UDC: 616.428

DOI: 10.52532/2663-4864-2023-1-67-50-53

KIKUCHI-FUJIMOTO DISEASE: THE FIRST CLINICAL OBSERVATION OF A RARE CASE IN KAZAKHSTAN

M.I. SELIVANOV[1], L.G. TURGUNOVA[1], A.V. ZINCHENKO[2], O.V. BRUNER[2]

[1]«Karaganda medical university» NCJSC, Karaganda, the Republic of Kazakhstan;
[2]«Center of Hematology» LLP, Karaganda, the Republic of Kazakhstan

ABSTRACT

Relevance: *Kikuchi-Fujimoto disease (KFD), also known as histiocytic necrotizing lymphadenitis, is a rare underlying cause of benign lymphadenopathy, typically accompanied by fever and fatigue. Diagnosing this rare condition causes difficulties. Even though more than half a century has passed since the first described case, KFD is still hard to diagnose. Therefore it is of utmost importance to perform all the necessary diagnostic tests to avoid misdiagnosing and prescribing the wrong and often too-aggressive treatment. This paper describes the first clinical case of KFD in the Republic of Kazakhstan.*

The study aimed to *share the clinical course and the specifics of a diagnostic search involving histological and immunohistochemical tests in KFD.*

Methods: *The paper describes a clinical case of KFD.*

Results: *We reported a case of KFD in a 35-year-old man who applied for cervical lymphadenopathy and fever. The diagnosis was made on histological and immunohistochemical analysis of a lymph node. Rapid regression of lymphadenopathy marked the evolution of the disease.*

Conclusion: *This clinical observation describes a rare case of KFD; its cases have not been previously described in Kazakhstan. KFD is prone to benign course and spontaneous regression. However, difficulties remain in KFD diagnosis since symptoms such as lymphadenopathy and fever more often resemble lymphoma or tuberculosis. Non-tumor lymphadenopathy can also produce high metabolic activity manifested by an intensive accumulation of radiopharmaceuticals, according to PET-CT. Clinicians should be highly suspicious of KFD in young patients with cervical lymphadenopathy and fever to avoid misdiagnosis.*

Keywords: *Kikuchi-Fujimoto disease (KFD), histiocytic necrotizing lymphadenitis, lymphoma, lymphadenopathy.*

Introduction: Kikuchi-Fujimoto disease (KFD), also known as histiocytic necrotizing lymphadenitis, is a rare underlying cause of benign lymphadenopathy, typically accompanied by fever and fatigue. The first case of KFD was reported in Japan in 1972. Since then, the disease has been reported worldwide, with most cases in Asia [1, 2]. In addition to lymphadenopathy, most commonly cervical, other symptoms such as nausea, weight loss, night sweats, and fatigue may be present in the clinic of KFD. Because of its rare occurrence and non-specific clinical picture, in 40% of cases, KFD is mistaken for other diseases accompanied by lymphadenopathy (e.g., lymphoma, tuberculous lymphadenitis, autoimmune diseases, and non-specific inflammation) [3]. Even though more than half a century has passed since the first described case, KFD is still hard to diagnose this disease in clinical practice. Therefore it is of utmost importance to perform all the necessary diagnostic tests to avoid misdiagnosing and prescribing the wrong and often too-aggressive treatment [4].

The study aimed to share the clinical course and the specifics of a diagnostic search involving histological and immunohistochemical tests in KFD.

Materials and methods: This paper describes a clinical case of KFD in a 35-year-old man. The patient was examined at Hematology Center LLP in Karaganda.

Histological examination of the lymph node was performed at the Department of Pathological Anatomy of the Pavlov First Saint Petersburg State Medical University of the Ministry of Health of the Russian Federation under the supervision of Professor V.V. Baikov, holder of a habilitation degree in Medicine.

Patient information: A young man of 35 years sought medical care due to increasing fever and painful cervical lymphadenopathy.

Clinical Data: Since January 2022, the patient has been bothered by sub-febrile fever up to 37.5°C. At the end of January 2022, the patient discovered a mass gradually increasing on the right side of his neck. Since then, periodic episodes of febrile fever up to 39.8-40.0°C have also occurred. Since early February 2022, the mass on the neck became painful on contact. The patient noted profuse night sweating and no weight loss. Asymmetry of the neck was notable during the objective examination. A volumetric mass up to 2 cm in diameter was palpable on the right side. It was dense and slightly painful on palpation, and displacement was preserved.

Diagnostics: *Laboratory indices* were within the acceptable values. PCR results for viral hepatitis B and C and HIV were negative. *Peripheral blood immunophenotyping* was performed due to suspected lymphoproliferative dis-

ease: no CD23/CD43/ FMC7/ CD20/ CD19 immunophenotype aberrations were found. No immunophenotypic evidence in peripheral blood for pathological lymphoproliferation (T or B linear) was obtained. *Whole-body PET-CT in February 2022:* showed high metabolic activity in enlarged lymph nodes of the jugular, supraclavicular, superficial and deep cervical groups on both sides, intrathoracic paratracheal on the right, bifurcation, subcarinal and axillary on two sides, which was consistent with lesions in lymphoma.

Histological examination of the lymph node (February 2022): The histological preparation had extensive fields/foci of macrophages/histiocytes and giant cells with plasmacytoid dendritic cell morphology. There were foci of necrosis without cellular reaction. Figure 1 shows pronounced cellular decay without cellular involvement, and the preparation contains extensive fields/foci of macrophages/histiocytes and giant cells with plasmacytoid dendritic cell morphology.

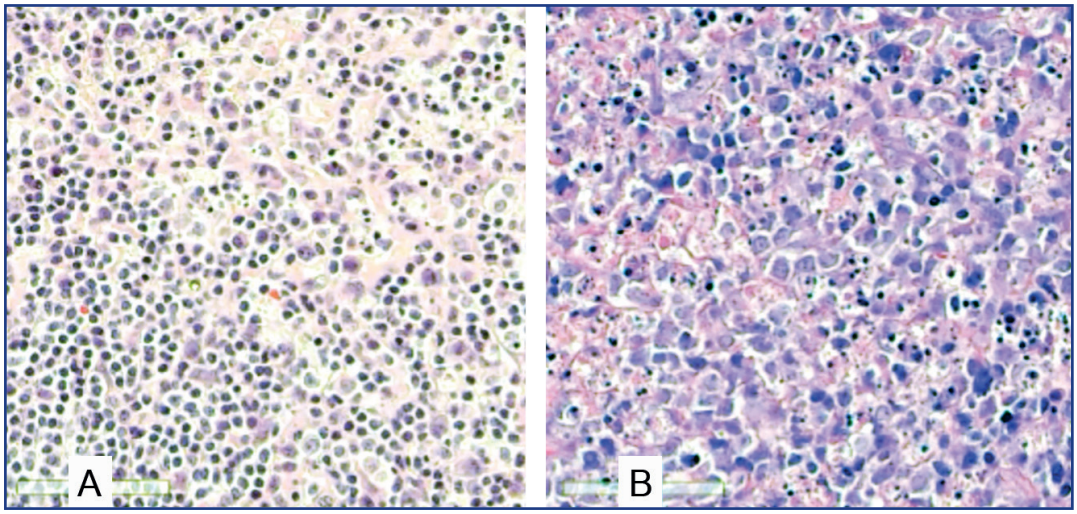

Figure 1 – Histological examination of a lymph node in a 35-year-old man with Kikuchi-Fujimoto disease: A – Hematoxylin-eosin staining, B – Azur-eosin staining. Magn. x400

Immunohistochemical study of the lymph node (February 2022): Most of the cells in the node express CD45(LCA). B-cell clusters (CD20+, Pax-5+) are not large, partly friable, and located mainly under the capsule. Part of them has follicular structures. T-cells (CD3+) sharply prevail, and CD8+ cells predominate in subpopulation composition. Some T-cells are moderately large, and nuclei are enlightened or with thinly vesicular chromatin patterns. Large dense or loose clusters of plasmacytoid dendritic cells (CD123+), macrophages/histiocytes (CD68+), some cells co-express MPO – T-cells and macrophages/histiocytes stained in reaction with antibodies to CD4. CD30+ cells are in moderate numbers, lying predominantly solitary. The proliferation index among infiltrate cells (outside residual follicles, by Ki-67) is about 30%. No expression of EBV (LMP), ALK, or TdI was detected (Figure 2).

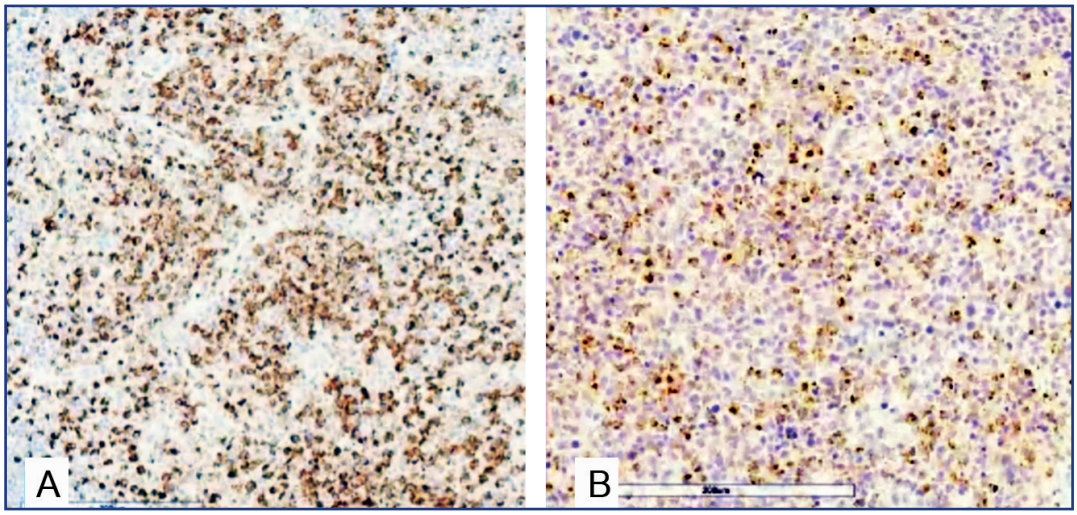

Figure 2 – Immunohistochemical examination of a lymph node in a 35-year-old man with Kikuchi-Fujimoto disease: A – cells expressing CD68, B – myeloperoxidase expression. Magn. x400

The immunohistochemical pattern was generally consistent with that observed in the histiocytic necrotizing lymphadenitis – necrotic stage of KFD. Considering that similar histological changes may correspond to autoimmune diseases, we screened for connective tissue diseases: antibodies to double-stranded DNA, antinuclear autoantibodies, and rheumatoid factor were examined. Screening results (March 2022) – negative. Based on the tests, the patient was diagnosed with KFD, necrotic stage.

Treatment: The patient received symptomatic treatment: nonsteroidal anti-inflammatory drugs for febrile spiral. No specific therapy was given.

Results: Since March 2022, the patient has had decreased clinical manifestations of the disease, normalized body temperature, and decreased size of peripheral lymph nodes. Since the middle of March 2022, the patient did not seek medical help, and his further fate is unknown.

Timeline: Figure 3 shows the dynamics of clinical manifestations of KFD in this patient with gradual regression of symptoms.

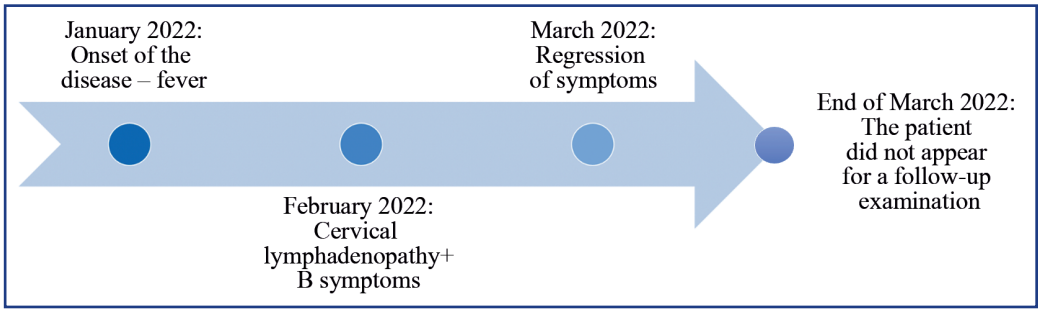

Figure 3 – Timeline of a clinical case in a 35-year-old man with Kikuchi-Fujimoto disease

Discussion: No possibility of determining the further course of the disease because the patient did not appear for the follow-up examination, did not seek medical attention after the regression of symptoms of the disease, and further fate is unknown.

KFD is a disease with a favorable prognosis and a tendency to regress independently. KFD primarily includes lymphadenopathy (most often cervical localization) and a fever of 38 to 40°C for 4-6 weeks, corresponding to the patient's clinic described above. A maculopapular rash with pronounced pruritus and mild hepatosplenomegaly up to +2 cm from under the costal margin may also occur. The difficulty of diagnosis is related to possible histological mimicry of KFD in other diseases, such as lymphomas. In a study by L.P. Menasce et al., among 27 patients with revision-assessed KFD, 88.8% of patients (n=24) were initially misdiagnosed with non-Hodgkin's lymphoma [5].

There is no standard treatment plan for KFD, as the disease is rare and individualized. The primary treatment for KFD is symptom relief, i.e., symptomatic therapy. Antibiotics are ineffective, but their use may be appropriate in immunocompromised patients to prevent the development of potential bacterial infections [6]. In addition, using glucocorticosteroids may alleviate symptoms and shorten the course of the disease. In addition, prednisolone has been used in treating pregnant women with KFD and effectively reduces disease manifestations.

Conclusion: KFD is a rare disease prone to benign course and spontaneous regression. However, there remain difficulties in diagnosing this disease. For example, differential diagnostics should be performed with malignant hematological neoplasms, infectious lymphadenopathy (of specific and non-specific etiology), and autoimmune diseases. The described clinical case is interesting because non-tumor lymphadenopathy can resemble a lesion in lymphoma and even produce high metabolic activity manifested by an intensive accumulation of radiopharmaceuticals, according to PET-CT data.

References:

1. Chiu C.F., Chow K.C., Lin T.Y., Tsai M.H., Shih C.M., Chen L.M. Virus infection in patients with histiocytic necrotizing lymphadenitis in Taiwan. Detection of Epstein-Barr virus, type I human T-cell lymphotropic virus, and parvovirus B19 // Am. J. Clin. Pathol. – 2000. – Vol. 113(6). – P. 774-781. https://doi.org/10.1309/1A6Y-YCKP-5AVF-QTYR

2. Bosch X., Guilabert A., Miquel R., Campo E. Enigmatic Kikuchi-Fujimoto disease: A comprehensive review // Am. J. Clin. Pathol. – 2004. – Vol. 122(1). – P. 141-152. https://doi.org/10.1309/YF08-1L4T-KYWV-YVPQ

3. Singh J.M., Shermetaro C.B. Kikuchi-Fujimoto Disease in Michigan: A Rare Case Report and Review of the Literature // Clin. Med. Insights Ear Nose Throat. – 2019. – Vol. 12. – Art. ID: 1179550619828680. https://doi.org/10.1177/1179550619828680

4. Lahma J., Arkoubi Z., Hejjouji R., Nitassi S., El Ayoubi A., Bencheikh R., Benbouzid M.A., Oujilal A., Essakalli L. About a rare disease misdiagnosed as malignant lymphoma or tuberculosis: Kikuchi-Fujimoto's disease // Pan. Afr. Med. J. – 2018. – Vol. 31. – P. 1-5. https://doi.org/10.11604/pamj.2018.31.77.16569

5. Potapenko V.G., Baĭkov V.V., Markova A.Yu., Mixajlova N.B., Ter-Grigoryan A.S., Krivolapov Yu.A. Bolezn' Kikuchi-Fudzhimoto: obzor literatury i chetyre klinicheskix nablyudeniya // Onkogematologiya. – 2022. – №17(4). – S. 48-59 [Potapenko V.G., Baikov V.V., Markova A.Yu., Mikhailova N.B., Ter-Grigoryan A.S., Krivolapov Yu.A. Kikuchi-Fujimoto disease: a literature review and four clinical observations // Oncohematology. – 2022. – Vol. 17(4). – P. 48-59 (in Russ.)]. https://doi.org/10.17650/1818-8346-2022-17-4-48-59

6. Xu S., Sun W., Liu J. Kikuchi-Fujimoto disease: A case report and the evaluation of diagnostic procedures // BMC Oral Health. – 2019. – Vol. 19. – P. 223. https://doi.org/10.1186/s12903-019-0920-4

АҢДАТПА

КИКУЧИ-ФУДЖИМОТО СЫРҚАТЫ: ҚАЗАҚСТАНДА СИРЕК КЕЗДЕСЕТІН ЖАҒДАЙДЫҢ АЛҒАШҚЫ КЛИНИКАЛЫҚ БАҚЫЛАУЫ

М.И. Селиванов[1], Л.Г. Тургунова[1], А.В. Зинченко[2], О.В. Брунер[2]

[1]«Қарағанды медицина университеті» КЕАҚ, Қарағанды, Қазақстан Республикасы;
[2]«Центр Гематологии» ЖШС, Қарағанды, Қазақстан Республикасы

Өзектілігі: *Кикучи-Фуджимото сырқаты, сондай-ақ гистиоцитарлық некротикалық лимфаденит деп те аталады, субфебрильді температурамен және жалпы әлсіздікпен бірге жүретін сирек қатерсіз лимфаденопатияның бірі болып табылады. Сырқат сирек кездесетіндіктен, диагностикалауда көптеген қиындықтар бар. Кикучи-Фуджимото сырқатының алғашқы жағдайын сипаттағаннан кейін жарты ғасырдан астам уақыт өтті, бірақ клиникалық тәжірибеде бұл сырқатты диагностикалауда әлі де қиындықтар бар, сондықтан қате диагноз қоюды және одан туындайтын дұрыс емес және жиі агрессивті емдеу тактикасын болдырмау үшін қажетті диагностикалық процедураларды жүргізу өте маңызды. Бұл мақала-Қазақстан Республикасындағы Кикучи-Фуджимото сырқатының клиникалық жағдайының ең алғашқы сипаттамасы.*

Зерттеудің мақсаты *– Кикучи-Фуджимото сырқатының гистологиялық және иммуногистохимиялық ерекшеліктерін ескере отырып, клиникалық ағымын және диагностикалық іздеу барысын сипаттау.*

Әдістері: *Кикучи-Фуджимото сырқатының клиникалық жағдайын сипаттау.*

Нәтижелері: *біз жатыр мойны лимфаденопатиясы мен безгегі туралы хабарлаған 35 жастағы ер адамда Кикучи-Фуджимото сырқатының жағдайы туралы хабарладық. Диагноз лимфа түйінінің биоптатын гистологиялық және иммуногистохимиялық талдау негізінде жасалды. Аурудың эволюциясы лимфаденопатияның жылдам регрессиясымен ерекшеленді.*

Қорытынды: *бұл клиникалық байқау Кикучи-Фуджимото сырқатының сирек жағдайын сипаттайды; авторлар Қазақстанда бұрын сипатталған ауру жағдайларын таппаған. Кикучи-Фуджимото сырқатының қатерсіз ағымға және өздігінен регрессияға бейімділікпен сипатталады. Алайда, бұл ауруды диагностикалауда қиындықтар қалады, өйткені лимфоаденопатия және қызба сияқты белгілер көбінесе лимфомаға немесе туберкулезге ұқсайды; сонымен қатар, ісіксіз лимфаденопатия тінті жоғары метаболикалық белсенділікті тудыруы мүмкін, бұл ПЭТ - КТ-ға сәйкес радиофармацевтикалық препараттың қарқынды жинақталуымен көрінеді. Қате диагнозды болдырмау үшін дәрігерлер жатыр мойны лимфаденопатиясы және безгегі бар жас пациенттерде Кикучи-Фуджимото ауруына жоғары күдікпен қарауы керек.*

Түйінді сөздер: *Кикучи-Фуджимото сырқаты, некротикалық гистиоцитарлық лимфаденит, лимфома, лимфаденопатия.*

АННОТАЦИЯ

БОЛЕЗНЬ КИКУЧИ-ФУДЖИМОТО: ПЕРВОЕ КЛИНИЧЕСКОЕ НАБЛЮДЕНИЕ РЕДКОГО СЛУЧАЯ В РЕСПУБЛИКЕ КАЗАХСТАН

М.И. Селиванов[1], Л.Г. Тургунова[1], А.В. Зинченко[2], О.В. Брунер[2]

[1]НАО «Медицинский университет Караганды», Караганда, Республика Казахстан;
[2]ТОО «Центр Гематологии», Караганда, Республика Казахстан

Актуальность: *Болезнь Кикучи-Фуджимото (БКФ), также известная как гистиоцитарный некротизирующий лимфа-денит, является редкой причиной доброкачественной лимфаденопатии, которая сопровождается субфебрильной лихорад-кой и общей слабостью. Прошло более полувека после описания первого случая БКФ, однако в клинической практике до сих пор существуют трудности в диагностики данного заболевания. Поэтому крайне важно провести необходимые диагно-стические процедуры во избежание постановки ошибочного диагноза и выбора неверной лечебной, часто агрессивной, так-тики. Данная статья – первое описание клинического случая БКФ в Республике Казахстан.*

Цель исследования *– описать клиническое течение болезни Кикучи-Фуджимото и ход диагностического поиска с учё-том гистологических и иммуногистохимических особенностей.*

Методы: *В статье приведено описание клинического случая БКФ.*

Результаты: *У 35-летнего мужчины, который обратился по поводу шейной лимфаденопатии и лихорадки, на основа-нии гистологического и иммуногистохимического анализа биоптата лимфатического узла была диагностирована БКФ. Эволюция заболевания была отмечена быстрой регрессией лимфаденопатии.*

Заключение: *Данное клиническое наблюдение описывает редкий случай БКФ; ранее описанных случаев заболевания в Казахстане авторы не нашли. БКФ характеризуется склонностью к доброкачественному течению и спонтанному регрес-су. Однако остаются трудности в диагностике данного заболевания, так как такие симптомы, как лимфаденопатия и лихорадка чаще напоминают лимфому или туберкулез. Кроме того, неопухолевая лимфаденопатия может даже давать высокую метаболическую активность, которая проявляется интенсивным накоплением радиофармпрепарата по данным ПЭТ-КТ. Клиницистам следует с высокой степенью подозрения относиться к БКФ у молодых пациентов с шейной лимфа-денопатией и лихорадкой, чтобы избежать ошибочного диагноза.*

Ключевые слова: *болезнь Кикучи-Фуджимото (БКФ), некротизирующий гистиоцитарный лимфаденит, лимфома, лимфаденопатия.*

Transparency of the study: *Authors take full responsibility for the content of this manuscript.*
Conflict of interest: *Authors declare no conflict of interest.*
Financing: *Authors declare no financing of the study.*
Authors' input: *contribution to the study concept – Turgunova L.G., Zinchenko A.V., Bruner O.V., Selivanov M.I.; study design – Zinchenko A.V., Turgunova L.G.; execution of the study – Selivanov M.I., Bruner O.V.; interpretation of the study – Turgunova L.G., Zinchenko A.V.; preparation of the manuscript – Selivanov M.I., Turgunova L.G., Zinchenko A.V., Bruner O.V.*
Authors' data:
Selivanov M.I. – Resident Hematologist of Internal Diseases Department, «Karaganda Medical University» NCJSC, Karaganda, Kazakhstan, tel. +77003863343, e-mail: maks7991@bk.ru, ORCID ID: 0000-0002-5726-2947;
Turgunova L.G. (corresponding author) – Doc. Med. Sci., Prof. at the Internal Diseases Department, «Karaganda Medical University» NCJSC, Karaganda, Kazakhstan, tel. +77012273536, e-mail: Turgunova@qmu.kz, ORCID ID: 0000-0002-6962-4247;
Zinchenko A.V. – Hematologist, Deputy Director for Medical and Preventive Activity, «Center of Hematology» LLP, Karaganda, Kazakhstan, tel. +77014955375, e-mail: gem_karaganda@mail.ru, ORCID ID: 0000-0002-0016-3147;
Bruner O.V. – Senior Resident at the Outpatient Unit, «Center of Hematology» LLP, Kazakhstan, tel. +77015740610, e-mail: olga.bruner@hemcenter.kz, ORCID ID: 0000-0002-0016-3548.

Address for correspondence: Turgunova L.G., «Karaganda Medical University» NCJSC, Gogol St. 40, Karaganda, Karaganda oblast M01K7G6, the Republic of Kazakhstan.