          | 9 (42.9)      | 55.6  | 37    |         |
| Weak                            | 11 (52.4)     | 42.4  | 42.4  |         |
| Negative                        | 1 (4.8)       | 100   | 100   |         |
| <b>FOXP3<sup>‡</sup> (n=24)</b> |               |       |       | 0.3     |
| Weak                            | 22 (91.7)     | 44.4  | 38.1  |         |
| Negative                        | 2 (8.3)       | 100   | 100   |         |

<sup>‡</sup>: Stromal area; <sup>†</sup>: Tumoral area

## Conclusions

This study finds that the expression of CD30 and CD38 was frequent in malignant cells, and CD30 in the stroma was associated with superior survival. The expression of CD4, CD8, CD30, CD38, and FOXP3 were different between malignant and stromal cells in ENKTL.

## References

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