

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 treat 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 Tuesday morning mainly for the decision-making of individual treatment plan. The pediatric staffs also join in the Transplant Conference on Monday and Thursday and the Orthopedic Surgery Conference on Tuesday. There are several academic meetings for educational purpose such as the Pediatric Oncology Data Center meeting on Thursday afternoon, and Pediatric Journal Club on Friday afternoon.

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 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 is a collaborative study with the SCT division.

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

(1) Local ophthalmic therapies for RB

Accurate evaluation for local ophthalmic therapies (LOT) is needed. We are currently making some retrospective studies to gather basic data of the safety and the efficacy of each LOT modality.

(2) Adjuvant chemotherapy for advanced RB

Adjuvant chemotherapy using a combination of cyclophosphamide, vincristine, pirarubicin, etoposide, carboplatin is needed in patients with advanced retinoblastoma (Makimoto). Patients with central nervous system disease need autologous SCT. The data of case series (Matsubara et al.) are accepted and being published.

Clinical Trials

I. The Pediatric Data Center and clinical trials using drugs commercially available

The Pediatric Oncology Data Center was established by a Grant-in-Aid for Scientific Research from the Ministry of Health, Labor and Welfare. 'The Phase II trial to test intensive induction chemotherapy and autologous stem cell transplantation for advanced rhabdomyosarcoma' is currently open for patients' entry. Other two trials for Ewing's sarcoma and acute lymphoblastic leukemia will be applied to the IRB in March.

II. Physician-initiating clinical trial for new drug approval

A GCP-based phase I-II trial using irinotecan for pediatric solid tumor is currently being planned. Although the infrastructures to perform physician-initiating clinical trials are still immature, we plan to start this trial in the early 2005 as one of the model cases of this type of trial.

Patient Statistics

A total of 92 patients were hospitalized to the pediatric ward in 2004. Most patients had a solid tumor including retinoblastoma, while less than 20 % of them had a hematological malignancy (see Table). The more activities to recruit newly diagnosed patients to the clinical trials are needed.

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Table: Number of Pediatric Inpatients

	2003	2004
Newly Diagnosed	22	26
Acute myelogenous leukemia	1	2
Acute lymphoblastic leukemia	4	2
Non-Hodgkin's lymphoma	1	7
Rhabdomyosarcoma	4	3
Ewing's sarcoma/PNET	2	4
Osteosarcoma	0	4
Neuroblastoma	2	1
Kidney tumors	1	1
Germ cell tumor	3	2
Advanced retinoblastoma	3	0
Histiocytosis	1	0
Relapsed	8	8
Acute lymphoblastic leukemia	2	6
Non-Hodgkin's lymphoma	2	0
Rhabdomyosarcoma	1	0
Neuroblastoma	1	0
Osteosarcoma	0	1
Localized Retinoblastoma	46	58
Total	76	92