DOI: https://doi.org/10.17816/dv626353

Case report

B-cell lymphoma of the skin: clinical observation

Yulia V. Karacheva, Anastasia N. Smykova

Professor V.F. Voino-Yasenetsky Krasnoyarsk State Medical University, Krasnoyarsk, Russia

ABSTRACT

Currently, there is an increase and an increase in the incidence of primary skin lymphomas worldwide. B-cell cutaneous lymphomas account for 25–30% of primary skin lymphomas. Among all skin lymphomas, primary cutaneous lymphoma from follicular center cells occurs in 10–11% of cases and is characterized by great diagnostic difficulties due to the great similarity of clinical manifestations with other dermatoses, such as benign lymphoplasia, Beck's sarcoidosis, Jessner–Kanof lymphocytic infiltration, skin metastases.

This paper presents a clinical case of B-cell lymphoma in a 29-year-old woman with a lesion of the facial skin in the form of a node, initially incorrectly interpreted as benign lymphoplasia. For five years, the patient received therapy with topical glucocorticosteroids with no effect from. Subsequently, histological examination and immunohistochemistry were performed for the purpose of differential diagnosis of sarcoidosis with B-cell lymphoma. Histologically, there is nodular proliferation of atypical lymphoid cells in the dermis, most of which have cytological characteristics of a centrocyte with an admixture of a small number of central blasts. Nodular proliferates contain an admixture of compactly arranged small lymphocytes. There are no signs of epidermotropism. During immunohistochemical examination, cells forming nodular proliferates express CD20, bc16 with an index of proliferative activity for the expression of nuclear protein K167 — 20–30%, a dissociated network of follicular dentritic cells expressing CD21 is determined at the base of nodular proliferates. They are not expressed by bc12, CD3, CD2, CD5 proliferate cells. CD117 is expressed by an admixture of discretely distributed mast cells. The morphological picture corresponds to primary cutaneous centrofollicular lymphoma. The node was excised. Radiation therapy was not prescribed due to the patient's pregnancy.

This clinical observation highlights the importance of considering the diagnosis of lymphoma in the differential diagnosis of treatment-resistant dermatological diseases.

Keywords: B-cell lymphoma of the skin; follicular lymphoma; primary lymphoma of the skin.

To cite this article:
Karacheva YuV, Smykova AN. B-cell lymphoma of the skin: clinical observation. *Russian journal of skin and venereal diseases.* 2024;27(3):241–248. DOI: https://doi.org/10.17816/dv626353

Received: 01.02.2024 **Accepted:** 15.04.2024 **Published online:** 04.07.2024

DOI: https://doi.org/10.17816/dv626353

Клинический случай

В-клеточная лимфома кожи: клиническое наблюдение

Ю.В. Карачева, А.Н. Смыкова

Красноярский государственный медицинский университет имени профессора В.Ф. Войно-Ясенецкого, Красноярск, Россия

АННОТАЦИЯ

В настоящее время во всём мире наблюдаются рост и увеличение заболеваемости первичными лимфомами кожи. В-клеточные кожные лимфомы составляют 25–30% первичных лимфом кожи. Среди всех лимфом кожи первичная кожная лимфома из клеток фолликулярных центров встречается в 10–11% случаев и характеризуется большими сложностями диагностики из-за схожести клинических проявлений с другими дерматозами, такими как доброкачественная лимфоплазия, саркоидоз Бека, лимфоцитарная инфильтрация Джесснера–Канофа, метастазы в кожу.

В статье представлен клинический случай В-клеточной лимфомы у женщины в возрасте 29 лет с поражением кожи лица в виде узла, изначально неверно интерпретированным как доброкачественная лимфоплазия. В течение 5 лет больная получала терапию топическими глюкокортикоидами без должного эффекта. В дальнейшем с целью дифференциальной диагностики саркоидоза с В-клеточной лимфомой было проведено гистологическое и иммуногистохимическое исследование. Гистологически в дерме выявлена нодулярная пролиферация атипичных лимфоидных клеток, имеющих в большинстве своём цитологические характеристики центроцита с примесью небольшого числа центробластов. Нодулярные пролифераты содержат примесь компактно расположенных мелких лимфоцитов. Признаков эпидермотропизма не прослеживается. При иммуногистохимическом исследовании клетки, формирующие нодулярные пролифераты, экспрессируют CD20, bc16 при индексе пролиферативной активности по экспрессии ядерного протеина К167 — 20–30%, в основе нодулярных пролифератов определяется диссоциированная сеть фолликулярных дентритных клеток, экспрессирующих CD21. Не экспрессированы клетками пролиферата bc12, CD3, CD2 и CD5; CD117 экспрессирован примесью дискретно распределённых тучных клеток. Морфологическая картина соответствует первичной кожной центрофолликулярной лимфоме. Проведено иссечение узла. Лучевая терапия не назначалась в связи с беременностью пациентки.

Данное клиническое наблюдение подчёркивает важность рассмотрения диагноза лимфомы в дифференциальной диагностике торпидных к терапии дерматологических заболеваний.

Ключевые слова: В-клеточная лимфома кожи; фолликулярная лимфома; первичная лимфома кожи.

Как цитировать:
Карачева Ю.В., Смыкова А.Н. В-клеточная лимфома кожи: клиническое наблюдение // Российский журнал кожных и венерических болезней. 2024. Т. 27, № 3. С. 241–248. DOI: https://doi.org/10.17816/dv626353

Рукопись получена: 01.02.2024 **Рукопись одобрена:** 15.04.2024 **Опубликована online:** 04.07.2024

INTRODUCTION

Primary cutaneous lymphomas are a heterogeneous group of extranodal non-Hodgkin lymphomas that develop due to neoplastic proliferation and accumulation of T-lymphocyte, NK-cell or B-lymphocyte clones [1]. Primary cutaneous lymphomas are the second most common type of extranodal non-Hodgkin lymphomas after lymphomas of the gastrointestinal tract. Compared to nodal neoplasias, they have a different clinical presentation, disease course, and specific chromosomal translocations and expression of various oncogenes [2, 3].

Currently, there is an increase in the incidence of primary cutaneous lymphomas worldwide. For example, in Europe the increase in the incidence of primary cutaneous lymphomas is about 3% and in the USA the incidence has increased from 0.5 to 1.27 cases per 100,000 over the last 20 years [2, 3]. Data on the incidence and the disease course in different ethnic groups indicate that lymphomas affect native Australians more frequently than non-native, and the overall incidence of lymphoid tumors is lower in Asia compared to Europe [4, 5].

Early stages of the primary cutaneous lymphomas can mimic various chronic inflammatory dermatoses, such as recurrent erysipelas, pyoderma, and shingles which makes them difficult to diagnose by dermatologists [1, 6].

Cutaneous B-cell lymphomas (CBCLs) account for 25%–30% of primary cutaneous lymphomas, while T-cell lymphomas are the most common type of neoplasia in this group [7]. CBCLs include primary cutaneous follicle center B-cell lymphoma, primary cutaneous marginal zone B-cell lymphoma, and primary cutaneous diffuse B-cell lymphoma, leg type [8].

Primary cutaneous follicle center lymphoma is a cutaneous lymphoma characterized by follicular growth of the B cells of the germinal center of the lymphoid follicle. It accounts for 10%–11% of all cutaneous lymphomas. It most often affects individuals aged 55–56 years, both males and females. Thus, in the study by I.A. Lamotkin et al. [8], the age ranged from 31 to 65 years (mean age 51.5±13.7 years) with the male to female ratio 1.5:1. The diagnosis was made within 1 to 5 (mean 2.9±1.4) months from the appearance of the lesion with primary tumor skin invasion at stages T1a and T2a. The average follow-up period was 1.2±0.5 years [8].

Clinically, follicular lymphoma usually presents as a well-defined single bluish nodule with dense elastic consistency, measuring 2–3 cm (not more than 4 cm) in the largest dimension. The most common localization is the head, neck, and trunk. Sometimes there may be ulcerations or multiple lesions present [8]. According to I.A. Lamotkin et al. [8], follicular lymphoma is characterized by an indolent course with five-year survival rate of 89%–96%. In single lesions located on the skin of the head and neck the five-year survival rate is greater than 96%, and in multiple lesions located on the skin of the legs it is less than 89%.

The diagnosis is made incidentally, after removing pseudolymphoma of the skin or basalioma and performing histologic and immunohistochemical examination. In some cases, the diagnosis of cutaneous lymphoma is suspected on cytologic examination. The diagnosis is usually made at early stages of T1aN0M0 and T2aN0M0 [8].

Histologically, follicle center lymphoma is characterized by the presence of a dense proliferate in the lower dermis with extension into the hypodermis. Follicular structures with small or absent mantle zone are seen among the proliferate cells. A clearly demarcated marginal zone is usually absent. Follicles contain centrocytes and centroblasts in different ratios. In the interfollicular zones there are accumulations of reactive small lymphocytes, histiocytes, some eosinophils and plasmocytes. When the tumor is ulcerated, it can infiltrate the dermis, subcutaneous fat and skeletal muscles [9].

Cutaneous B-cell lymphomas vary in malignancy. Low-grade cutaneous B-cell lymphoma (CBCL I) is represented by nodular and plaque forms. The disease occurs at any age, and malignization occurs after 20–30 years from the beginning of the process. The nodular form is characterized by the formation of one or more pink-brown nodules up to 3 cm in diameter with dense elastic consistency and smooth surface, which gradually increase in size and number. The plaque form is characterized by large yellowish-pink or brown spots, further transforming into plaques and nodules [10]. Intermediate CBCL (CBCL II) is represented by dense, purple-colored nodules which are initially located on the head and neck and further disseminate over the body, and malignization occurs after 2–3 years from the onset of the disease [10]. High-grade CBCL (CBCL III) is characterized by the rapid progression of the process with dissemination of the deep subcutaneous nodules within six months and a fatal outcome in 1–2 years [10].

Although CBCLs represent a minority of primary cutaneous lymphomas, they require close attention of dermatologists and oncologists in terms of differential diagnosis with benign lymphoplasias and other nodular dermatoses. The clinical picture of CBCLs is homogeneous and is characterized by red-purple nodules and plaques on the skin of the scalp, trunk, and extremities [9]. Nodules are not accompanied by desquamation due to the absence of epidermotropism of the tumor infiltrate in this form of neoplasia. Most often B-cell lymphomas must be differentiated from benign lymphoplasia, Beck's sarcoidosis, Jessner-Kanoff's lymphocytic infiltration, and metastases. Patients at early stages of the disease are closely observed in dermatologic clinics with the initial diagnosis including a wide range of dermatoses, not always coinciding with the final diagnosis [1].

Treatment depends on the extent of the lesion and is most often limited to surgical excision. In some cases, radiation therapy is additionally administered. Single nodes are excised within healthy tissues. Surgery is sometimes combined with pre- or postoperative close-focus radiotherapy. In preoperative radiotherapy 5 sessions of 340 Rad are

performed, to shrink the tumor which is then surgically removed. In postoperative radiotherapy after the excision of the node close-focus radiotherapy of a total dose of 5100 Rad at the excision site is performed.

Follicle center cutaneous B-cell lymphoma is characterized by indolent course with a five-year survival rate of 95%. After treatment, patients are often removed from follow-up after 1–2 years [10, 11].

In this article, we present a clinical case of CBCL in a 29-year-old woman with a nodular lesion on the facial skin initially misdiagnosed as benign lymphoplasia. This case report emphasizes the importance of inclusion of lymphoma in the differential diagnosis of therapy-resistant dermatologic diseases.

CASE DESCRIPTION

Patient information

Patient P., 29 years old, in 2017 visited a dermatologist of Krasnoyarsk Regional Skin and Venereological Dispensary No. 1 with complaints of a forehead skin mass not associated with anything. The dermatologist clinically diagnosed benign lymphoplasia, therefore topical hormonal therapy was prescribed. Despite the lack of effect from treatment for 5 years, the patient did not repeatedly seek for medical help. In September 2022 she was referred to the Department of Dermatovenereology of Krasnoyarsk State Medical University by the women's health clinic where she was observed for pregnancy.

On examination there was a horseshoe-shaped burgundy-red painless nodule, 3 × 2 cm in size with a dense elastic consistency and smooth surface located on the skin of the left forehead (Fig. 1).

The patient denied chronic somatic diseases.

Physical, laboratory and instrumental examination results

Screening examination results: no pathology revealed. Conclusion: biopsy of the nodule is recommended for differential diagnosis of sarcoidosis and CBCL.

Histologic examination results: there is a dense lymphoid infiltrate in the papillary and reticular layers of the dermis; nuclei with polymorphism and mitoses are seen. Conclusion: "B-cell lymphoma." Immunohistochemical examination with immunophenotyping of the infiltrate cells is recommended.

The patient was immediately referred to the oncology clinic, where excision of the node with subsequent immunohistochemical examination was performed.

Results of immunohistochemical examination dated 19/10/2022 (Fig. 2): the material is represented by skin biopsy; in the dermis there is nodular proliferation of atypical lymphoid cells mostly with cytologic features of a centrocyte with an admixture of a small number of centroblasts. Nodular proliferates contain an admixture of

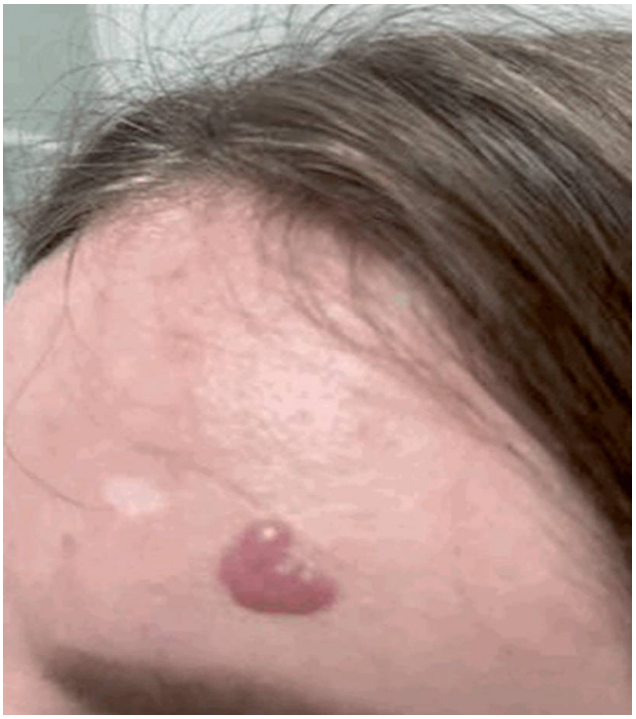


Fig. 1. Patient P., 29 years old. A horseshoe-shaped burgundy-red nodule of 3×2 cm in size, painless, dense-elastic consistency, with a smooth surface was located on the skin of the forehead on the left side.

closely arranged small lymphocytes. There are no signs of epidermotropism. Immunohistochemical examination shows CD20 expression by the cells forming nodular proliferates; bc16 with proliferative activity index by expression of nuclear protein K167 is 20%–30%; the base of nodular infiltrates is represented by a dissociated network of follicular dendritic cells with CD21 expression. There is no bc12, CD3, CD2, CD5 expression by the cells of the proliferate. CD117 is expressed by an admixture of discretely distributed mast cells. Conclusion: the morphologic picture is consistent with primary cutaneous follicle center lymphoma.

Treatment and follow-up

The patient underwent surgical excision of the node within healthy tissues. Radiation therapy was not performed due to 30-week pregnancy at the time of surgery. The postoperative period was uncomplicated. At the excision site a scar was formed (Fig. 3).

DISCUSSION

The clinical case presented supports the difficulties of the clinical diagnosis of primary cutaneous follicle center lymphoma described by different authors [1, 8]. At an outpatient visit cutaneous lymphoma can be initially misdiagnosed as various dermatologic diseases, such as benign lymphoplasia, Beck's sarcoidosis, Jessner-Kanoff's lymphocytic infiltration, or metastases to the skin from a tumor of an internal organ [1]. The patient

DOI: https://doi.org/10.17816/dv626353

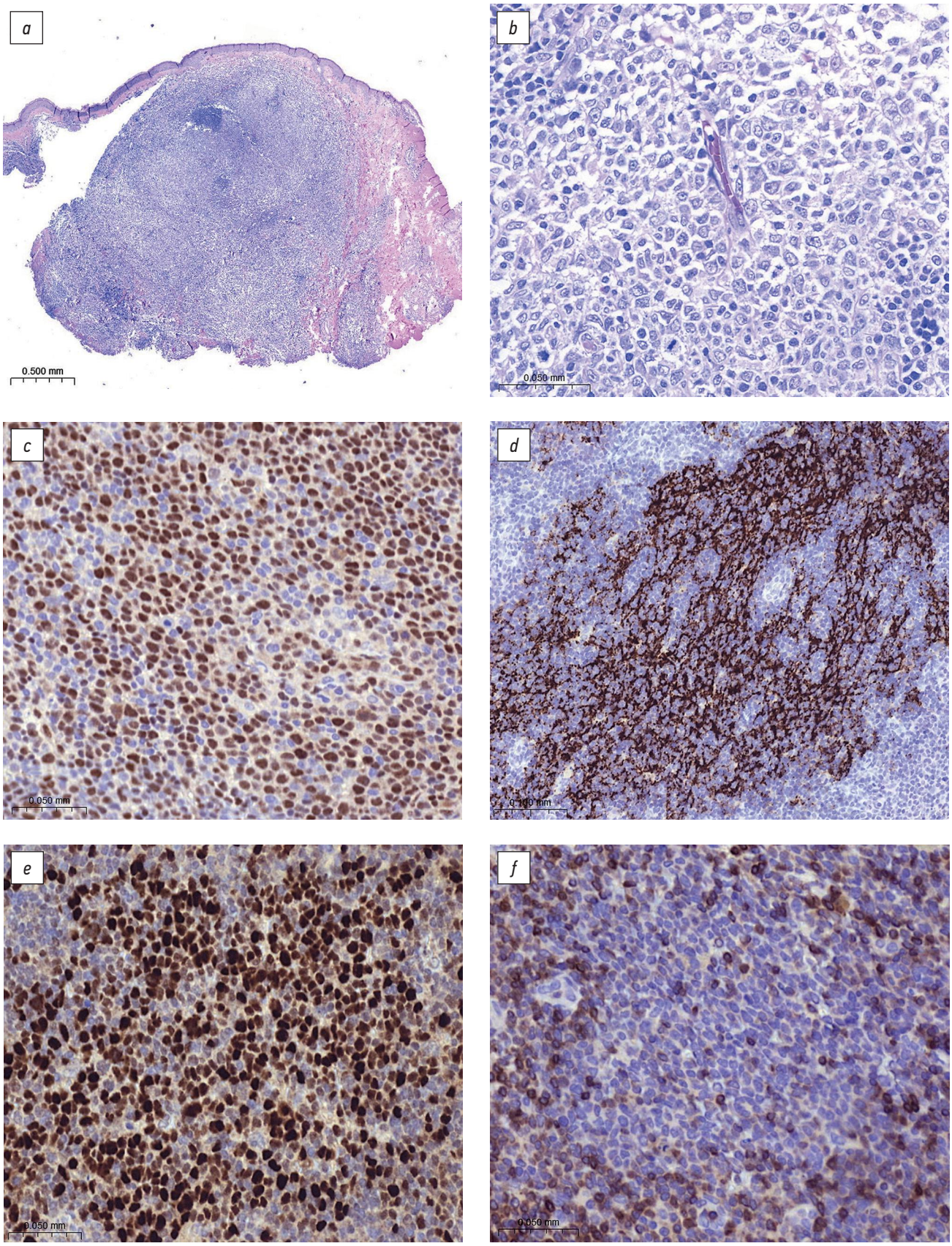
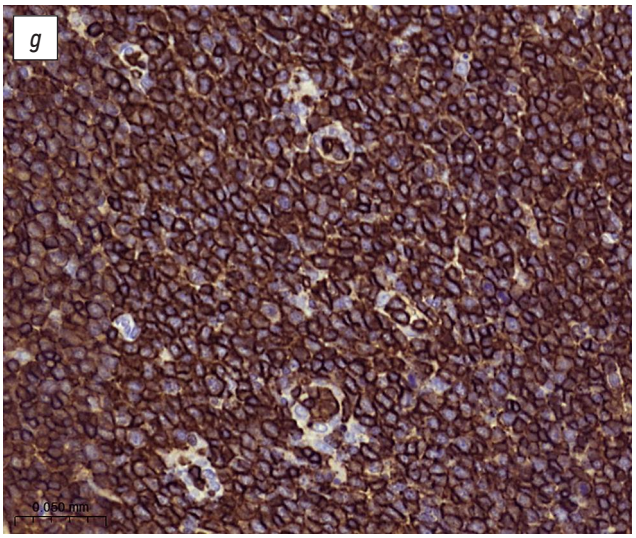


Fig. 2. Results of histological and immunohistochemical examination: *a* — overview view of skin preparation with nodular proliferate tumour lymphoid cells; *b* — predominantly centrocytic composition of nodular tumour proliferates with admixture of a small number of centroblasts; *c* — nuclear expression of bcl6 by tumour cells; *d* — dislocated network of follicular dendritic cells expressing CD23 at the base of tumour proliferates; *e* — nuclear expression of LMO2 by tumour cells; *f* — tumour cells do not express bcl2; *g* — expression of CD20 by tumour cells; *h* — expression of Ki67 nuclear protein by tumour cells.

DOI: https://doi.org/10.17816/dv626353



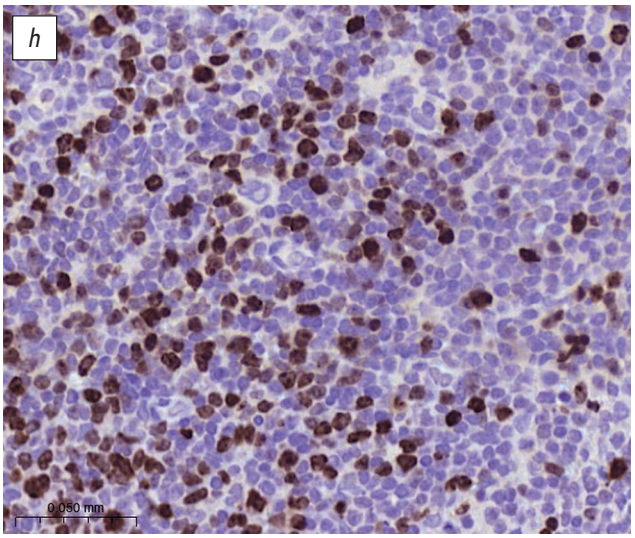


Fig. 2. Ending.

we presented was also initially misdiagnosed with benign lymphoplasia and the topical hormonal therapy prescribed had no positive effect. The time from the appearance of the lesion to the correct diagnosis was more than 5 years. Since CBCLs are malignant neoplasms, delays in treatment may lead to dissemination of the process and an increase in malignancy [8].

CONCLUSION

Thus, primary cutaneous lymphoma is one of the most important problem of the contemporary medicine due both to its high rate of incidence and difficulties in diagnostics and treatment requiring taking in account a lot of factors and using a wide range of up-to-date methods of investigation: histological, immunological, and based on molecular genetics. Lymphoproliferative diseases should undoubtedly be included in the differential diagnosis of treatment-resistant dermatologic diseases. The clinical case we presented once again emphasizes the importance of diagnostic skin biopsy in the diagnosis of indolent dermatologic diseases.

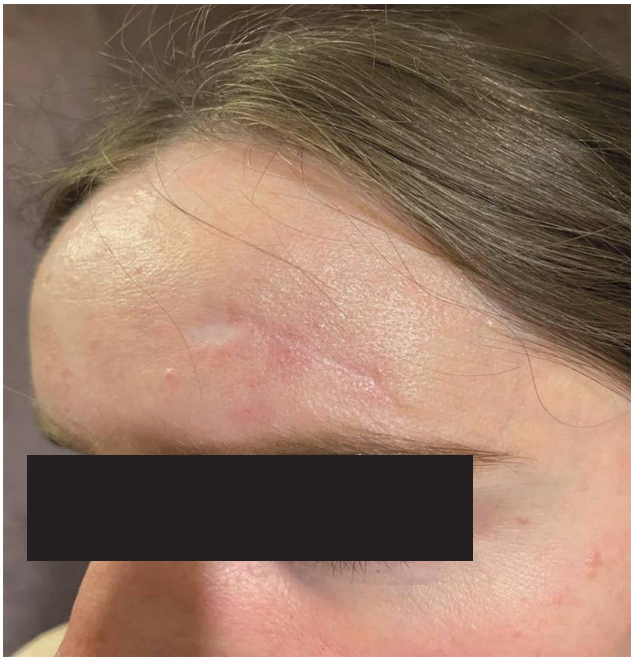


Fig. 3. Postoperative scar on the forehead skin as a result of tumour excision.

ADDITIONAL INFORMATION

Funding source. This publication was not supported by any external sources of funding.

Competing interests. The authors declare that they have no competing interests.

Authors' contribution. All authors made a substantial contribution to the conception of the work, acquisition, analysis, interpretation of data for the work, drafting and revising the work, final approval of the version to be published and agree to be accountable for all aspects of the work. Yu.V. Karacheva — data collection, writing a draft of the manuscript, scientific revision of the manuscript, consideration and approval of the final version of the manuscript; A.N. Smykova — writing a draft of the manuscript, technical revision, design, layout.

Consent for publication. Written consent was obtained from patients for publication of relevant medical information and all associated images in the manuscript.

REFERENCES

1. Kuklin IA, Kohan MM, Demidov SM. Primary lymphomas of the skin. *Practitioner.* 2018;(5):27–29. EDN: XQSAHR
2. Eder J, Kern A, Moser J, et al. Frequency of primary cutaneous lymphoma variants in Australia: Retrospective data from a dermatology referral centre between 2006 and 2013. *Eur Acad Dermatol Venereol.* 2015;29(8):1517–1523. doi: 10.1111/jdv.12907
3. Blaizot R, Ouattara E, Fauconneau A, et al. Infectious events and associated risk factors in mycosis fungoides/Sézary syndrome: A retrospective cohort study. *Br J Dermatol.* 2018;179(6):1322–1328. doi: 10.1111/bjd.17073
4. Potekaev NN, Khamaganova IV, Almazova AA, et al. The problems of epidemiology, diagnosis, and organization of medical care for patients with cutaneous lymphomas. *Russ J Clin Dermatol Venereol.* 2013;11(4):4–7. EDN: RBMEGT
5. Zhang X, Condon JR, Rumbold AR, et al. Estimating cancer incidence in Indigenous Australians. *Aust NZ J Public Health.* 2011;35(5):477–485. doi: 10.1111/j.1753-6405.2011.00762.x
6. Bulanova NV, Semochkin SV. Difficulties in diagnosing ALK-negative anaplastic large cell lymphoma manifesting from a skin lesion. *Russ J Skin Venereal Dis.* 2022;25(6):25–32. EDN: DYLDIB doi: 10.17816/dv115012
7. Denisjuk N, Kerl K, Cozzio A. Primary cutaneous B-cell lymphoma. *J Deutschen Dermatologischen Gesellschaft.* 2012;10(1):12–22; quiz 23. doi: 10.1111/j.1610-0387.2011.07852.x
8. Lamotkin IA, Rukavitsyn AO, Gladko VV, et al. Skin B-cell lymphomas: 20 years experience in observation and treatment. *Russ J Skin Venereal Dis.* 2017;20(5):260–266. EDN: YLWZAS doi: 10.18821/1560-9588-2017-20-5-260-266
9. Lamotkin IA. *Oncodermatology. Atlas.* Textbook. Moscow: Laboratoriya znanii; 2017. 878 p. (In Russ).
10. Fingers MA, Potekaev NN, Kazantseva IA, et al. *Clinical and morphological diagnosis of skin diseases (Atlas):* Textbook. Moscow: Meditsina; 2004. 428 p. (In Russ).
11. Lauren P. Diagnosis and management of cutaneous B-cell lymphoma. *Dermatologic Clin.* 2015;33(4):835–840. doi: 10.1016/j.det.2015.05.003

СПИСОК ЛИТЕРАТУРЫ

1. Куклин И.А., Кохан М.М., Демидов С.М. Первичные лимфомы кожи // Лечащий врач. 2018. № 5. С. 27–29. EDN: XQSAHR
2. Eder J., Kern A, Moser J., et al. Frequency of primary cutaneous lymphoma variants in Australia: Retrospective data from a dermatology referral centre between 2006 and 2013 // Eur Acad Dermatol Venereol. 2015. Vol. 29, N 8. P. 1517–1523. doi: 10.1111/jdv.12907
3. Blaizot R., Ouattara E., Fauconneau A., et al. Infectious events and associated risk factors in mycosis fungoides/Sézary syndrome: A retrospective cohort study // Br J Dermatol. 2018. Vol. 179, N 6. P. 1322–1328. doi: 10.1111/bjd.17073
4. Потекаев Н.Н., Хамаганова И.В., Алмазова А.А., и др. Проблемы эпидемиологии, диагностики и организации медицинской помощи пациентам с лимфомами кожи // Клиническая дерматология и венерология. 2013. Т. 11, № 4. С. 4–7. EDN: RBMEGT
5. Zhang X., Condon J.R., Rumbold A.R., et al. Estimating cancer incidence in Indigenous Australians // Aust NZ J Public Health. 2011. Vol. 35, N 5. P. 477–485. doi: 10.1111/j.1753-6405.2011.00762.x
6. Буланова Н.В., Сёмочкин С.В. Трудности диагностики ALK-негативной анапластической крупноклеточной лимфомы, манифестировавшей с поражения кожи // Российский журнал кожных и венерических болезней. 2022. Т. 25, № 6. С. 25–32. EDN: DYLDIB doi: 10.17816/dv115012
7. Denisjuk N., Kerl K., Cozzio A. Primary cutaneous B-cell lymphoma // J Deutschen Dermatologischen Gesellschaft. 2012. Vol. 10, N 1. P. 12–22; quiz 23. doi: 10.1111/j.1610-0387.2011.07852.x
8. Ламоткин И.А., Рукавицын А.О., Гладько В.В., и др. В-клеточные лимфомы кожи: 20-летний опыт наблюдения и лечения // Российский журнал кожных и венерических болезней. 2017. Т. 20, № 5. С. 260–266. EDN: YLWZAS doi: 10.18821/1560-9588-2017-20-5-260-266
9. Ламоткин И.А. *Онкодерматология. Атлас.* Учебное пособие. Москва: Лаборатория знаний, 2017. 878 с.
10. Пальцев М.А., Потекаев Н.Н., Казанцева И.А., и др. *Клинико-морфологическая диагностика заболеваний кожи (атлас).* Москва: Медицина, 2004. 428 с.
11. Lauren P. Diagnosis and management of cutaneous B-cell lymphoma // Dermatologic Clin. 2015. Vol. 33, N 4. P. 835–840. doi: 10.1016/j.det.2015.05.003

AUTHORS' INFO

*** Anastasia N. Smykova,** MD, Cand. Sci. (Med.);
address: 1 Partizan Zeleznyak street, 660022 Krasnoyarsk, Russia;
ORCID: 0000-0001-5846-4244;
eLibrary SPIN: 2226-9685;
e-mail: smykova.a@mail.ru

Yulia V. Karacheva, MD, Dr. Sci. (Med.), Associate Professor;
ORCID: 0000-0002-7025-6824;
eLibrary SPIN: 4789-9178;
e-mail: julkar19@yandex.ru

* Corresponding author / Автор, ответственный за переписку

ОБ АВТОРАХ

*** Смыкова Анастасия Николаевна,** канд. мед. наук;
адрес: Россия, 660022, Красноярск, ул. Партизана Железняка, д. 1;
ORCID: 0000-0001-5846-4244;
eLibrary SPIN: 2226-9685;
e-mail: smykova.a@mail.ru

Карачева Юлия Викторовна, д-р мед. наук, доцент;
ORCID: 0000-0002-7025-6824;
eLibrary SPIN: 4789-9178;
e-mail: julkar19@yandex.ru