

Pediatric Oncology Division

Introduction

The Pediatric Oncology Division handles a wide variety of malignancies in children and adolescents. The pediatric ward (12A) has gathered around 100 patients with pediatric malignancies per year, who are referred from hospitals located throughout Japan and other Asian countries including Taiwan, Korea, and so forth. The diseases we treat include both hematological malignancies such as acute leukemias and malignant lymphomas, and solid tumors such as soft tissue sarcomas, neuroblastoma, Wilms tumor and retinoblastoma.

Based on the heterogeneity of the disease-spectrum, we have built up a multidisciplinary network with other divisions, such as surgery (including orthopedic surgery, neurosurgery, urology, and ophthalmology), radiation oncology, and hematopoietic stem cell transplantation (SCT). Although SCT procedure is usually performed in the transplantation ward (12B), the 12A also can accept patients undergoing autologous SCT.

A special nursing care system in the ward helps young patients and families physically as well as psychologically. Nurses provide appropriate information to help patients and families to keep their ideal relationship. To elevate the quality of hospital life of young patients, an educational opportunities ranging from elementary school to a high school are available in the pediatric ward, where 9 teachers work daily. For inpatients' families who come from distant areas, the Family Houses are available with inexpensive accommodation fees in several areas in Tokyo.

Routine Activities

The division has two staff pediatricians, and several trainees. The pediatric outpatient service opens on Monday, Wednesday, and Thursday to see new

patients and provide follow-up treatment to patients who have completed intensive treatment course. The pediatric staffs and trainees discuss various issues in pediatric inpatients on round on a daily basis. Patients undergo various procedures in a timely manner, sometimes under IV sedation. These procedures include diagnostic bone marrow aspiration/biopsy, central venous catheter placement, and lumbar puncture/ intrathecal chemotherapy. The Pediatric Conference is held in Wednesday afternoon mainly for the decision-making of individual treatment plan. The pediatric staffs also join in the Transplant Conference on Monday, Wednesday and Friday and the Orthopedic Surgery Conference on Tuesday. There are several academic meetings for educational purpose such as the Hemato-oncology Journal Club on Wednesday morning.

The common approach to the diseases is "risk-adapted therapy" regarding the long-term life-expectancy. Patients with solid tumors receive multidisciplinary therapy, including surgical removal of the tumor, radiation therapy, chemotherapy, and sometimes SCT as indicated. Patients with hematological malignancies usually receive induction or re-induction chemotherapy first. Then, they are assigned either to chemotherapy course or SCT course based on the risk of the disease. Since the main reason of referral of the patients is the refractoriness of the diseases to conventional therapies, many of the patients are applied SCT in either autologous or allogeneic settings.

Research Activities

I. New treatment strategy for refractory solid tumors in children and young adults

(1) Double autologous SCT following high-dose chemotherapy

This strategy is now applied for Ewing sarcoma and germ cell tumor. Because the data seem

promising, study protocols are under construction.

(2) Nonmyeloablative/reduced intensity SCT (Mini-SCT)

The objective of this study is to evaluate safety and efficacy of mini-SCT on refractory solid tumors with an expectation of immunological eradication of residual tumors by allografts (graft-versus-tumor effect). This collaborative study with the SCT division is ongoing and results of case-series were presented at annual meeting of American Society of Pediatric Hematology Oncology.

II. Establishment of optimal treatment strategy for patients with retinoblastoma (RB)

(1) Local ophthalmic therapies for RB

In order to facilitate the strategy in local ophthalmic therapies (LOT), we need to develop strong salvage therapies for patients who relapsed on or after the LOT. We are pursuing a risk-adapted treatment strategy for RB patients with good QOL, based on the retrospective data of risk factors. A manuscript for publication is in process.

(2) Adjuvant chemotherapy for advanced RB

Adjuvant chemotherapy using a combination of cyclophosphamide, vincristine, pirarubicin, etoposide, carboplatine is needed in patients with advanced retinoblastoma. Patients with central nervous system disease need autologous SCT. The data of case series are currently being gathered to make retrospective analyses to evaluate safety and efficacy of this strategy.

Clinical Trials

As a result of our activity on renewing systems for multi-center clinical studies in pediatric oncology in Japan, a Grant-in-Aid for Scientific Research from the Ministry of Health, Labor and Welfare was awarded in order to facilitate our activity. A pediatric data center is being organized in our department as several study protocols are being made. The protocols listed below will be submitted to IRB in early 2004.

(1) Phase III open randomized controlled trial to compare bone marrow and blood stem cell as an allogeneic graft for treatment of leukemia.

(2) Phase II trial to test intensive induction chemotherapy and autologous stem cell transplantation for advanced rhabdomyosarcoma.

(3) A GCP-based phase I-II trial using irinotecan for pediatric solid tumor is currently being planned. The purpose of this study is to have this medicine approved by the Ministry of Health, Labor and Welfare in terms of usage for pediatric solid tumors.

Patient Statistics

A total of 98 patients were hospitalized to the pediatric ward in 2002. Most patients had a solid tumor; less than 20 % of them had a hematological malignancy. Four patients underwent autologous SCT and three patients underwent allogeneic SCT in 2003.

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Table: Number of Pediatric Inpatients

	2003
Retinoblastoma	34
Acute myelogenous leukemia	3
Acute lymphoblastic leukemia	6
Osteosarcoma	10
Brain tumor	7
Non-Hodgkin's lymphoma	6
Rhabdomyosarcoma	6
Neuroblastoma	4
Ewing's sarcoma/PNET	3
Synovial sarcoma	1
Germ cell tumor	3
Others	14
Total	98