Clinical results of high-dose chemotherapy followed by autologous peripheral blood stem cell transplantation in children with advanced stage rhabdomyosarcoma

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Clinical results of high-dose chemotherapy followed by autologous peripheral blood stem cell transplantation in children with advanced stage rhabdomyosarcoma

Directed by Professor Chuhl Joo Lyu

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ABSTRACT

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Purpose: Rhabdomyosarcoma (RMS) is most common soft-tissue sarcoma and highly malignant tumor in children. Regardless of improvement in cure of RMS, the results in treatment of advanced stage of RMS are still dismal. Recently, high-dose chemotherapy followed by autologous peripheral blood stem cell

transplantation (HDC/APBSCT) has been tried to manage the advanced high-risk RMS patients. We investigated the effectiveness of HDC/APBSCT by reviewing the clinical records of high-risk RMS patients in single institute data base.

Methods: Over twenty years, 37 patients were diagnosed as RMS with high-risk at the time of first diagnosis in Severance Hospital, Seoul, Korea. High-risk patients were defined as clinical group III or IV. These patients were classified as two groups according to treatment method. The first group was HDC/APBSCT and the other was conventional multi-agent chemotherapy group. Differences of clinical results between the two groups were analyzed. The data of patients were reviewed retrospectively.

Result: Seventeen and twenty patients were female and male, respectively. The median age of patients was 5 years, ranging from 6 months to 15 years. The 5-year overall survival rate (OS) of all patients was about 25.1±7.6%. HDC/APBSCT group and conventional multi-agent chemotherapy group were 40.5±16.5% and 16.7±7.6% for 5-year OS, respectively (p=0.028). There was a

significant difference in the result of HDC/APBSCT between complete remission or very good partial response group and poor response group. The difference of OS between two groups was 51.4±20.4% versus 25±21.7% (p=0.04). Especially, in the very high-risk group (Group IV or Stage IV over 10 years of age with embryonal histology or all alveolar histology), there was statistically significant different OS between HDC/APBSCT and conventional multi-agent chemotherapy group (32.7±17.3% vs. 0%).

Conclusion: HDC/APBSCT can be a promising treatment modality, especially in very high-risk RMS patients. It should be performed to patients with good response to conventional multi-agent chemotherapy because good outcome and tolerable treatment related toxicity are expected.

Key words: rhabdomyosarcoma, pediatric solid tumor, high-dose chemotherapy, autologous stem cell transplantation

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I.INTRODUCTION

Rhabdomyosarcoma (RMS) is the most common type of soft-tissue sarcoma occurring in childhood and adolescence in Korea. In spite of its highly malignant characteristics, cure rate of RMS has been improved during past 40

years from approximately 20% in 1970 to greater than 70% currently[1-3]. Since 1972, Intergroup Rhabdomyosarcoma Study (IRS) committee has conducted various treatment strategies for pediatric soft tissue sarcoma patients. With contemporary multimodal therapy, much more children and adolescents with this disease are cured.[3]

However, high risk disease such as clinical group III or IV and alveolar type RMS have shown dismal results until now. The IRS has used therapeutic window studies to confirm the predictive nature of preclinical xenograft models and to identify several newly developed agents and combinations of agents with activity in high-risk patient group.[4] Despite these efforts, the outcome for these high-risk patients has not improved.[5] Recently, high dose chemotherapy followed by autologous peripheral blood stem cell transplantation (HDC/APBSCT) has tried for these clinical group III or IV high-risk patients by some institutes. However, the result seems controversial up until these days.[6,7]

Multimodal therapy including surgery, radiation, and multi-agent combination chemotherapy was performed during over two decades in our

institution. In the current years, some patients with high-risk features have been treated with HDC/APBSCT. We reviewed the clinical records of pediatric high-risk RMS over twenty years in single institute and explored the clinical implication of HDC/APBSCT in these patients.

II. PATIENTS AND METHODS

This study was performed by retrospective review of medical records for patients with RMS in a single institute. Between 1982 and 2006, 37 patients who have been diagnosed as RMS high-risk group and treated in Severance Hospital, Seoul, Korea were reviewed in this study. All patients have been classified by Tumor-Node-Metastasis (TNM) staging system and clinical group stage system employed in IRS. The treatment results were reviewed to compare the patients who have undergone HDC/APBSCT and the patients treated with conventional multi-agent chemotherapy alone. The patients reviewed in this study have not been included in any other published reports.

The chemotherapeutic regimen composed with ifosfamide, carboplatin and etoposide (ICE) was used for hematopoietic stem cell mobilization in the patients with HDC/APBSCT. Serial subcutaneous injections of recombinant granulocyte colony stimulating factor (G-CSF) were given until recovery phase of chemotherapy. The peripheral blood stem cells were collected by continuous flow apheresis.

Criteria for high-risk RMS were as follows; Group III or IV patients at diagnosis by IRS clinical group stage system, and Stage III or IV disease by TNM staging. Especially, the patients with Group IV or Stage IV patients regardless of tumor site and size, embryonal histology over 10 years old or all alveolar histology were classified to very high-risk group.[8]

The patients treated with HDC/APBSCT were categorized as good response group and poor response group according to radiographic measurement of disease after conventional multi-agent chemotherapy. Patients with complete resolution of disease (complete resolution, CR) or decrease maximum perpendicular diameter of mass more than 50% (partial response, PR) were defined as good response group. Patients with increased diameter of mass or decreased diameter less than 50% were considered as poor response group.

All of these 37 patients were classified as high-risk RMS. Medical records of these high-risk patients were closely reviewed to analyze the relationship between treatment modality and outcome, retrospectively. We compared the effect of HDC/APBSCT between good response group and poor

response group, also. Kaplan-Meier curve was generated to compare the 5-year overall survival rate (OS) of each groups. The differences between groups were analyzed using univariate analysis with the log-rank test. The differences of the mean between the two groups were analyzed by Student's t-test. A *p*-value less than 0.05 was regarded as statistically significant. Toxicities were reviewed by the Eastern Cooperative Oncology Group (ECOG) common toxicity criteria for all patients.

III. RESULTS

Patient Characteristics

The clinical characteristics of the patients are summarized in Table 1. All the thirty-seven patients were diagnosed as RMS clinical group III or IV. The median age of patients was 5 years which was ranged from 6 months to 15 years. Seventeen patients were female and other 20 patients were male. Twenty four patients were treated with conventional multi-agent chemotherapy and other thirteen patients were treated with HDC/APBSCT. Local treatment of disease was operation or radiation therapy. Eleven patients have undergone cytoreductive surgery as a local treatment, and 28 patients received radiotherapy as a local treatment. The modality of local treatment was chosen by clinical situation of each patient.

The differences of clinical manifestation between conventional multi-agent chemotherapy group and HDC/APBSCT group were described in Table 2. The age of patients in each group was 5.9±4.3 and 8.7±5.3 which was not

statistically different (p=0.084). The most frequent primary site were genitourinary area in conventional multi-agent chemotherapy group (group 1) and trunk area in HDC/APBSCT group (group 2). And the most frequent histologic type was embryonal type in group 1 and alveolar one in group 2.

The proportion of patients according to primary site at diagnosis and histological findings are shown in Table 3. Fifteen patients were embryonal type (41%) and sixteen patients were alveolar type (43%). The patients with embryonal type were usually clinical group III. On the contrary, the patients with alveolar type were mainly clinical group IV patients. The proportion of alveolar type in this study was more than generally reported proportion of overall RMS patients.[9] Other histology included undifferentiated and pleomorphic types. There was no botryoidal patient.

The clinical characteristics of the patients undergone HDC/APBSCT are summarized in Table 4. Thirteen patients were treated with HDC/APBSCT, and the clinical group of patients at the time of diagnosis was group IV, except 1 patient (patient number 29). Nine patients had showed very good partial

response or complete remission before HDC/APBSCT. The conditioning regimens for HDC/APBSCT varied as mentioned in Table 4.

Table 1. Clinical characteristics of patients enrolled in this study

Patient number	Age (year)	Sex	Primary site	Histologic type	Stage	Group	PBSCT	Operation	Radiation Therapy	outcome	OS (year)
1	3	F	GU	Embryonal	3	3	-	+	+	Dead	1
2	5	M	H&N	Others	3	3	-	-	+	Alive	25.2
3	2	F	PM	Embryonal	4	4	-	-	+	Dead	0.75
4	11	M	H&N	Alveolar	3	3	-	-	+	Dead	3.42
5	4	M	GU	Embryonal	3	3	-	-	+	Alive	19
6	9	M	Ext	Alveolar	4	4	-	+	+	Dead	2.3
7	3	F	H&N	Embryonal	4	4	-	-	-	Dead	0.8
8	1	F	GU	Others	3	3	-	-	+	Dead	1.25
9	4	F	GU	Embryonal	3	3	-	+	+	Dead	1.34
10	5	M	GU	Embryonal	3	3	-	-	+	Dead	2
11	3	F	H&N	Embryonal	3	3	-	-	+	Dead	1.92
12	2	M	GU	Others	3	3	-	-	+	Dead	1.4
13	5	F	H&N	Embryonal	3	3	-	-	-	Alive	19.2
14	1	F	T	Alveolar	4	4	-	-	+	Dead	0.08
15	15	F	T	Embryonal	4	4	-	-	+	Dead	0.4
16	1	M	GU	Others	3	3	-	-	+	Dead	1
17	12	M	T	Others	4	4	-	-	-	Dead	1.5
18	4	M	GU	Embryonal	3	3	-	+	+	Alive	9.8
19	4	M	PM	Embryonal	3	3	-	-	-	Dead	0.6
20	10	M	PM	Alveolar	3	3	-	-	-	Dead	1.2
21	12	F	GU	Alveolar	4	4	-	-	-	Dead	0.5
22	1	M	GU	Alveolar	3	3	-	-	+	Dead	4
23	12	M	PM	Alveolar	4	4	-	+	+	Dead	0.7
24	1	M	T	Others	4	4	-	-	-	Dead	0.45
25	15	M	Ext	Alveolar	2	4	+	+	+	Dead	2.84
26	2	M	Ext	Alveolar	2	4	+	-	+	Dead	4.25
27	7	M	H&N	Alveolar	4	4	+	-	-	Alive	9.55
28	15	F	T	Alveolar	4	4	+	-	+	Dead	1
29	3	M	H&N	Embryonal	3	3	+	+	+	Alive	4.37
30	2	F	H&N	Alveolar	4	4	+	-	-	Alive	5.1
31	6	M	PM	Embryonal	4	4	+	-	+	Alive	4.2
32	1	F	T	Alveolar	4	4	+	-	+	Dead	2
33	11	F	T	Embryonal	4	4	+	+	+	Dead	1.8
34	14	F	T	Alveolar	4	4	+	-	+	Dead	1
35	6	F	T	Alveolar	4	4	+	+	+	Alive	1.7
36	14	M	Ext	Embryonal	4	4	+	+	+	Alive	2.5
37	12	F	Ext	Alveolar	4	4	+	+	+	Alive	1

*Note.*Primary site: H&N= Head and neck, PM= Parameningeal, GU= Genitourinary, Ext= Extremity, T= Trunk; OS= overall survival

Table 2. Differences of clinical characteristics between conventional multi-agent chemotherapy group (Group 1) and high-dose chemotherapy and autologous peripheral blood stem cell transplantation group (Group 2)

	Group 1 (n=24)	Group 2 (n=13)
Age (year)	5.9±4.3	8.7±5.3
Most frequent primary site	Genitourinary (n=10)	Trunk (n=5)
Most frequent histologic type	Embryonal (n=11)	Alveolar (n=9)
TNM stage	III (n=15), IV (n=9)	III (n=1), IV (n=10)
Clinical group	III (n=15), IV (n=9)	III (n=1), IV (n=12)

*Note.*M: male, F: female, TNM: tumor-node-metastasis

Table 3. Proportion of patients according to histology and primary site (n=37)

	Embryonal (n=15, 41%)		Alveolar (n= 16, 54%)		Others (n= 6, 16%)	
	Group III	Group IV	Group III	Group IV	Group III	Group IV
Head and neck	3	1	1	2	1	-
Parameningeal	1	2	1	1	-	-
Genitourinary	5	-	1	1	3	-
Extrimity	-	1	-	4	-	-
Trunk	-	2	-	5	-	2
Total	9	6	3	13	4	2

Table 4. Patients treated with high-dose chemotherapy and autologous peripheral blood stem cell transplantation

Patient number	Group at diagnosis	Status at SCT	HDC regimens	Outcome
25	IV	CR	TBI-EM	Progressive disease
26	IV	VGPR	CEM	Relapse
27	IV	PR	CEM	No evidence of disease
28	IV	PD	TBI-EM	Partial response
29	III	CR	CEM	No evidence of disease
30	IV	CR	CEM	No evidence of disease
31	IV	CR	CCE	Relapse
32	IV	VGPR	CCM	Progressive disease
33	IV	PR	CEM	Progressive disease
34	IV	PR	Cy-Mel-TBI	Progressive disease
35	IV	CR	CEM	No evidence of disease
36	IV	VGPR	CEM	Relapse
37	IV	CR	CEM	No evidence of disease

Note. SCT: stem cell transplantation, CR: complete remission, VGPR: very good partial response, PR: partial response, PD: Progression disease, HDC: high dose chemotherapy, TBI-EM: total body irradiation-etopocide-melphalan, CEM: cyclophoaphamide-etoposide-melphalan, CCE: cyclophosphamide-carboplatin-etoposide, Cy-Mel-TBI: cyclophoaphamide-melphalan-total body irradiation

Toxicity

There was no patient who died of toxicity directly related to HDC/APBSCT. However, every patient had grade III or IV hematologic complications such as thrombo-cytopenia or neutropenia. These hematologic complications were shown equally, regardless of treatment modalities which were conventional chemotherapy or HDC/APBSCT. There was one case of treatment related mortality in the conventional chemotherapy group. A 12 year-old male patient (Patient number 23) was treated with multi-agent chemotherapy consisted with ICE. After 6-cycles of scheduled chemotherapy, he failed to recover from myelosuppression and died due to invasive bacterial infection.

Survival and Outcomes

The overall survival rate of all patients reviewed in this study is shown in Figure 1, estimated by Kaplan-Meier methods. The 5-year OS was 25.1±7.6%. The patients with HDC/APBSCT were higher OS than conventional chemotherapy group. The 5-year OS of each group were 40.5±16.5% and 16.7±7.6%, separately. As shown in Figure 2, *p*-value was less than 0.028 and median follow-up duration was 7.3 years. Figure 3 shows the difference of OS that had been in complete remission or very good partial response versus partial response, which means poor response to conventional multi-agent chemotherapy. The 5-year OS was better in the patients who had achieved complete remission or very good partial response (51.4±20.4%) than in patients with partial response or disease progression (25±21.7%) at the time of HDC/APBSCT. The 5-year OS difference was statistically significantly between two groups (p=0.04). The 5-year OS according to treatment method in very high-risk group are shown in Figure 4. In this group, the difference of survival rate between HDC/APBSCT group (12 patients) and conventional

chemotherapy group (9 patients) was statistically significant (p<0.001). The 5-year OS was 32.7±17.3% for HDC/APBSCT group and 0% for conventional chemotherapy group.

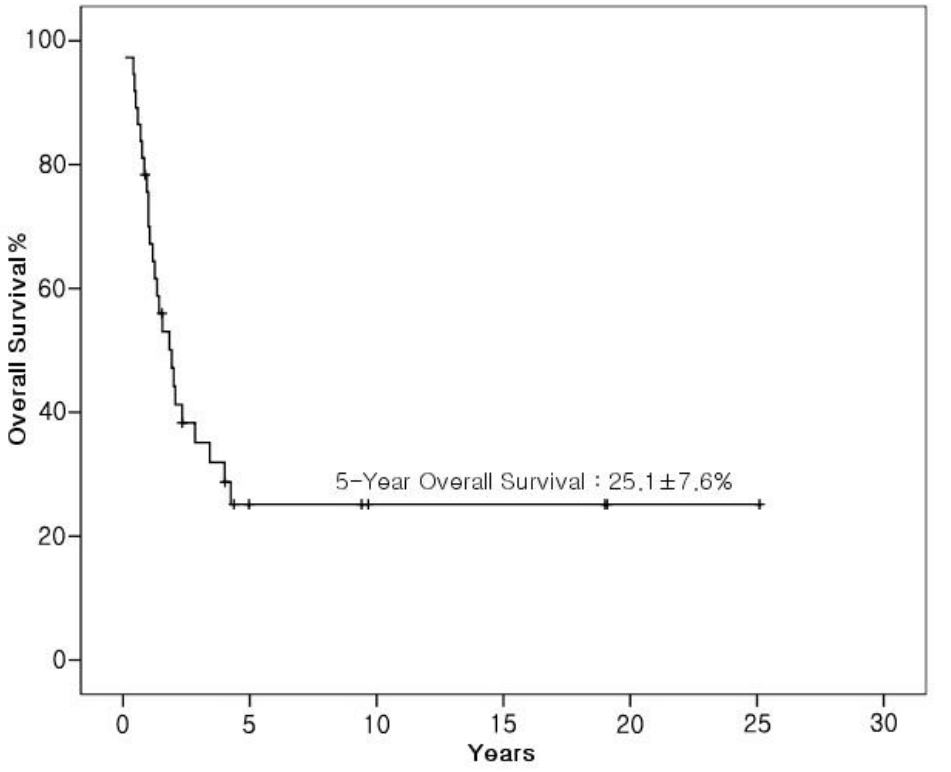

Figure 1. Overall survival in patients with advanced rhabdomyosarcoma.

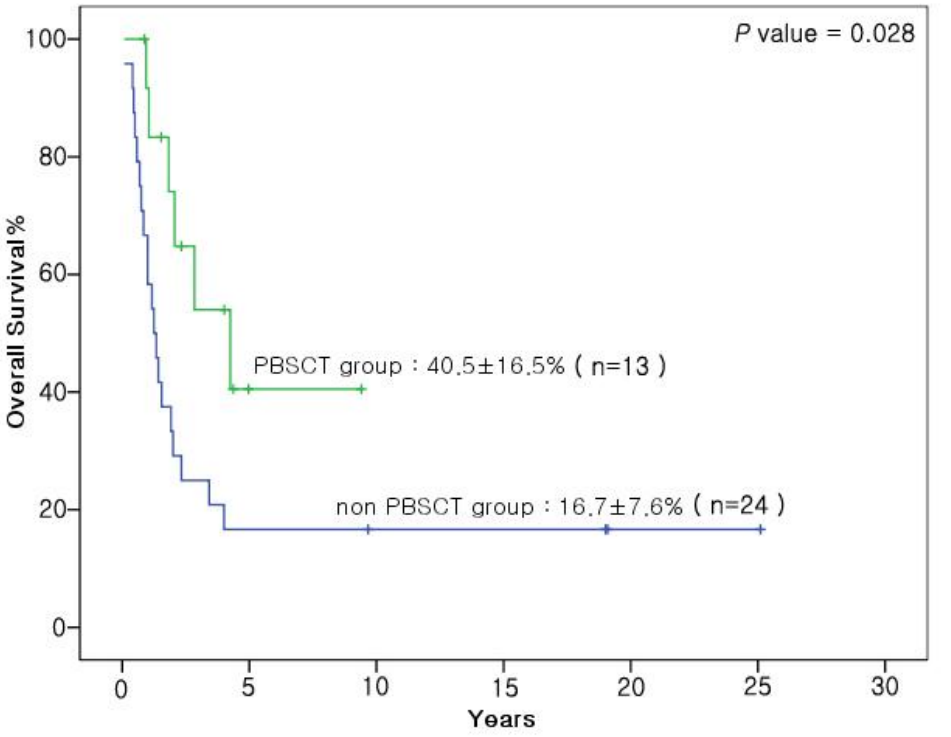

Figure 2. Overall survival in patients with high risk rhabdomyosarcoma according to high dose chemotherapy and autologous peripheral blood stem cell transplantation or not.

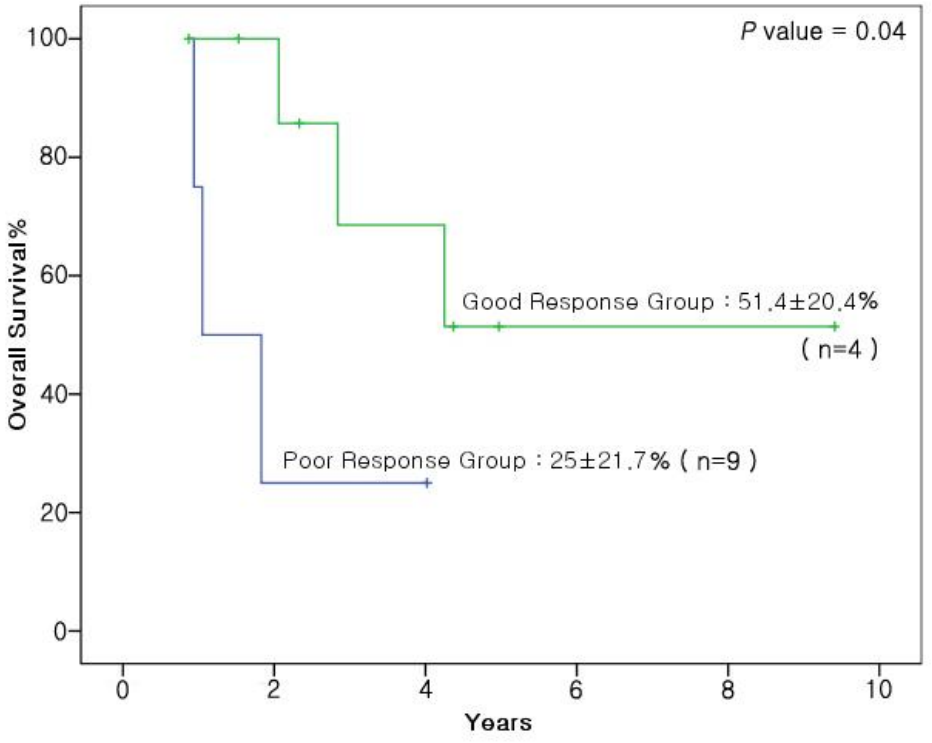

Figure 3. Overall survival in patients with high risk rhabdomyosarcoma according to the status at the time of hematopoietic stem cell transplantation.

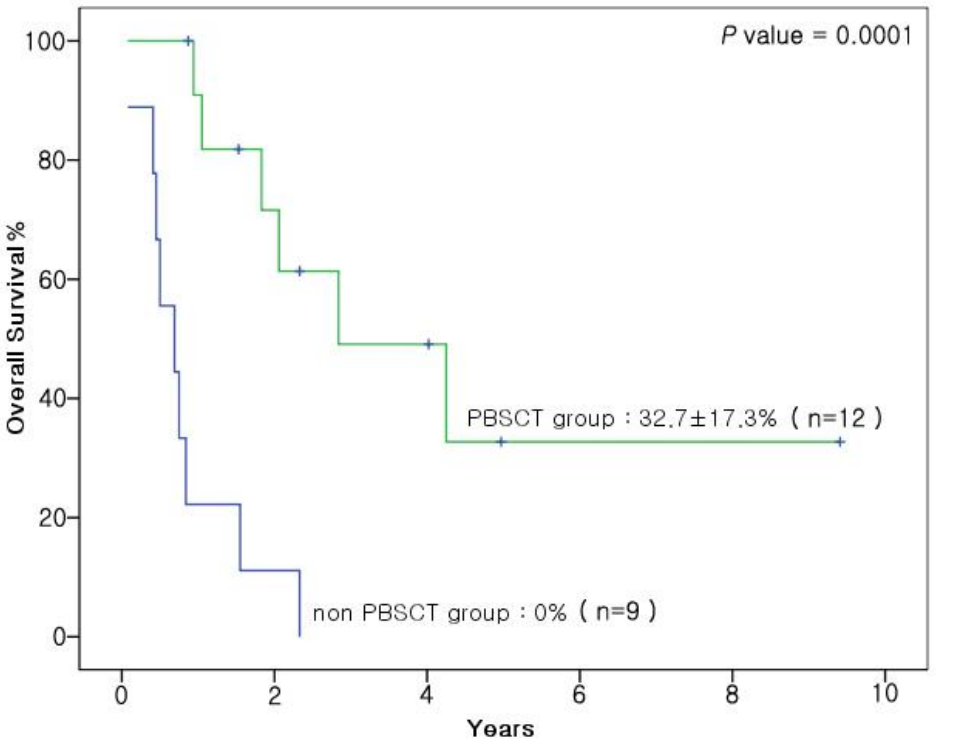

Figure 4. Overall survival in patients with very high risk rhabdomyosarcoma according to high dose chemotherapy and autologous peripheral blood stem cell transplantation or not.

IV. DISCUSSION

Chemotherapy has critical role in treatment of advanced stage RMS, because RMS is chemosensitive. Until now, several effective multi-agent chemotherapies were studied.[10,11] Van Winkle P and his fellows reported the Children's Cancer Group (CCG) experience of combination chemotherapy regimen consisted with ICE[12]. The overall response rate of 97 enrolled patients was 51% (27% complete response). After that report, conventional multi-agent chemotherapy in RMS was well established and considered as standard therapy. Finding and investigating the most effective combination of multi-agent chemotherapeutic agent is still the main stream to improve survival rate of high-risk RMS patients. But, dismal treatment results for these patients were reported until nowadays.[4,5] Therefore, HDC/APBSCT can be a new treatment option for these patients. But, it has controversy in treatment effect and safety.[6,7] This study was performed to investigate the efficacy and safety of HDC/APBSCT in pediatric high-risk RMS patients.

The aim of the present study was to report our experience on clinical

impact of HDC/APBSCT in pediatric high-risk RMS patients, which seems to be promising result as a new standard modality of treatment at high-risk pediatric RMS. Therefore, the result of this study seems to present the indication and advantage of HDC/APBSCT. Analysis of these 37 cases indicated that HDC/APBSCT can be considered as reasonable treatment option in the high-risk pediatric RMS patients with good response to conventional multi-agent chemotherapy and especially in the very high-risk group HDC/APBSCT can be a last chance to survive.

The 5-year OS of all 37 patients was 25.1±7.6%. It means that the patients reviewed in this study were classified as poor prognosis group. However, the patients undergone HDC/APBSCT had shown better prognosis than the other group. The OS of these patients was 40.5±16.5%. One of the important factors to decide whether to do HDC/APBSCT is the response to conventional multi-agent chemotherapy before HDC/APBSCT. The patients with complete remission or very good partial response had better prognosis than patients with poor response to conventional multi-agent chemotherapy before

HDC/APBSCT. As mentioned, the high-risk patients with good response to conventional chemotherapy had much more longer survival rate than poor response patients (5-year OS was 51.4±20.4%). At the time of diagnosis, far advanced patients who were classified to very high-risk patient may have no treatment option except systemic multi-agent chemotherapy. For these patients, HDC/APBSCT might be an only chance to cure. Because our study was not prospective, double blinded and controlled, our data may have selection bias. Therefore, to make a more worthy information, prospective controlled study will be needed. However, depending on these data, we can conclude that HDC/APBSCT must be considered in very high-risk or far advanced RMS patients to cure their disease. For very high-risk patients, effective and powerful local treatment methods such as radiation or operation cannot be performed. Therefore, HDC/APBSCT will be a key treatment option. However, preference towards HDC/APBSCT may lead to over treatment. The long-term complication and quality of life of patients who have undergone HDC/APBSCT is not confirmed yet. We must decide to treat with HDC/APBSCT under careful

consideration. Patient who are eligible for multi-modality of treatment must be treated with multi-modal therapy before being considered as a candidate for HDC/APBSCT.

In spite of establishment of effective conventional multi-agent chemotherapy, many advanced stage high-risk RMS show poor response to usual dose chemotherapy. Children with metastatic disease at presentation, those older than 10-years old or bone and bone marrow metastasis, had much poorer outcome. This may show that high-dose chemotherapy may have a key role in these patients.[13] Therefore, high-risk RMS patients not only with good response to usual dosage multi-agent chemotherapy but also with poor response to conventional chemotherapy can be candidates for HDC/APBST. In our study, overall survival rate in HDC/APBSCT group was higher than that of conventional multi-agent chemotherapy group and the 5-year OS in the very high-risk patients were also higher, regardless of the response to conventional multi-agent chemotherapy.

Several previous studies have shown the clinical effectiveness and survival advantages in advanced high risk RMS patients with HDC/APBSCT.[13-

[18] It is very important to decide whether RMS patient will undergo HDC/APBSCT or not. Matsubara H. and his colleagues reported a single institute experience about HDC/APBSCT in high risk RMS patients. They emphasized that high-risk RMS patients who had good response to multi-agent combination chemotherapy will have a good treatment result with HDC/APBSCT.[14] On the contrary, RMS patients with refractory nature to conventional chemotherapy will show response to HDC/APBSCT. There was a case report on a 17 year-old girl with refractory RMS after conventional chemotherapy who achieved partial remission after HDC/APBSCT.[15] In our study, about 25% of patients with poor response to conventional multi-agent chemotherapy showed efficacy to HDC/APBSCT. It means that HDC/APBSCT can be a treatment option in these extremely hopeless patents.

The patients with good response to conventional chemotherapy may be considered as a candidate for HDC/APBSCT group. However, the patients with relatively poor response to conventional multi-agent chemotherapy may not be considered as a candidate for treatment because of the high cost and uncertain

effect of HDC/APBSCT. Some decades ago, HDC/APBSCT had relatively high treatment related mortalities. This was because, there were not enough conservative treatment methods that were available, such as G-CSF. However, currently, vast methods in conservative management has improved, which resulted in a relatively safer environment for HDC/APBSCT. Therefore, HDC/APBSCT in patients refractory to conventional multi-agent chemotherapy may be possible, therefore it is necessary to conduct a randomized-controlled prospective trial in this group of patients.

However, HDC/APBSCT is not always effective and safe. As the dose of chemotherapeutic agent escalates, the effectiveness and toxicity are elevated together.[17,18] Therefore, regimen related toxicity must be considered to patients when planning HDC/APBSCT. Cancer cell contamination or resistance to high-dose chemotherapy can be a problem for HDC/APBSCT. Some patients with stage IV alveolar RMS who have experienced relapse were reported to have poor response to HDC/APBSCT.[19] It must be considered to the high-risk RMS patient that regimen related toxicity, pre-transplantation conditioning regimen,

stem cell source, cancer cell contamination for the autologous stem cell transplantation. Studies in management of long term complication and quality of life in patient with HDC/APBSCT will be needed.

Recently, other target therapy for high-risk RMS has been investigated. Topoisomerase-I and monoclonal antibody such as 8H9 will be a new window of opportunity for treatment of RMS.[8,20] It is important not only to treat RMS and reach complete remission, but also to prevent recurrence of the disease. There are some known methods which may prevent metastasis and recurrence of the disease. All-trans retinoic acid is known to be blocker of tumor recurrence and metastasis.[21]

V. CONCLUSION

HDC/APBSCT seems to achieve prolonged remission in pediatric high-risk RMS. It may be considered as a treatment option in high-risk RMS patients who are in complete remission or who show very good partial response following conventional chemotherapy. In conclusion, HDC/APBSCT will be a promising treatment modality in high-risk RMS patients for its tolerable treatment related toxicity and effectiveness.

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ABSTRACT (IN KOREAN)

고위험군 소아 횡문근육종에서 고용량 항암 치료 후 자가 조혈모세포 이식의 치료 결과

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목적: 횡문근육종은 소아에서 가장 흔한 연부조직 육종으로 높은 악성도를 보인다. 횡문근육종의 치료 성적의 향상에도 불구하고 진행된 단계의 횡문근육종의 치료 결과는 실망스러운 실정이다.

최근에 고용량 항암치료 후 자가조혈모세포이식을 하는 치료법이 진행된 단계의 횡문근육종환자에서 시도되고 있다. 우리는 이러한 고용량 항암치료 후 자가조혈모세포이식의 치료 효과를 분석해 보기 위해 단일기관에서 치료 받은 고위험군의 횡문근육종 환자의 의무 기록을 후향적으로 분석해 보았다.

방법: 세브란스병원에서 20년간 37명의 환자가 고위험군의 횡문근육종을 진단받았다. 고위험군의 환자는 stage III 혹은 IV의 환자이거나 clinical group III 혹은 IV의 환자들로 정의 하였다. 이 대상 환자들을 치료 방법에 따라 고용량 항암치료 후 자가 조혈모세포 이식을 시행한 환자군과 일반적인 다약제를 사용한 항암치료를 시행한 환자군으로 분류하였으며 이 두 환자군 사이의 5년 생존율을 비교하였다. 이 환자들의 임상 정보는 후향적으로 분석하였다.

결과: 대상환자에서 남녀 성비는 각각 남자 21명과 여자 17명 이었다.

대상 환자 연령의 중앙값은 5세 였으며 분포는 6개월에서 15세에 이르렀다. 전체 환자의 5년 생존율은 25.1±7.6%였다. 고용량 항암치료 후 자가조혈모세포이식을 한 경우와 다약제를 이용한 항암제 치료만을 한 환자군의 각각 5년 생존율은 40.5±16.5%과 16.7±7.6%로 차이를 보였다(P=0.028). 완전관해를 보이거나 항암제 치료에 반응이 좋았던 환자군에서는 고용량 항암치료 후 자가조혈모세포이식의 시행여부에 따라 더욱 큰 생존율의 차이를 보였다 (51.4±20.4% 및 25±21.7%, P =0.04). 특이 초고위험군 환자에서는 고용량 항암치료 후 자가조혈모세포이식의 여부에 따라 더욱 큰 생존율의 차이를 보였다(32.7±17.3% 및 0%).

결론: 고용량 항암치료 후 자가조혈모세포이식은 향후 좋은 치료 성적을 보이는 치료 법으로 인정받을 수 있을 것이며 특히 고위험군 환자일수록 그 효과가 더 있을 것으로 생각된다. 또한 고용량 항암치료 후 자가조혈모세포이식의 치료는 일반적인 다약제를 이용한

항암 치료에 비교적 반응을 잘 하는 고위험군 횡문근육종 환자에서 좋은 치료 결과 및 적은 독성 효과를 기대할 수 있으므로 이러한 환자군에서 하나의 치료 방법으로 고려되어야 할 것이다.

핵심되는 말: 횡문근육종, 소아암, 고용량 항암치료, 자가 조혈모세포 이식