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The history of oncohematology development at the Kazakh Institute of Oncology and Radiology

The article is devoted to the history of the creation and development of the Oncohematology Department at the Kazakh Institute of Oncology and Radiology (KazIOR). For the first time, the authors talk about the development of oncohematology at KazIOR during the Soviet period in the USSR and the Kazakh SSR, and later – in independent Kazakhstan. They also describe the role of the institute directors and the contribution of the department heads at different stages of its history and share information about introducing new modern methods of diagnosing malignant lymphomas and new technologies for treating hemoblastosis. The authors also highlight the current topical problems of oncohematology and ways to solve them.

Keywords: *the establishment of hematological service, harmful anthropogenic factors.*

Healthcare is designated as the national priorities of the modern social and economic development in Kazakhstan as a sovereign state. The National Programme for Healthcare Reform and Development prioritizes a systematic transition to international standards, new technologies, modern methods of treatment, and medical care, as well as the prevention, diagnosis, and treatment of socially significant diseases. The problems of oncohematology are topical issues today in this context.

The establishment and development of the hematological service in the Republic of Kazakhstan (RK) occurred in the mid-1960s when hematological hospitals were opened for the first time in the USSR; the training of specialists began. Its need was caused by the gradual increase in the incidence of malignant tumors (MT), including hematological diseases. The first hematological departments in Kazakhstan were opened in 1963 in two cities – 60 beds in Alma-Ata (in City Clinical Hospital (CCH) No. 7 of Kalkaman Village) for and Karaganda for 40 hospital beds. The number of hematological beds for adult patients increased up to 129 in the 1970s in Kazakhstan.

The number of patients with hematological diseases in Kazakhstan has grown because of the increase in the influence on the harmful anthropogenic factors on the human body (the result of Semipalatinsk Nuclear Test Site (SNTS) activity, the accident at the Chernobyl Atomic Power Station (APS), uranium mining by an open method in Stepnogorsk, the Ust-Kamenogorsk zinc-lead plant activity, etc.).

In 1983, hematological departments were established in various regions of the USSR, including the Hematological Center based at the Central Order of Lenin Institute of the blood transfusion (COLIBT) in Moscow, by order of the USSR Minister of Healthcare. A lymphogranulomatosis (LGM) department based on the Kazakh Research Institute (RI) of Oncology and Radiology for 20 beds was organized in summer 1983 by order of the USSR Minister of Healthcare and the corresponding Order of the Kazakh SSR Minister of Healthcare. At that time, Professor Odak Kabievich Kabiev, the then Director of the Institute, made a tremendous contribution to the Department's organization and development.

From 1983 to 1988, the Department was headed by an excellent hematologist, Candidate of Medical Sciences Shakar Zhartovna Balgozhina, who graduated from postgraduate school at the Hematological Center in Moscow and defended her thesis under the authority of the Academician Joseph Abramovich Kassirskiy. Later, Sh.Zh. Balgozhina trained and raised several generations of hematologists.

The Department mainly treated patients with LGM, lymphosarcoma (Non-Hodgkin lymphomas, NHL), myeloma, less often – chronic lymphoid and myeloid leukemia. At that time, the Department acted as the Republican Center for Diagnostics and Treatment of Malignant Lymphomas and provided specialized medical care to all Kazakhstani citizens.

Treatment was performed only under cytological examination of bone marrow and histological examination of biopsy material. Shakar Zhartovna herself performed bone marrow aspirations, deciphered myelograms, and made a diagnosis.

In 1989, the Director of KazIOR Professor A.A. Beisebayev combined the LGM department with the tumor chemotherapy department led by a chemotherapist Professor Boris Vasilievich Monakhov. They emphasized the polychemotherapy method in the treatment of patients having MT. Combined treatment was the main therapy method for patients with MT in the Department. Drug therapy was performed in COPP, CVPP, and ACOP regimens, including such medicines as cyclophosphamide, vincristine, vinblastine, methotrexate, natulan, 6-MP, adriablastin, prednisolone, etc.

Later, radiation therapy became the dominant method in the treatment of LGM patients. With the occurrence of the linear accelerators ЛУЭВ 15M1 and Clinac 2100, treatment with fast electrons was widely introduced into clinical practice in the form of radical radiation therapy above and below the diaphragm up to cumulative dose (CD) of 40-42 Gy. With this therapy, a five-year relapse-free survival (RFS) of patients with I-IIA and B LGM stages reached 85.0-90.0%. The author of this program – Professor G.D. Baisogolov from the Institute of Medical Radiology (Obninsk, Russia) of the RF Ministry of Healthcare – was awarded the Lenin Prize.

The name of the LGM department changed with the arrival of each new head of the institute. In 1991, the Corresponding Member of the Academy of Sciences of the Kazakh SSR, Professor Zh.N. Abdrakhmanov, was appointed the Director of the Institute. He renamed the LGM department to the Lymphoma Radiation Therapy Department under its work direction.

From 1991 to 1995, the Department was led by a radiologist, Doctor of Medical Sciences, Professor N.A. Agigaliev. As a specialist in radiology, he concentrated on radiation therapy in the treatment of lymphomas. Besides patients having lymphoma, the Department began to take patients with other serious tumors for radiation therapy.

From 1998 to 2006, the Department was led by the Doctor of Medical Sciences, Professor R.K. Karakulov, one of the originators of this Department's creation. Professor Karakulov always defended the status of the Department at the Kazakh SSR Ministry of Healthcare. At that time, the Department had 30 hospital beds. The patients with Hodgkin's lymphoma, NHL, multiple myelomas, chronic myeloid leukemia, chronic lymphocytic leukemia, and other localizations were treated at the Department. New diagnostic methods were introduced: the immune histochemical test (IHC) method for lymphomas, a study of the proliferative tumor pool for patient-specific treatment. Besides, new technologies of treating refractory lymphomas using a radio modifier were introduced, e.g., intratumoral administration of metronidazole with subsequent radiation therapy. The use of immunomodulators (interferon inducers) during radiation therapy has reduced post-radiation complications, particularly post-radiation pulmonitis, by 40%. Monoclonal antibodies (rituximab, brentuximab, etc.) were used for the first time in Kazakhstan for refractory forms of the NHL and CL.

The Department had its scientific direction for the first time in its history: "The use of radio modifiers and immunomodulators in the radiation therapy of malignant lymphomas." Employees of the Department received ten patents for inventions, twice won Grants from the RK Ministry of Education and once – from the RK National Academy of Sciences. Candidate's and doctoral theses were defended on that topic. When being the head of the Department, Professor Karakulov prepared 5 Candidate of Medical Sciences and two Doctors of Medicine.

The Department is an educational base for KazNMU bachelors, KazIOR, and KazNMU interns and residents. The Department has trained nine resident hematologists for the RK regions during the last five years. Two employees study for a higher doctorate at KazIOR and Al-Farabi Kazakh National University. The Department employees take an active part in annual congresses of the European Hematological Association (ENA) and the annual Eurasian Hematological Congress in Turkey. Employees received advanced training at the Institute of Pediatric Oncology, Hematology, and Transplantology named after R.M. Gorbacheva (St. Petersburg) for stem cell separation and HSC autotransplantation.

Professor Karakulov published more than 350 scientific papers, including 53 foreign publications, two monographs, one book, one methodological recommendation. For a decade, he headed the primary NurOtan party cell at KazIOR, which took first place thrice among other party cells of the Almalinsky district and was second among other NurOtan party cells in Almaty. Several times R.K Karakulov was awarded diplomas of the First President of Kazakhstan N.A. Nazarbayev and President of Kazakhstan K.-J. Tokayev, the medal "Excellent Healthcare Worker of the USSR," "Jubilee Medal," and the badge "Inventor of the USSR."

In 2009-2010, the Department was led by a hematologist, Doctor of Medical Sciences S.Ye. Sultangazieva. Under her leadership, the Department retained its name as the Hemoblastosis Department. The 30-beds Department provided care to patients with chronic lymphomas and leukemia. Svetlana Yeleusizovna was the first to introduce cytological and molecular-genetic analysis for lymphomas and chronic leukemia. The research was performed under the contract based on the Research Institute of Obstetrics and Gynecology of the RK Ministry of Healthcare.

From 2011 up to this day, the Department is headed by Saule Telembaevna Gabbasova, Ph.D., hematologist of the highest category. When she came, positive changes occurred in the Department. Almost all Department employees were trained at the R.M. Gorbacheva Institute of Pediatric Oncology, Hematology, and Transplantology. They mastered such new modern methods to diagnose leukemia, as cytogenetic studies of the bone marrow, FISH-study of the biopsy, and bone marrow. For the first time, the high-dose PCT method was used in refractory forms of lymphomas, leukemia, and multiple myelomas. Since 2014, the method of HSC autotransplantation was implemented into the Department's practice. In six years, more than 40 HSC autotransplantations were performed in patients with hemoblastoses. The introduction of this method has improved the RFS and the patients' quality of life. Since 2018, as part of the Grant Study, the Department is studying the gene expression profile to identify molecular subgroups in B-cell NHL for patient-specific therapy. All the positive changes in the Department happened thanks to the support of the current Director of the Institute, Doctor of Medical Sciences, Academician D.R. Kaidarova. A 45-beds Center for Hematology and Bone Marrow Transplantation was established at KazIOR due to the growing number of patients admitted to the Department.

Since 2019, the oncohematology department changed its name to the Center for Hemoblastosis and Bone Marrow Transplantation. Patients come from all RK regions; they are provided with highly specialized care (high-dose PCT and HSC autotransplantation in lymphomas, leukemia, and multiple myeloma). Besides, a new generation of monoclonal antibodies is used in lymphomas and multiple myeloma.

Considering the constant growth in the number of patients with hemoblastoses in Kazakhstan, especially in the southern and western regions of the country, and the incomplete coverage with sanitary and epidemiological measures to prevent post-transplantation complications, it is advisable to create a separate hematological institute that would develop and widely apply modern methods of auto- and allogeneic transplantation and immune polychemotherapy for patients from western and southern RK regions.

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ТҰЖЫРЫМ

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Қазақ онкология және радиология ғылыми-зерттеу институтындағы онкогематологияның даму тарихы

Мақала Қазақ онкология және радиология ҒЗИ-ның онкогематология бөлімшесінің құрылу және даму тарихына арналған. Алғаш рет мақала авторлары Қазақ онкология және радиология ғылыми – зерттеу институтында КСРО мен Қазақ КСР дәуіріндегі, кейінірек Тәуелсіз Қазақстандағы онкогематологияның даму тарихы туралы ақпарат берді. Сондай-ақ, институт директорларының рөлі мен бөлім басшыларының бөлімше тарихына әртүрлі кезеңдерде қосқан үлесі туралы айтылады. Мақалада бөлімшенің даму кезеңінде қатерлі лимфомаларды диагностикалаудың жаңа заманауи әдістері және гемобластоздарды емдеудің жаңа технологиялары енгізілгені туралы мәліметтер келтірілді. Сонымен қатар, мақала авторлары онкогематологияның өзекті мәселелерін және оларды шешу жолдарын көрсетеді.

Түйін сөздер: *гематологиялық қызметтің қалыптасуы, зиянды антропагенді факторлар.*

АННОТАЦИЯ

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История развития онкогематологии в Казахском НИИ онкологии и радиологии

Статья посвящена истории создания и развития отделения онкогематологии в Казахском НИИ онкологии и радиологии. Впервые авторами статьи приведены сведения о развитии онкогематологии в Казахском НИИ онкологии и радиологии в эпоху СССР и Казахской ССР, позже – в независимом Казахстане. Также рассказывается о роли директоров института и вкладе руководителей отделения на разных этапах его истории. Приведены сведения о том, на каком этапе развития отделения были внедрены новые современные методы диагностики злокачественных лимфом и новые технологии лечения гемобластозов. Кроме того, авторы статьи указывают на актуальные проблемы онкогематологии и пути их решения.

Ключевые слова: *становление гематологической службы, вредные антропогенные факторы.*