Original Research

PRELIMINARY RESULTS OF TREATMENT EXTRANODAL NK/T-CELL LYMPHOMA, NASAL TYPE STAGE I-II AT K HOSPITAL

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ABSTRACT

Background: *Extranodal NK/T-cell lymphoma, nasal type, is a rare subtype of non-Hodgkin lymphoma, origin from natural killer (NK) cells and T cells. This is a rare, fast-growing and poor prognosis disease. Currently there have been not many studies in Vietnam on this issue. We conduct this research with two objects: to describe characteristics of patients and evaluate preminary results of treatment extranodal NK/T cell lymphoma, nasal type, stage I to II at K hospital.*

Methods: *Retrospective study. From January 2017 to June 2020, we enrolled 26 patients with extranodal NK/T cell lymphoma, nasal type, stage I to II. Patients were treated concurrent chemoradiotherapy with cisplatin, followed by 3 cycles of VIPD adjuvant regimen.*

Results: *Patient characteristics: The average age was 43.2. Male/female ratio was 1.36. The most common symptoms were stuffy of nose 84.6%; runny nose 65.4%. Peripheral lymph nodes observed in 19.2%; 50% with B symptom. Staged I was dominated with 73.1%.*

Treatment results: *Concurrent chemoradiotherapy phase: completed response was 26.9%, partial response 53.8% and progression disease 19.2%. At the end of treatment course, the overall response rate was 73% (including 61.5% completed response and 11.5% partial response), 26.9% cases with disease progression.*

Toxicity: *Leukopenia was the most common toxicity (61.1%). Grade III and IV leukopenia were observed in 18.4%.*

Conclusions: *Concurrent chemoradiotherapy followed by adjuvant VIPD regimen with stage I, II is effective regimen and acceptable toxicity.*

Keywords: *extranodal NK/T-cell lymphoma, nasal type, concurrent chemoradiotherapy, VIPD*

I. INTRODUCTION

Extranodal natural killer (NK)/T-cell lymphoma, nasal type is a malignant proliferation disease of cells mainly originated from natural killer cells and T-lymphocytes. This is a rare, fast-growing and poor prognosis subtype of non-Hodgkin lymphoma. Clinical characteristics are typically in the nasal cavity, nasopharynx. But it can also invade adjacent organs such as: paranasal sinus, orbit, peripheral lymph nodes… This disease is usually associated with Epstein-Barr virus [1]. It accounts for about 7-10% non-Hodgkin lymphoma [2].

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About 70-80% of patients are newly diagnosed at localized stages (stage I, II) with several common clinical symptoms such as: stuffy nose, runny nose, epistaxis, stinky facial necrosis... [3]in general, are associated with a poor clinical outcome.\nPATIENTS AND METHODS: A cohort of 1,314 cases of PTCL and NKTCL was organized from 22 centers worldwide, consisting of patients with previously untreated PTCL or NKTCL who were diagnosed between 1990 and 2002. Tissue biopsies, immunophenotypic markers, molecular genetic studies, and clinical information from consecutive patients at each site were reviewed by panels of four expert hematopathologists and classified according to the WHO classification.\ nRESULTS: A diagnosis of PTCL or NKTCL was confirmed in 1,153 (87.8%. The treatment of NK/ T-cell lymphoma depends on the disease stage. Previously, NK/T-cell lymphoma stage I or II was commonly treated with chemotherapy or radiation therapy alone. However, the efficacy was limmited, response rate was low and systemic recurrence rate was high [4],[5]. Recently, the concurrent chemoradiotherapy with weekly cisplatin followed by VIPD adjuvant regimen has showed relatively high response rate and the toxicity during the treatment course is acceptable [6]. In Vietnam, there is not any research mentioning completely about this issue. Therefore we conducted this study for two objects:

1. Describing some characteristics of patients diagnosed with extranodal NK/T-cell lymphoma, nasal type, stage I to II at K Hospital.

2. Evaluating preliminary results and toxicity of treatment regimen.

II. PATIENTS AND METHODS

2.1. Patients: Twenty-six patients with confirmed diagnosis of NK/T-cell lymphoma, stage I or II from January 2017 to June 2020 were enrolled to study. All patients were treated with concurrent chemoradiotherapy with or without adjuvant chemotherapy.

2.1.1. Eligibility Criteria

- Patients were diagnosed with biopsy samples that confirmed NK/T-cell lymphoma, nasal type according to WHO 2006 classification.

- All patients were staged IE-IIE according to the Lugano modification of the Ann Arbor staging system.

- The target lessions can be evaluated by: CT, MRI, PET/CT

- There are no contradication of chemotherapy

2.1.2. Exclusion criteria: Patients with synchronous cancers, lost follow up information.

2.2. Methods: *Retrospective study*

Treatment regimen protocol:

- Phase 1 (Concurrent chemoradiothrapy): weekly cisplatin 30mg/m^2,IV concurrent with radiation. The total dose was 50 Gy, 2 Gy/Fraction.

- Phase 2 (Adjuvant chemotherapy): three cycles of VIPD (Etoposide, Ifosfamide, Cisplatin, Dexamethasone), every 21 days.

2.3. Statistical Analysis: The collected information is encrypted and processed on SPSS 16.0 software.

2.4. Medical ethics: Treatment regimen is approved by Indepentdent Ethics Committee at K hospital, the study procedure was be implied with the eligible patients's acceptance. Results of study are used for researching and advancing therapeutic effect.

III. RESULTS AND DICUSSION

3.1. Characteristics of patients

3.1.1. Sex, age: The median age was 43.2 (range, 21 to 71 years); most commonly seen in the age group 40-49 (26.9%). Male/female ratio was 1.36. According to Au WY (2009) report, the median age at the time of diagnosis was 52 years, male/female ratio was 1.5 [7]136 cases (11.8%.

3.1.2. Clinical features

Table 1: Common clinical features

		n	%
Symptom	Stuffy nose	22	84.6
	Runny nose	17	65.4
	Epistaxis	10	38.5
	Dyspnea	2	7.7
Sign	Orbit tumor	2	7.7
	Swollen face	6	23.1
	Stinky necrosis tumor	4	15.4
	Peripheral lympho nodes	5	19.2
Systemic symptom	"B" symptoms	13	50

Most of patients have nasal and pharynx symptoms, while stuffy nose (84.6%) and runny nose (65.4%) are two most common symptoms. Swelling of the face (23.1%) and stinky necrosis tumor (15.4%) are specific signs but they seem to be less common in early stages. Dyspnea symptom is rare with 7.7%.

Peripheral lymph nodes were observed in 19.2% of all patients. Systemic "B" symptoms occured in half of patients (50%). LiYX author (2009) conducted research on this disease and the result showed that the proportion of peripheral lymph nodes was 17% in all of stages, 34% of patients had systemic "B" symptoms [8].

3.1.3. Work-up findings

Table 2: Work-up findings

	n	%
Pre-treatment serum LDH level		
- Increased	3	15
- Normal	17	85
β2-microglobulin level		
- Increased	11	91.7
- Normal	1	8.3
Peripheral nodes		
- Present	7	26.9
- Absent	19	73.1
Stage		
- IE	19	73.1
- IIE	7	26.9

The proportion of patients with regional lymph nodes were 26.9%. Pre-treatment high level of serum LDH was uncommon (15%), high level of **β2-microglobulin** was observed in most of cases (91.7%).

In this study, the proportion of patients with stage IE was dominated (73.1%), while the number of patients with stage IIE only accounted for 26.9%.

3.2. Treatment results

3.2.1. Characteristics of treatments

In this research, 84.6% of patients were treated with five cycles of concurrent chemoradiotherapy with full dose 50Gy. The remaining patients did not receive enough five cycles due to intolerance to cisplatin or complication of radiation therapy.

In the adjuvant chemotherapy phase, 21 patients (80.7%) continued to receive VIPD regimen. Of which, 14 patients (66.7%) received three cycles of VIPD, 5 patients (23.8%) appeared serve toxicity, so they received two cycles before treatment discontinuation. Two patients (9.5%) had to switch to treatment regimen because of disease progression.

3.2.2. Treatment response

Table 3: Response assessment to treatment according to RECIST 1.1

Response	After phase I		After phase II		Whole treatment	
	n	%	n	%	n	%
Completed response	7	26.9	16	76.2	16	61.5
Partial response	14	53.8	3	14.3	3	11.5
Stable disease	0	0.0	0	0.0	0	0.0
Progression disease	5	19.2	2	9.5	7	26.9
Total	26	100	21	100	26	100

Table 3 shows that the overall response rate was 80.8% after concurrent chemoradiotherapy phase (including 26.9% completed response, 53.8% partial response). Five patients (19.2%) had progression disease. After the whole treatment regimen, the overall response rate was 73%, of which 61.5% patients had completed response, 11.5% patients had partial response. 26.9% cases progressed during whole of treatment. A phase II study (Kim, 2009) with similar regimen showed results: 100% of patients achieved response after concurrent chemoradiotherapy phase. The overall response rate was 83.3% after the whole treatment, the completed response rate was 80% [6].

3.2.3. Toxicity

Toxicity in phase I (concurrent chemoradiotherapy)

Table 4: Toxicity in phase I

Toxicity (n=125 cycles)	Grade 0		Grade 1		Grade 2		Grade 3		Grade 4	
	n	%	n	%	n	%	n	%	n	%
Neutropenia	110	88	7	5.6	4	3.2	4	3.2	0	0.0
Thrombocytopenia	119	95.2	3	2.4	1	0.8	2	1.6	0	0.0
Anemia	77	61.6	39	31.2	9	7.2	0	0.0	0	0.0
Increased liver enzymes	101	80.8	18	14.4	5	4	0	0.0	1	0.8
Increased creatinine	124	99.2	0	0.0	0	0.0	1	0.8	0	0.0

- *Leukopenia and neutropenia:* Grade 1 to 3 neutropenia were observed in 12% of patients. Grade 4 neutropenia was not reported.

- *Anemia:* 38.4% patients had anemia but grade 1 or 2 only.

- *Thrombocytopenia:* less common, with a rate of 4.8%

- *Increased liver enzymes*: 19.2%, mainly grade 1.

- *Kidney failure:* one patient with Hemophagocytic lymphohistiocytosis during phase 1 had grade 3 kidney failure.

Toxicity in phase II (adjuvant chemotherapy)

Table 5: Neutropenia in phase II

Toxicity (n=54 cycles)	Grade 0		Grade 1		Grade 2		Grade 3		Grade 4	
	n	%	n	%	n	%	n	%	n	%
G-CFS prophylaxis (n= 34)	29	85.3	2	5.8	0	0.0	1	2.9	2	5.8
No G-CFS prophylaxis (n= 20)	4	20	1	5	6	30	4	20	5	25
Total (n= 54)	33	61.1	3	5.5	6	11.1	5	5.5	7	12.9

Adjuvant chemotherapy is more toxic than phase I, mainly neutropenia.

- *Febrile neutropenia:* 14.3% patients were observed febrile neutropenia that requires antibiotic therapy.

- *Neutropenia:* In the entire chemotherapy cycles, neutropenia rate was quite high (38.9%). In which neutropenia rate of using G-CFS prophylaxis and not using G-CFS were 14.7% and 80%, respectively. When using G-CFS prophylaxis, only 8.7% of cases had grade 3,4 neutropenia. In which this rate was 45% at the remaining group

and 18.4% for both groups. According to a research (Kim, 2009) with similar regimen, the proportion of grade 3,4 neutropenia was 46.7% [6]. It can be seen that, VIPD adjuvant regimen has high rate of neutropenia, febrile neutropenia and it is necessary to use G-CFS prophylaxis.

Table 6: Toxicity in phase II

Toxicity (n=54 cycles)	Grade 0		Grade I		Grade II		Grade III		Grade IV	
	n	%	n	%	n	%	n	%	n	%
Thrombocytopenia	49	90.7	2	3.7	1	1.8	0	0.0	2	3.7
Anemia	9	16.6	22	40.7	18	33.3	4	7.4	1	1.8
Increased liver enzymes	53	98.1	0	0.0	1	1.8	0	0.0	0	0.0
Increased creatinine	54	100	0	0.0	0	0.0	0	0.0	0	0.0

- *Anemia:* the rate of this event was 83.4%, commonly meet at grade 1 or 2 in adjuvant chemotherapy

- *Thrombocytopenia:* This adverse event was quite uncommon with 9.3%. However, two patients had grade 4 thrombocytopenia because of myelosuppression and requiring platelet trasfusion.

- *Increased liver enzymes and creatinin level:* were rare in phase II

IV. CONCLUSIONS

Concurrent chemoradiotherapy regimen (50Gy radiation 2Gy/fraction and weekly cisplatin 30mg/m^2) followed by VIPD adjuvant chemotherapy for NK/T-cell non Hodgkin lymphoma, nasal type, stage I and II is effective regimen. The overall response rate was 73% (61.5% completed response). Grade 3,4 neutropenia were observed in 18.4% within phase II, so it is necessary to follow-up carefully. G-CFS primary prophylaxis is recommend.

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