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Clinical and Paraclinical Features, Outcome, and Prognosis of Extranodal Natural Killer/T-Cell Lymphoma, Nasal Type: A Retrospective Study of 31 Vietnamese Patients

Kien Hung Do[1], Tu Anh Do[1], Tai Van Nguyen[1], Duc Thanh Le[1], Linh Van Phan[1], Chu Van Nguyen[1,2]

[1]National Cancer Hospital, Hanoi, Vietnam
[2]Hanoi Medical University, Hanoi, Vietnam

Corresponding Author: Chu Van Nguyen, National Cancer Hospital, Hanoi, Vietnam
E-mail: nguyenvanchu@hmu.edu.vn

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ABSTRACT

Background: Extranodal natural killer (NK)/T-cell lymphoma, nasal type is a rare, aggressive, and poor prognostic subtype. The concurrent chemoradiotherapy followed by chemotherapy showed a relatively high response rate and the toxicity due to the treatment is acceptable. The study attempted to report the clinicopathological features, the survival outcome, and response rates of stages I-II, nasal type ENKTL patients treated with CCRT followed by adjuvant VIPD chemotherapy in Vietnam.

Materials and Methods: The current study was conducted on 31 stage I or II NK/T cell lymphoma, nasal-type patients received by CCRT, followed by adjuvant VIPD chemotherapy. Information on patient demographics, disease stage, clinical symptoms, tumor, and paraclinical characteristics were collected. The primary endpoints of this study were OS and response rates.

Results: After CCRT, 26 out of 31 (83.9%) patients had stable disease or response. Overall response rate (ORR) was observed in 80.6% of patients with a complete response rate of 67.7%. Low-risk PINK patients had a higher response rate than the intermediate- risk group (p=0.038). Mean disease-free survival was 44.3±4.5 months (95% CI, 35.4-53.1 months). Mean overall survival was 46.8±4.5 months (95% CI, 37.99-55.8 months). The intermediate-risk PINK patients had a significantly lower OS rate than low-risk patients.

Conclusion: Concurrent chemoradiotherapy followed by adjuvant VIPD chemotherapy showed a high response rate and survival benefit in stages I-II, nasal type, and extranodal natural killer (NK)/T-cell lymphoma Vietnamese patients.

Keywords: NK/T-cell; Lymphoma; Concurrent chemoradiotherapy; VIPD; Prognosis

INTRODUCTION

Extranodal natural killer (NK)/T-cell lymphoma (ENKTL), nasal type is a malignant proliferation disease of cells mainly originated from natural killer cells and T-lymphocytes. This is a rare, aggressive and poor prognostic subtype of non-Hodgkin lymphoma, accounts for about 7-10% of all periperal T-cell lymphomas[1,2]. Clinical characteristics are typically in the nasal cavity, nasopharynx, but it can also involve adjacent organs such as: paranasal sinus, orbit, peripheral lymph

nodes. This disease is relatvely common in Asia and usually associated with Epstein-Barr virus[3,4].

About 70-80% of patients are newly diagnosed at localized stages (stage I, II) with several common clinical symptoms such as: nasal stuffy, runny, epistaxis, stinky facial necrosis[5,6]. Previously, NK/T-cell lymphoma stage I or II was commonly treated with chemotherapy or radiation therapy alone.[6] However, the efficacy was limited, response rate was low and systemic recurrence rate was high.[7] Recently, the benefit of concurrent chemoradiotherapy (CCRT) followed by chemotherapy has been confirmed in several studies, showed relatively high response rate and the toxicity during the treatment course is acceptable[8-10]. Clinically, L-asparaginase showed a significant single-agent activity in relapsed/refractory NK/T-cell lymphoma[11-13]. Therefore, to show the benefit of L-asparaginase in local stage patients, a phase II study using CCRT followed by adjuvant L-asparaginase-containing chemotherapy was conducted, the complete response (CR) rate was 86.7% of all cases[9]. In Vietnam, in context of indisponibility of L-asparaginase, CCRT with cisplatin weekly followed by adjuvant VIPD chemotherapy (etoposide, ifosfamide, mesna, cisplatin, dexamethasone) according to the National Comprehensive Cancer Network (NCCN) guideline[14] is still a standard of care regimen for the treatment of stages I-II, nasal-type ENKTL patients. Here, we report the clinicopathological features, the survival outcome and response rates of stages I-II, nasal type ENKTL patients treated with CCRT followed by adjuvant VIPD chemotherapy in Vietnam.

MATERIALS AND METHODS

Patient and sample selection

This retrospective analysis included stage I-II NK/T cell lymphoma, nasal type, who were treated with concurrent chemoradiotherapy followed by adjuvant chemotherapy from January 2017 to June 2022. The eligibility criteria were as histopathological and immunohistochemical (IHC) diagnosis of the primary NK/T cell lymphoma nasal type, without previous treatment. Patients of the primary NK/T cell lymphoma, nasal type combined with extra-nasal sites such as gastrointestinal tract or skin were excluded in this study. By using clinical examination and imaging of computerized tomography (CT) scan, magnetic resonance imaging (MRI) and laryngoscopic exam, disease staging was performed by physicians at the time of diagnosis. All patients were staged according to the Costwold modification of Ann Arbor staging system. Quantitative polymerase chain reaction (PCR) for EBV DNA in peripheral blood was performed to determine the EBV viral load. According to study of Kim HS *et al.*, EBV DNA will be detectable if EBV viral load is equal or more 64 copies/μL[15]. Clinical and paraclinical information was extracted from the medical records included patient characteristics (age, gender), clinical symptoms (ECOG, B symptoms) and tumor characteristics (location, lymph-node, histopathological type, IHC expressions). The written informed consent was obtained from the patients for publication of details of their medical cases. All private information was deleted or disguised in order to ensure patient anonymity. The study protocol was validated by the Hanoi Medical University, Vietnam, National Cancer Hospital of Vietnam.

Treatment, outcomes, and follow-up

The treatment scheme was shown in Figure 1. All patients were received by the concurrent chemoradiotherapy, followed by adjuvant chemotherapy. Three-dimensional (3D) conformal radiotherapy was delivered at a dose of 50 Gy in 25 fractions concomitantly with weekly cisplatin at a dose of 30mg/m^2 for 5 weeks. Response to concurrent chemoradiotherapy was asssed after 4 weeks of CCRT using MRI and CT scan according to WHO criteria[11]. Three to five weeks after the completion of CCRT, adjuvant VIPD chemotherapy was applied up to three cycles. The adjuvant chemotherapy of VIPD regimen included: etoposide 100mg/m² from days 1-3, ifosfamide 1200mg/m² from days 1-3, mesna 240mg/m² from days 1-3, cisplatin 33 mg/m² from days 1-3, dexamethasone 40mg/day from days 1-4, every three weeks.

All patients were followed up until June 2022. During follow-up, clinical, biological and radiological evaluations, laryngoscopic exam, whole body CT

scan and MRI of the involvement lesions were performed every three months for the first two years, then every 6 months up to 5 years after the end of treatment.

Overall survival (OS) was defined as the time interval between the date of diagnosis and the date of death from any cause or the last follow-up. Disease-free survival (DFS) was defined as the time interval between the date of diagnosis and the date of the first relapse at any site or death from any cause. The primary end points of the current study were OS and response rates. The secondary end points were DFS, toxicities.

Statistical analysis

Data were managed and analyzed using the SPSS ver. 20.0 statistical software. Chi-quare and Fisher's exact tests were used to test the difference of clinical response by clinical and subclinical features. Survival estimates were calculated using the Kaplan-Meier method. In subgroup analyses, survival compared using the log-rank test and hazard ratio was estimated by Cox regression. A two-sided p-value < 0.05 was considered to be significant.

RESULTS

Patient's baseline characteristics

Thirty-one patients with stage stage I-II NK/T cell lymphoma, nasal type were included in this study from January 2017 to June 2022 at National Cancer Hospital of Vietnam. Table 1 shows the patients' baseline clinicopathological features. Mean age was 42.8 years (range, 21-71 years). The most patients presented with ECOG 0 (67.7%). B symptoms were observed in 14 out of 31 patients (45.2%). Twenty-one of 31 (67.7%) patients occurred in the nasal cavity. Peripheral lymph nodes were not observed in 19.4% of all patients. Low-risk PINK score was the most common feature in our study (83.9%), whereas intermediate-risk was seen in 16.1%.

Efficacy analysis

Table 2 shows response to treatment according to RECIST v1.1. At the end of CCRT, 26 of 31 (83.9%) patients that were stable disease or response to CCRT received adjuvant chemotherapy. Overall response rate (ORR) was observed in 80.6% of patients (25 out of 31) evaluated by Lugano criteria, with complete response rate of 67.7% (21 out of 31) and partial response rate of 12.9% (4 out of 31). There were 4 patients (12.9%) of progressive disease after CCRT and 2 patients (6.6%) of progressive after adjuvant chemotherapy.

In the adjuvant chemotherapy phase, 26 patients (83.9%) continued to be received by the VIPD regimen. Of which, 17 of 26 patients (65.4%) were received three cycles of VIPD, 6 of 26 patients (23.1%) appeared toxicity grade 3-4, then received two cycles before treatment discontinuation. Two patients (9.5%) had to switch to other regimens because of disease progression. Group of low-risk PINK score had higher response rate, compared with group of intermediate risk (p=0.038). For multivariate analysis, there was no independent factor which affected the response rate (Table 3).

During follow-up, 12 of 31 patients (38.7%), who presented with disease progression or death. Mean disease-free survival was 44.3$\pm$4.5 months (95% CI, 35.4-53.1 months) and the estimated 4-year DFS was 61.3% (Figure 2). Ten of 31 patients (32.3%) died during the follow-up period. The mean overall survival was 46.8$\pm$4.5 months (95% CI, 37.99-55.8 months) and the estimated 4-year OS was 65.3% (Figure 3). Table 4 and Figure 4 display the DFS according to some characteristics of NK/T cell lymphoma, type nasal. Patients aged less 50 years old, who shown the better DFS rate than one of over 50 years old. For overall survival, patients of the intermediate-risk PINK score had a significant lower OS rate than low-risk patients (Table 5 and Figure 5).

Toxicity

Table 6 showed the detailed information on toxicities during CCRT and VIPD phases. During CCRT phase, hematologic toxicities were not frequently reported, grades 1 to 2 anemia were observed in six patients (19.3%); all grades neutropenia were seen in 4 patients (12.9%), including 1 patients presented with grade 3. For non-hematologic toxicities, the most toxicities were grades 1 and 2; one patietns experienced grade 3 hepatic toxicity and one patients with grade 3 renal toxicity (both of 3.2%). For acute toxicities related

to radiation, the most patients presented with mucositis and dermatitis (3.2%). During VIPD phase, grades 3 to 4 hematologic toxicities were more often, two patients experienced grades 3-4 anemia (6.4%); five patients (16.1%) presented with grades 3-4 neutropenia and 3 patients (9.7%) experienced grades 1 and 2, one patient experienced grade 3 febrile neutropenia. For nonhematologic toxicities, one patients experienced both grade 3 of liver and kidney toxicity (3.2%). There was no report of death related to toxicity of treatment protocol.

Table 1: Patient demographics

Characteristics	Number (n=31)	Percentage (%)
Age (years)		
<50	22	71.0
≥50	9	29.0
Mean (range): 42.8 ± 13.2 (21-71)		
Sex		
Male	19	61.3
Female	12	38.7
ECOG performance status		
0	21	67.7
1-2	10	32.3
B symptoms		
Presence	14	45.2
Absence	17	54.8
Tumor location		
Nasal cavity	21	67.7
Other	10	32.3
Lymph-node involvement		
Regional	6	80.6
None	25	19.4
LDH level before treatment		
Increased	4	12.9
Normal	27	87.3
Epstein-Barr virus DNA in peripheral blood*		
Detectable	8	32.3
Non-detectable	10	25.8
Unknown	13	41.9
Stage		
I	24	77.4
II	7	22.6
PINK score		
0 (low risk)	26	83.9
1 (intermediate risk)	5	16.1
Ki-67 index		
> 75%	8	25.6
50-75%	7	22.6
Not specified	16	51.6

ECOG: Eastern Cooperative Oncology Group, DNA: Deoxyribonucleic acid, PINK: Prognostic Index of Natural Killer Cell Lymphoma

Table 2: Response to treatment according to RECIST v1.1

Response category	After CCRT		After adjuvant chemotherapy		Total		P
	n	%	n	%	n	%	0.781
CR	12	38.7	21	77.8	21	67.7	
PR	15	48.4	3	11.1	4	12.9	
SD	0	0.0	1	3.7	0	0.0	
PD	4	12.9	2	7.4	6	19.4	
Total	31	100.0	27	100.0	31	100.0	

CCRT: concurrent chemoradiotherapy, CR: complete response, PR: partial response, SD: stable disease, PD: progressive disease

Table 3: Univariate and multivariate analyses for treatment response by clinical features

Clinical features	No. Response N (%)	Univariate P value	Multivariate		
			HR	95% CI	P value
Age		0.320	0.833	0.19-3.64	0.808
< 50	19/22 (86.4)				
≥50	6/9 (66.7)				
Sex		0.574	0.161	0.006-4.117	0.270
Male	15/19 (78.9)				
Female	10/12 (83.3)				
B symptoms		0.571	1.647	0.10-27.204	0.727
Yes	11/14 (78.6)				
No	14/17 (82.3)				
ECOG		0.067	4.617	0.37-57.596	0.235
0	19/21 (90.5)				
1-2	6/10 (60.0)				
Tumor location		0.358	3.310	0.292-37.53	0.334
Nasal cavity	18/21 (85.7)				
Other	7/10 (70.0)				
Stage		0.490	0.928	0.047-18.231	0.961
I	19/24 (79.2)				
II	6/7 (85.7)				
PINK score		0.038	26.545	0.179-3927.324	0.198
Low	23/26 (88.4)				
Intermediate	2/5 (40.0)				

ECOG: Eastern Cooperative Oncology Group, PINK: Prognostic Index of Natural Killer Cell

Table 4: Disease-free survival according to some characteristics of NK/T cell lymphoma, type nasal

Features	No reccurence N (%)	No. Events N (%)	Mean DFS	3-year DFS rate (%)	p value
Age					0.041
< 50	16 (72.7)	6 (27.3)	44.6±5.8	67.0	
≥50	3 (33.3)	6 (66.7)	40.6±6.2	65.6	
Sex					0.859
Male	12 (63.2)	7 (36.8)	49.3±5.1	77.3	
Female	7 (58.3)	5 (41.7)	29.9±6.8	40.0	
B symptoms					0.390
Yes	10 (71.4)	4 (28.6)	40.9±6.2	62.7	
No	9 (52.9)	8 (47.1)	45.7±5.4	70.7	
ECOG					0.205
0	15 (71.4)	6 (28.6)	48.8±5.2	74.7	
1-2	4 (40.0)	6 (60.0)	34.1±7.4	50.0	
Tumor location					0.294
Nasal cavity	14 (66.7)	7 (33.3)	47.4±5.1	75.2	
Other	5 (50.0)	5 (50.0)	35.0±7.6	48.0	
Stage					0.312
I	14 (58.3)	10 (41.7)	38.6±4.8	59.9	
II	5 (71.4)	2 (28.6)	53.6±6.4	85.7	
EBV DNA					0.466
Detectable	3 (37.5)	5 (62.5)	32.7±7.7	46.9	
Non-detectable	6 (60.0)	4 (40.0)	39.1±7.4	56.0	
PINK score					0.073
Low	18 (69.2)	8 (30.8)	47.7±4.8	72.1	
Intermediate	1 (20.0)	4 (80.0)	28.0±9.2	20.0	

ECOG: Eastern Cooperative Oncology Group, DNA: Deoxyribonucleic acid, PINK: Prognostic Index of Natural Killer Cell Lymphoma

Table 5: Overall survival according to some characteristics of NK/T cell lymphoma, type nasal

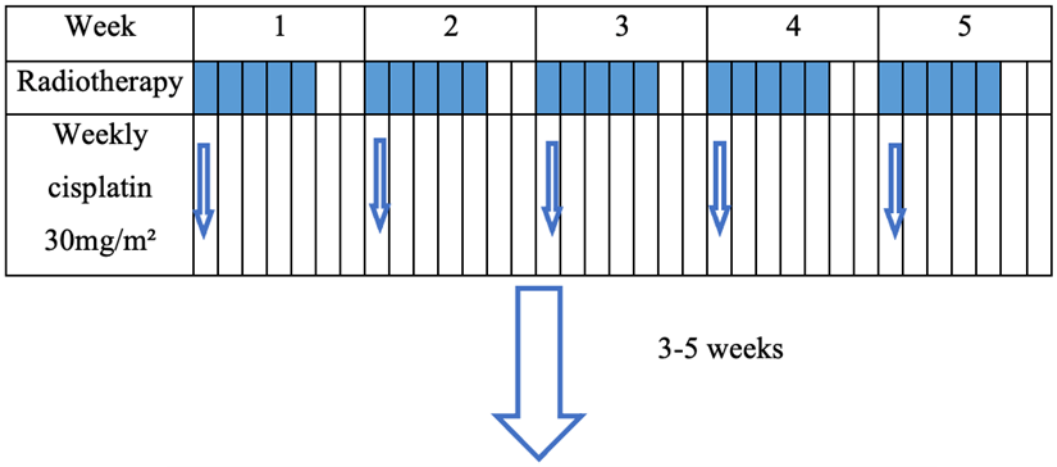
Features	Alive patients N (%)	No. Events N (%)	Mean OS (months)	3-year OS rate (%)	p value
Age					0.086
< 50	17 (77.3)	5 (22.7)	51.4±4.99	77.3	
≥50	4 (44.4)	5 (55.6)	33.7±7.6	53.3	
Sex					0.465
Male	14 (73.7)	5 (26.3)	48.9±5.7	73.7	
Female	7 (58.3)	5 (41.7)	40.6±6.3	65.6	
B symptoms					0.662
Yes	10 (71.4)	4 (28.6)	44.9±6.3	70.6	
No	11 (64.7)	6 (35.3)	45.7±5.4	70.7	
ECOG					0.186
0	16 (76.2)	5 (23.8)	50.8±5.1	81.0	
1-2	5 (50.0)	5 (50.0)	35.3±7.7	50.0	
Tumor location					
Nasal cavity	15 (71.4)	6 (28.6)	49.1±5.2	75.2	0.499
Other	6 (60.0)	4 (40.0)	38.0±7.8	60.0	
Stage					0.220
I	15 (62.5)	9 (37.5)	40.0±4.8	65.4	
II	6 (85.7)	1 (14.3)	57.3±6.2	85.7	
EBV DNA					0.487
Detectable	4 (50.0)	4 (50.0)	33.6±7.2	46.9	
Non-detectable	7 (70.0)	3 (30.0)	42.6±7.5	70.0	
PINK score					0.017
Low	20 (76.9)	6 (23.1)	51.1±4.7	76.9	
Intermediate	1 (20.0)	4 (80.0)	28.0±9.2	40.0	

ECOG: Eastern Cooperative Oncology Group, DNA: Deoxyribonucleic acid, PINK: Prognostic Index of Natural Killer Cell Lymphoma

Table 6: Adverse events of treatment according to CTCAE

Adverse events	CCRT phase (grade) N (%)				VIPD phase (grade) N (%)			
	1	2	3	4	1	2	3	4
Anemia	4 12.9	2 6.5	0 0.0	0 0.0	7 26.9	3 11.5	1 3.8	1 3.8
Neutropenia	2 6.5	1 3.2	1 3.2	0 0.0	2 7.7	3 11.5	2 7.7	3 11.5
Thrombocytopenia	1 3.2	1 3.2	1 3.2	0 0.0	1 3.8	1 3.8	1 3.8	0 0.0
Febrile neutropenia	0 0.0	0 0.0	1 3.2	0 0.0	0 0.0	0 0.0	2 7.7	1 3.8
Elevated liver enzymes	7 22.6	2 6.5	1 3.2	0 0.0	5 19.2	2 7.7	1 3.8	0 0.0
Elevated creatinine	1 3.2	0 0.0	1 3.2	0 0.0	4 15.4	0 0.0	1 3.8	0 0.0
Dermatitis	16 51.6	4 12.9	1 3.2	0 0.0	0 0.0	0 0.0	0 0.0	0 0.0
Mucositis	10 32.2	2 6.5	1 3.2	0 0.0	0 0.0	0 0.0	0 0.0	0 0.0
Dry mouth	6 19.3	3 9.7	0 0.0	0 0.0	0 0.0	0 0.0	0 0.0	0 0.0

CCRT: concurrent chemoradiotherapy, VIPD: etoposide/ ifosfamide/ cisplatin/ dexamethasone regimen chemotherapy



3-5 weeks

VIPD chemotherapy every three weeks, up to three cycles		
Etoposide	100mg/m² intravenous	D1-3
Ifosfamide	1200mg/m² intravenous	D1-3
Mesna	240mg/m² intravenous	D1-3
Cisplatin	33 mg/m² intravenous	D1-3
Dexamethasone	40mg/day oral	D1-4

Figure 1. Scheme of protocol for the treatment of NK/T cell lymphoma, type nasal

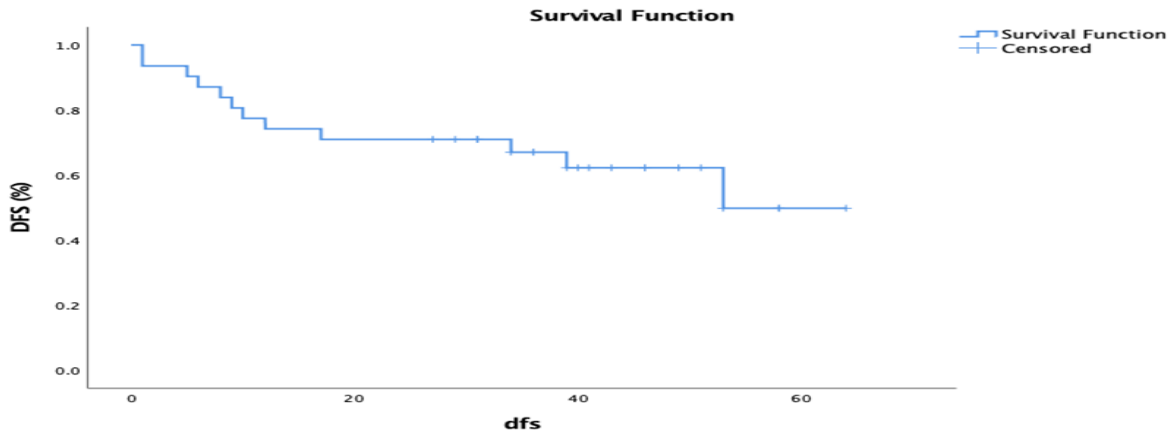


Figure 2. Disease-free survival of patients with NK/T cell lymphoma, type nasal. Kaplan-Meier curve displayed the estimated 3-year DFS was 61.3%

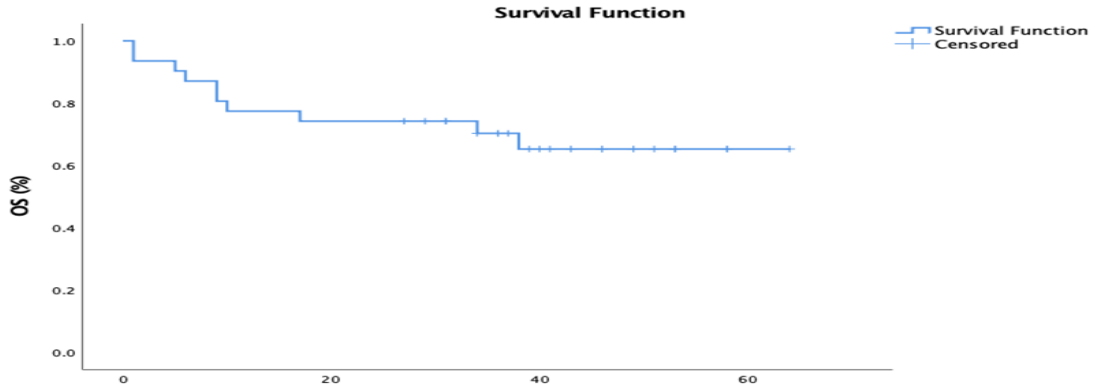


Figure 3. Overall survival of patients with NK/T cell lymphoma, type nasal. Kaplan-Meier curve displayed the estimated 3-year OS was 65.3%

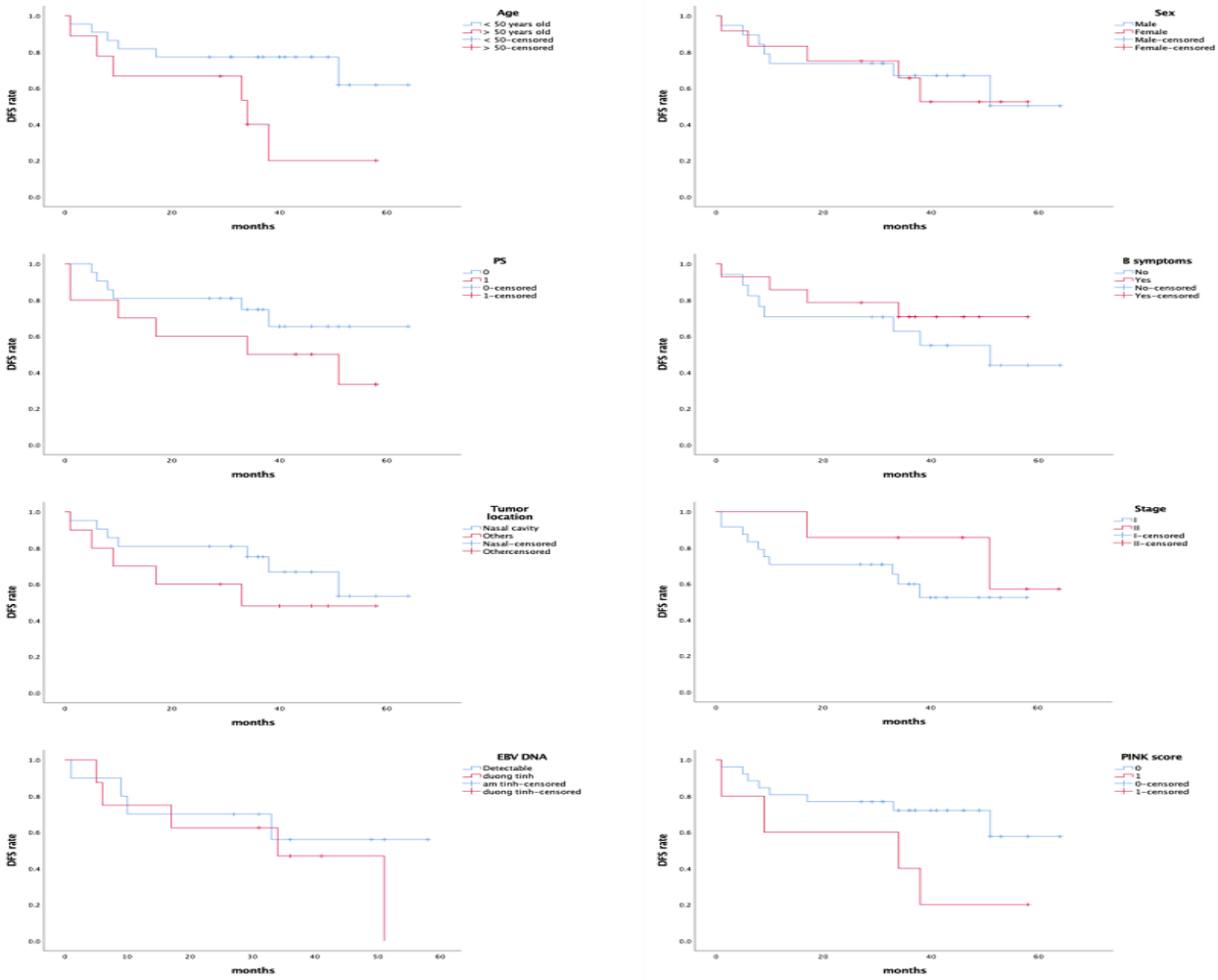


Figure 4. Kaplan-Meier for disease-free survuval according to some characteristics of NK/T cell lymphoma, type nasal

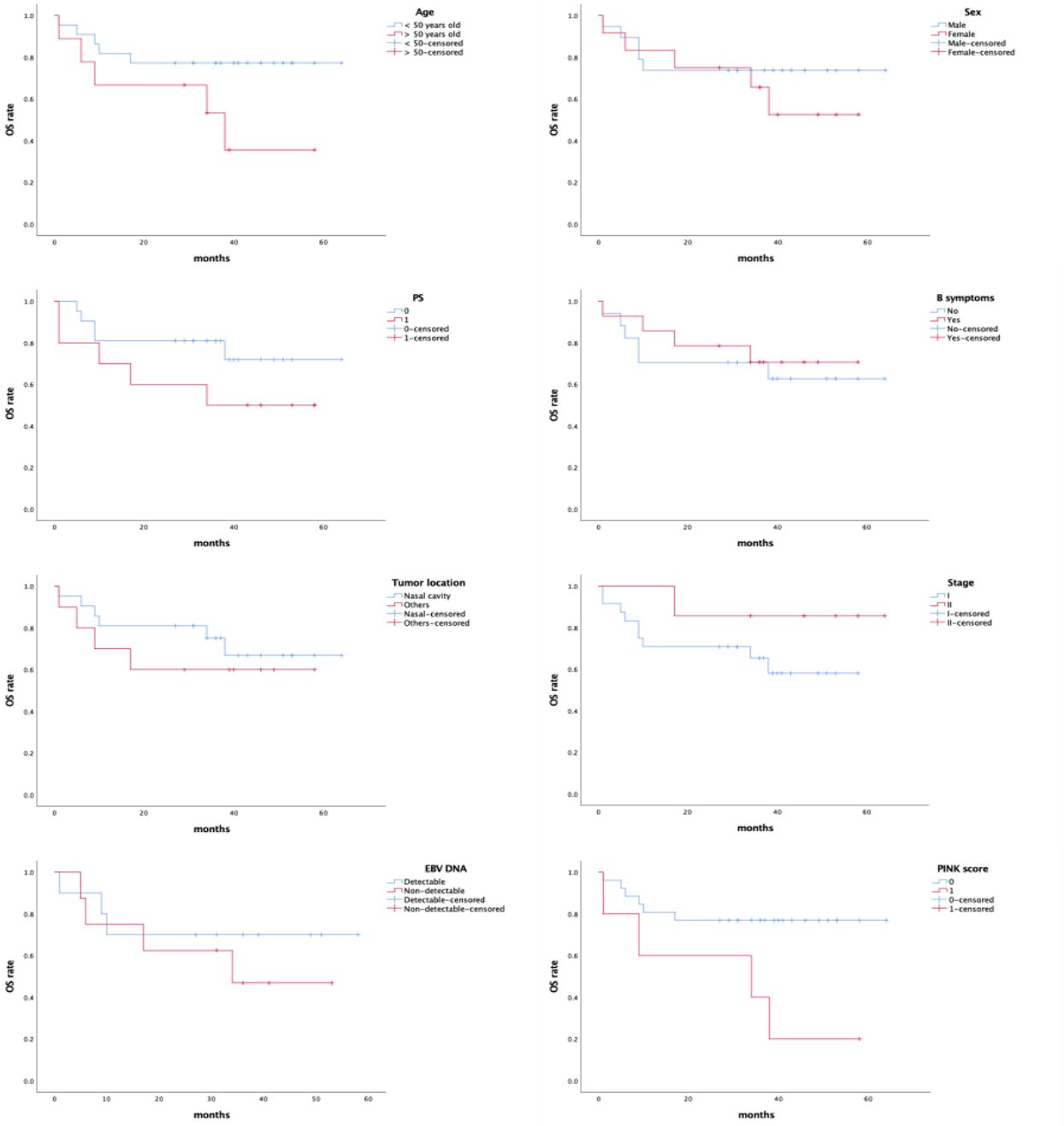


Figure 5. Kaplan-Meier for overall survuval according to some characteristics of NK/T cell lymphoma, type nasal

DISCUSSION

Extranodal NK/T-cell lymphoma, nasal type (ENKTCL) is an aggressive malignancy associated with Epstein-Barr virus infection, mostly of NK-cell and occasionally of T-cell lineage, with a geographic and racial predilection for some Asian and Latin American countries[3,16]. ENKTCL, nasal type is divided into nasal, non-nasal, and disseminated subtypes. Nasal NK/T-cell lymphomas involve the nose, nasopharynx and the upper aerodigestive tract. Diagnosis of extranodal NK/T cell lymphoma nasal type are typically positive for CD3 (cytoplasmic), CD56, cytotoxic markers (granzyme B, TIA1) and Epstein Barr virus (EBV). Plasma EBV DNA is an accurate surrogate biomarker for lymphoma load. Prognostically models based on clinicopathologic parameters and EBV DNA load are useful in stratification of patients for therapy[17].

Conventional anthracycline-containing regimens used for other lymphomas are less effective and should not be used for NK/T-cell lymphomas, due to expression of the multidrug resistance (MDR) P-glycoprotein on NK lymphoma cells[18-20]. For non-metastatic disease, the previous studies showed that combination of radiotherapy and chemotherapy provided superior benefits in both response rate and survival outcomes compared to group receiving chemotherapy alone or radiotherapy alone for the treatment of locally staged NK/T-cell lymphomas[21-23]. A phase II study of 30 newly diagnosed, stages I-II, nasal ENKTL patients received CCRT with cisplatin, then followed by VIPD chemotherapy showed the ORR and the CR rate were 83.3% and 80.0%, respectively[8]. An important advance in the treatment of NK/T-cell lymphoma is the use of L-asparaginase.[24] This is an MDR-unrelated anticancer agent that exerts antitumor effects in both ENKL cell lines and primary ENKL cells[25]. The dramatic response to L-asparaginase observed in patients with disseminated ENKL led to the development of L-asparaginase-containing regimens[26,27]. Conventional Escherichia coli–derived L-asparaginase is the prototype. If an allergic reaction to conventional E coli–derived L-asparaginase occurs, Erwinia asparaginase can be used instead[28]. Pegaspargase, a pegylated E coli–derived L-asparaginase, showed lower toxicity than E coli–derived L-asparaginase[25]. Clinically, L-asparaginase showed the significant single-agent activity in relapsed/refractory NK/T-cell lymphoma[11-13]. Therefore, to show the benefit of L-asparaginase in local stage patients, a phase II study using CCRT followed by adjuvant L-asparaginase-containing chemotherapy was conducted, the CR rate was 86.7% and disease progression was observed in only 3 out of 27 patients (11.1%)[9]. Another study using adjuvant DeVIC chemotherapy (dexamethasone, etoposide, ifosfamide, and carboplatin) for the treatment of localized nasal natural killer (NK)/T-cell lymphoma reported a similar overall response rate of 81% with CR of 77%[10].

Since the early 2000s, new approaches to treating localized ENKL have included concurrent chemoradiotherapy and sequential chemoradiotherapy with non-anthracycline chemotherapy[25]. The current study conducted the first-time of ENKTCL, nasal type of Vietnamese patients with stages I-II, who were treated by concurrent chemoradiotherapy followed by adjuvant VIPD chemotherapy in the National Cancer Hospital of Vietnam, an Asian population had not been yet previously published. After chemoradiotherapy, the present findings showed that the rate of response was 87.1% (27 out of 31 patients) with complete response rate of 38.7%. Using adjuvant VIPD chemotherapy, complete response raised up to 67.7%. Five out of 31 patients (16.1%) presented with progressive diseases during treatment, two with cervical node progressions, one with inguinal node metastasis, two with progression of skin and confirmation of hemophagocytic lymphohistocytosis. The ORR of the current study was similar to both two studies of Kim *et al.*,[8,9] but the CR rate was lower, there might be difficult in assessing treatment response after radiotherapy related to areas of post-radiation fibrosis and inflammation. To the best of the author's knowledge, no study has been conducted to evaluate the factors predicting response to treatment. In the current study, low-risk PINK score patients had a higher response rate, compared with intermediate-risk one for univariate analysis but there is no significant difference in multivariate

analysis. There was no significant association between ORR and age, gender, B symptoms, tumor location, performance status and stage. The relative small sample size in our study migh have limited these findings.

ENKTCL, nasal type was characterized by its poor prognosis irrespective of clinical stage and therapy. However, during the last two decades, advances of tests such as pathologic, genetic and molecular characterization have been achieved, as have changes in the chemotherapy regimens, combination with radiotherapy, that are significantly improving the survival of these patients, especially the initial stages[16]. For survival outcome, 38.7% patients presented with disease progression or death. Mean disease-free survival was 44.3±4.5 months and the estimated 4-year DFS was 61.3%. Ten of 31 (32.2%) patients died during the study period. The mean overall survival was 46.8±4.5 months and the estimated 4-year OS was 65.3%. A Japan study of 358 patients with localized ENKL received radiotherapy with dexamethasone, etoposide, ifosfamide, and carboplatin (RT-DeVIC) showed a 5-year OS of 72.0% and a 5-year PFS of 61.0%[24]. In this analysis, patients aged less 50 years old had the better DFS rate than one of over 50 years old. For overall survival, intermediate-risk PINK score patients had a significant lower OS rate than low-risk patients.

In the context of indisponibility of L- asparaginase in Vietnam, data on the clinical benefit of CCRT followed by adjuvant VIPD chemotherapy in stages I-II, nasal ENKTL patients remain the importance and practice. Information from this analysis would therefore be clinically relevant to our daily practice.

CONCLUSION

The concurrent chemoradiotherapy followed by adjuvant VIPD chemotherapy showed a high response rate and the survival benefit in stages I-II, nasal type, extranodal natural killer (NK)/T-cell lymphoma Vietnamese patients.

CONFLICT OF INTERESTS

The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Ethical considerations

All objects of the protocol's this study was approved by the Ethical Committee of Hanoi Medical University, Vietnam as number: 3955/QĐ-ĐHYHN.

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