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Retrospective analysis of adolescent and young adult with lymphoma at two cancer facilities in Japan

The concept of the adolescent and young adult (AYA) period has only recently emerged. Most important activities in human life are done in this period. It has therefore become usual to think about this group separately from children and adults. However, in Japan, treatment of lymphoma in this group is split between pediatrics and hematology [1]. This results in poor information-sharing and some confusion about who should treat and follow this group. There is therefore no precise data about lymphoma in this group collected in Japan. We aimed to clarify the prevalence of lymphoma subtype, outcomes, and long-term adverse events in this group.

We retrospectively analyzed 50 patients aged from 16 to 39 years old, who were diagnosed with lymphoma at Kansai Medical University Hospital and Kansai Medical University Medical Center from July 2004 to July 2018. All patients were treated by adult hematologist/oncologist. Their median age was 34 (16–39) years old and 62% were male. The median follow-up period was 67 (0.3–176) months. The most frequent type of lymphoma was B cell lymphoma (58%), following Hodgkin lymphoma (24%), and T cell lymphoma (18%) (Table 1). The most frequent subtype of B cell lymphoma was diffuse large B cell lymphoma (DLBCL) (21 cases), followed by follicular lymphoma (four cases), Burkitt lymphoma (two cases), and lymphoblastic lymphoma (two cases). The most frequent T cell lymphoma was mycosis fungoides (four cases), then peripheral T-cell lymphoma, not otherwise specified (PTCL, NOS) (two cases), followed by cutaneous T cell lymphoma, extranodal NK/T-cell lymphoma (ENKL), nasal type, and anaplastic large cell lymphoma, ALK positive (all one case). Among 50 patients, 48 patients received treatment in our facilities and two patients moved to other hospitals. Then, we analyzed 48 patients whom we could follow. Median overall survival (OS) and progression free survival (PFS) are not reached. 3-year OS was 91.2(78.1–96.6)% and 3-year PFS was 70.8 (54.9–81.9)%. Over all response rate was 85.4%. Mortality was 12.5%(n = 6), and the cause of death in each case was disease progression. Subtype of fatal lymphoma was DLBCL, and Hodgkin lymphoma (two cases each), and PTCL, NOS and ENKL (one case each). Relapse rate was 31.3%(n = 15). Among relapsed patients, four received a stem cell transplantation (two autologous and two allogeneic). Late onset adverse events were seen in six patients and were secondary breast cancer, hepatitis B virus reactivation, interstitial pneumonia, recurrent herpes zoster (all one case), and infertility (three cases; two female and one male). Five patients are still under treatment, and the patient with interstitial pneumonia died of disease progression. There were two patients who had sperm preservation, whereas, no patient had ovum preservation prior to treatment.

Incidence of lymphoma in AYA in Japan is different from that in Western countries [2,3]. More T cell lymphomas were seen in Japan, most of which were mycosis fungoides, and all of them had a good prognosis with oral methoxsalen (psoralen) and ultraviolet A radiation (PUVA). Recently, retrospective multicenter study of Japanese AYA-DLBCL was reported [4]. The incidence of B cell lymphoma in our study is consistent with their data, however, the frequency of T cell lymphomas is different. Our study included mycosis fungoides, which are mostly followed by dermatologists.

There were very few adverse events, but the effects were lasting. Secondary malignancy is life-threatening, and other adverse events that interfere with daily life are also serious. One thing to note is that there are three patients of infertility in this small study. Up to now, there are a few reports on infertility in lymphoma. Behringer et al. reported that low birth rate was seen in advanced stage Hodgkin lymphoma; 6.5% in women and 3.3% in men [5]. Paoli et al. detected that a high number of intensive regimens for Hodgkin lymphoma induced a permanent absence of sperm in the seminal fluid [6]. These are all reports on Hodgkin lymphoma. Regarding other lymphomas, rate of infertility is unknown. Thus, it is necessary to investigate of it as soon as possible and arrange the measures to prevent it. In our cohort, only two patients had sperm preservation and no patient had ovum preservation. We can assume various reasons for this low rate. First, it is costly. As insurance does not cover, it is self-expenses. Second, if the disease progression is aggressive, there is no time to preserve them. Furthermore, there is no smooth network to urology or gynecology department and it takes time. Now that, infertility has come to problem, we need to construct the smooth network between urology or gynecology department to preserve sperm/ovum quickly before the treatment.

Another problem in this generation is that it is difficult to follow this group effectively. Depending on life events, they may move and not attend the same hospital if they have a relapse or late onset adverse events. This cannot be helped, but it is important to encourage them to attend health checks after treatment.

The main limitation of this study was its small cohort in only two facilities. However, we believe that our data probably reflect the population of adolescents and young adults with lymphoma in Japan. It is, however, necessary to investigate the actual situation using a large-scale survey in the near future. The problem in Japan is that confusion remains about this group of patients. It is therefore important to expand awareness of their needs among healthcare workers and clarify who should treat them, as well as provide a suitable system for preservation of sperm/ovum and their follow-up care.

Declaration of Competing Interest

The authors declare no competing financial interest in relation to the work.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.lrr.2019.100174.

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Table 1
Patients' characteristics.

No. of patients(n)	50
Median age, range(y/o)	34(16–39)
Male sex(%)	62
HL(%)	24
MC	16
NS	4
LP	2
Unknown	2
B cell(%)	58
DLBCL	42
FL	8
Burkitt	4
LBL	4
T cell(%)	18
MF	8
PTCL,NOS	4
CTCL	2
ENKL	2
ALCL	2

HL: Hodgkin Lymphoma; MC: mixed cellularity; NS: nodular sclerosis; LP: lymphocyte predominant; DLBCL: diffuse large B cell lymphoma; FL: follicular lymphoma; LBL: Lymphoblastic lymphoma; MF: mycosis fungoides; PTCL, NOS: peripheral T-cell lymphoma, not otherwise specified; CTCL: cutaneous T cell lymphoma; ENKL: extranodal NK/T-cell lymphoma; ALCL: anaplastic large cell lymphoma.

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