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History of the Center of Morphological Research of the Kazakh Research Institute of Oncology and Radiology and its contribution to the development of oncological service in the Republic of Kazakhstan

The article is devoted to the history of the Center of morphological research at the Kazakh Institute of Oncology and Radiology (KazIOR). The initial Pathomorphology Laboratory was established in 1960 under the leadership of the Candidate of Medical Sciences I.A. Zakhvatkina. The Problem Laboratory of Pathomorphology and Geographic Pathology of Tumors was created later in 1964 and was headed by the Doctor of Medical Sciences, Professor N.I. Kolychev since 1972.

Modern morphological diagnostics methods introduced into practice during the laboratory existence included an immunohistochemical examination of tumors, electron microscopic examination, and FISH (fluorescent in situ hybridization) diagnostics.

Today, the Center for Morphological Studies provides methodological, organizational, and advisory assistance to oncological dispensaries and other medical institutions of the Republic of Kazakhstan in malignant neoplasms' diagnostics.

Keywords: Pathomorphological Laboratory, geographical pathology, Center of Morphological Studies.

The Pathomorphology Laboratory at the Kazakh Institute of Oncology and Radiology (KazIOR) was established in 1960 as part of the implementation of one of the priority tasks set by Saken Nugmanovich Nugmanov, the first director of the Institute, Honored Doctor of the Kazakh SSR, associate professor of the Department of Obstetrics and Gynecology of

Kazakh State Medical Institute. The task was to construct additional clinical buildings and an independent building for pathomorphology and cytology needs.

The Pathomorphology Laboratory, headed by Iraida Afrikanovna Zakhvatkina, was arranged in the experimental morphology building (Figures 1, 2).

Figure 1 – The first director of KazIOR, Prof. S.N. Nugmanov; Doctor of Medical Sciences N.I. Kolycheva; a pathologist from India; Associate Professor, Candidate of Medical Sciences Iraida Afrikanovna Zakhvatkina (the first head of the Pathomorphology Laboratory)

Figure 2 – Employees of the Pathological Anatomy Department of the Alma-Ata State Institute for Advanced Medical Studies (AGIUV): Associate Professor, Candidate of Medical Sciences I.A. Zakhvatkina; the Head of AGIUV Pathological Anatomy Department, Prof., Doctor of Medical Sciences A.I. Zikeeva; assistants of the Department A.Ya. Khatskeles, G.N. Kiykbaeva and others (1960-63)

In 1964, the development of a new direction in oncology – morphological epidemiology provoked the establishment of the Problem laboratory of pathomorphology and geographical pathology of tumors on the basis of the Pathomorphology Laboratory. In 1972, both laboratories were combined under the leadership of Doctor of Medical Sciences, Professor Nelli Ivanovna Kolycheva.

Main scientific areas of the Laboratory activities included geographical pathology and epidemiology of precancer and cancer of the upper digestive tract, the study of the boundary of the propagation of malignant tumors in the Kazakh SSR, the elucidation of the role of the climatic characteristics of the various areas of the country, the impact of nutrition, bad habits, some national customs in the occurrence of precancerous diseases and malignant tumors.

This served for the establishment in the city of Guryev (current Atyrau) of a KazIOR branch studying esophagus pathology. From 1976 to 1985, Doctor of Medical Sciences Kh.A. Abisatov was the head of the branch and the chief physician of the regional oncological dispensary. The branch staff, together with the staff of the laboratories of morphological epidemiology (headed by Prof. N.A. Kolycheva), cytology (headed by Prof. A.I. Shibanova), and carcinogenesis and tumor prophylaxis (headed by Prof. M.A. Karimov), studied the endogenous and exogenous factors contributing to the emergence of precancerous diseases and cancer of the esophagus in the population living in the Caspian lowlands and the pathogenesis of pathological processes in the esophageal mucosa. Together with the staff of the Clinical Cancer Prevention Department (headed by Prof. M.I. Dauletbakov, then Prof. B.V. Monakhov), they actively conducted secondary prevention of esophageal cancer under the Republican program "Esophagitis."

The results obtained established the possibility of preventing esophageal cancer. The esophageal cancer incidence of in the Guryev region has decreased from 84.2°/0000 in 1974 to 41.4°/0 in 1985. In the Republic as a whole, the esophageal cancer incidence has decreased from 27.8 to 11.2°/0000, that is more than twice over 30 years (1970-2000) (Figure 3).

The Laboratory was the basis for the WHO reference centers that created International histological classifications on the complex topic of "Malignant neoplasms" (oropharyngeal tumors, tumors of the esophagus and stomach, tumors of the upper respiratory tract) together with the CMEA member countries. The Laboratory has extensively collaborated with many scientific teams of Kazakhstan and the USSR and participated in the International IARC projects (Figure 4).

In 1982, prof. N.I. Kolycheva was awarded the USSR State Award for the research in the morphological epidemiology of precancer and cancer of the esophagus in the Kazakh SSR. Twenty-five candidates' and five doctoral theses on this topic were defended under her leadership.

The Laboratory became the basis for the first cancer epidemiology researches in Kazakhstan. A series of works on morphological epidemiology of esophageal precancer and cancer conducted by N.I. Kolycheva, N.M. Alexandrova, G.K. Kusakina, A.P. Pozdnyakova, G.V. Fedotovskikh, K.A. Ayapov, S.Kh. Adilgireeva, M.A. Sharipova, S.S. Samratova, M.N. Kadyaikina, V.A. Chizhov, and others contributed to a sharp decrease in esophageal cancer incidence in Kazakhstan. The morphology and epidemiology of breast cancer (N.N. Serova, A.Zh. Abdrakhmanova), colorectal cancer (G.A. Khamidullina), lung cancer (E.G. Sokolenko), and some other cancer localizations were also studied.

Figure 3 – At a microscope in the Laboratory: Head of the Laboratory, Prof. N.I. Kolycheva; junior researcher S.S. Samratova; senior researcher, Candidate of Medical Sciences G.K. Kusakina; senior researcher, Candidate of Medical Sciences N.M. Alexandrova (1979)

Figure 4 – International conference (Prof. N.N. Blokhin, Prof. N.I. Kolycheva, Prof. O.K. Kabiev, senior researcher, Doctor of Medical Sciences M.A. Karimov, et al.).

Figure 5 – Candidate of Medical Sciences G.A. Khamidullina, head of the Pathomorphology Laboratory (2002-2010)

In 2002-2007, the Pathomorphology Laboratory was headed by the Candidate of Medical Sciences Galina Asgadulovna Khamidullina. She supervised the introduction of immunohistochemistry as a diagnostic method for tumor histological clarification and electron microscopic

examination for scientific and practical use. The laboratory team began cooperation with scientists from the UK, Japan, Austria, Hungary, and other countries on IHC diagnostics of tumors (Figure 5). From 2007 to 2010, the Laboratory was headed by Zarihto Vladimirovich Takhayev.

From 2010 to 2017, Candidate of Medical Sciences Ekaterina Grigorievna Sokolenko was the head of the Laboratory of Pathomorphology, Cytology, and Molecular Pathology of Tumors. In 2013, they introduced the FISH (fluorescent in situ hybridization) method to determine the HER2 gene amplification with breast cancer. The laboratory equipment for preparation, staining, and examination of micro preparations was updated (Figure 6).

Since 2017, the Laboratory became a Center for Morphological Studies headed by Candidate of Medical Sciences Elvira Bolatovna Satbaeva. Today, the Center staff includes

physicians: Candidate of Medical Sciences N.A. Mukhametgaliev, Candidate of Medical Sciences M.N. Akhmetkaliev, Candidate of Medical Sciences N.T. Artykbaeva, Candidate of Medical Sciences G.N. Orzbekova, N.B. Anarbaev, I.O. Kovchegov, Candidate of Medical Sciences E.E. Iskakova, R.E. Eslyamov, D.T. Zhandildina, B.T. Kusainova, and Zh.B. Eleubaeva; biologists: S.A. Lyubko and I.A. Perova; senior laboratory assistant A.B. Koishybaev. Vladimir Pavlovich Merkulenko, the oldest employee of the Center, who untimely died of the coronavirus, was posthumously awarded the Order of "Kurmet" [Respect] on behalf of the President of Kazakhstan.

Figure 6 – Employees of the Department of Pathomorphology, Cytology, and Molecular Pathology, 2010:

E.G. Sokolenko, F.Kh. Mukhamedova, M.A. Nursuleimenova, M.V. Ivakin, K.A. Fayzullaeva, Zh. Musabekova, Zh. Umirgalieva, M.M. Zhamanov, A.Kh. Tokbaeva, V.P. Merkulenko, G. Kusakin (left to right)

In total, the Center has 43 employees who conduct all kinds of morphological diagnostics: histological, immunohistochemical diagnostics of cancerous and precancerous processes, tests for sensitivity to targeted, biological and immunological drugs, cytological diagnostics of puncture biopsy material and smears, immunophenotyping of bone marrow and peripheral blood, molecular genetic studies – SISH for determining HER2-status with breast and stomach cancers, FISH-studies of ALK-status with non-small cell lung cancer, PD-L1 examination with non-small cell lung cancer, bladder cancer, head and neck cancer.

The Center for Morphological Studies provides methodological, organizational and advisory assistance in cancer diagnostics to oncological dispensaries and other medical institutions of the Republic of Kazakhstan. The Center staff have developed and introduced into daily practice international standards for the study of the breast, prostate, lung, stomach, colon, esophagus cancer, and other tumors. In their daily routine, doctors use modern WHO classifiers and specialized literature, participate in numerous master classes, conferences, seminars, round tables, and webinars. The wide use of

the telepathology system allows providing consultations online and discussing diagnoses with domestic and foreign colleagues. The Center trains future pathologists and laboratory assistants-histologists for regional dispensaries, as well as residents, undergraduates, doctoral students of various departments of the Institute. The Center's employees participate in research grants in various fields, including lung cancer, colorectal cancer, lymphoproliferative diseases, thyroid cancer, head and neck cancer.

Academician D. Kaidarova, director of KazIOR, and E.B. Satbaeva, head of the Center for Morphological Research, provided methodological and advisory support in creating a laboratory of pathomorphology and immunohistochemical diagnostics at the Mangistau Oncological Dispensary and equipping pathomorphology laboratories in the cities of Petropavlovsk, Taraz and Atyrau.

Employees of the Center of Morphological Studies participate in the preparation and holding of congresses, conferences with international participation, webinars, and workshops. The Center is among the developers and implementers of the Comprehensive Cancer Control Plan 2018 - 2022 (Figure 7).

Figure 7 – Pathomorphology Section of the VII Congress of Oncology and Radiology, Nur-Sultan, 2019.

ТҰЖЫРЫМ

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Қазақ онкология және радиология ғылыми-зерттеу институты морфологиялық зерттеулер орталығының тарихы және оның Қазақстан Республикасының онкологиялық қызметін дамытуға қосқан үлесі

Мақала Қазақ онкология және радиология ғылыми-зерттеу институтының (бұдан әрі – ҚазОжРФЗИ) морфологиялық зерттеулер орталығының тарихына арналады. Патоморфологиялық зертханасы 1960 жылы м.ғ.к. И.А. Захваткинаның жетекшілігімен ұйымдастырылды. 1964 жылы ісіктердің географиялық патологиясы және патоморфология проблемалық зертханасы құрылды, оны 1972 жылдан бастап медицина ғылымдарының докторы, профессор Н.И. Колычева басқарды.

Зертхана жұмыс істеген кезеңде морфологиялық диагностиканың заманауи әдістері - ісіктерді иммуногистохимиялық зерттеу, электрондық-микроскопиялық зерттеу, FISH-диагностикасы (in situ флуоресценттік будандастыру) енгізілді.

Морфологиялық зерттеулер орталығы қатерлі ісіктерді диагностикалауда Қазақстан Республикасының онкологиялық диспансерлеріне және басқа да емдеу мекемелеріне әдістемелік, ұйымдастырушылық және консультациялық көмек көрсетеді.

Түйінді сөздер: патоморфология, патоморфологиялық зертхана, географиялық патология, морфологиялық зерттеу орталығы.

АННОТАЦИЯ

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История центра морфологических исследований Казахского НИИ онкологии и радиологии и его вклад в развитие онкологической службы Республики Казахстан

Статья посвящена истории Центра морфологических исследований Казахского НИИ онкологии и радиологии (КазНИИОР). Лаборатория патоморфологии была организована в 1960 году под руководством к.м.н. И.А. Захваткиной. В 1964 году была создана Проблемная лаборатория патоморфологии и географической патологии опухолей, которую с 1972 года возглавляла д.м.н., профессор Н.И. Колычева.

За период существования лаборатории были внедрены современные методы морфологической диагностики - иммуногистохимическое исследование опухолей, электронно-микроскопическое исследование, FISH-диагностика (флуоресцентная гибридизация in situ).

Центр морфологических исследований оказывает методическую, организационную и консультативную помощь в диагностике злокачественных новообразований онкологическим диспансерам и другим лечебным учреждениям Республики Казахстан.

Ключевые слова: лаборатория патоморфологии, географическая патология, центр морфологических исследований.