DOI: 10.20514/2226-6704-2025-15-3-199-205
УДК 616.833-006.38.03
EDN: HJYYBD

Р.Н. Мустафин

ФГБОУ ВО «Башкирский государственный медицинский университет», Уфа, Россия

КЛИНИЧЕСКАЯ ХАРАКТЕРИСТИКА НЕЙРОФИБРОМАТОЗА 1-ГО ТИПА В РЕСПУБЛИКЕ БАШКОРТОСТАН

R.N. Mustafin

Bashkir State Medical University, Ufa, Russia

Clinical Characteristics of Neurofibromatosis Type 1 in the Republic of Bashkortostan

Резюме

Актуальность. Нейрофиброматоз 1-го типа (НФ1) — это наследственный опухолевый синдром, встречающийся с частотой 1:3164 населения в мире. Болезнь характеризуется тяжелыми клиническими проявлениями в виде множественных кожных и подкожных опухолей, плексиформных нейрофибром, скелетных аномалий, когнитивных расстройств и различных осложнений. **Цель исследования.** Определение частоты встречаемости НФ1 в Республике Башкортостан и ее динамики, клинических особенностей НФ1 для совершенствования организационных и лечебно-диагностических подходов при оказании медицинской помощи пациентам с НФ1. **Материал и методы.** Проведено клинико-эпидемиологическое исследование больных НФ1 в Республике Башкортостан и сравнительный анализ с данными за 2009 и 2021 годы. **Результаты.** В Республике Башкортостан зарегистрировано 544 больных НФ1 из 433 семей в возрасте от 1 до 85 лет (средний возраст 30 лет и 7 месяцев), частота встречаемости составила 1:7407 человек. Характерные для НФ1 пигментные пятна определены у всех пациентов, кожные и подкожные нейрофибромы у 58 %, плексиформные нейрофибромы — у 7 %, сколиоз — у 17,4 %. Трудности в обучении выявлены у 14 %, эпилепсия — у 3,7 %, гидроцефалия — у 4 %, глиомы зрительных нервов — у 6 %, опухоли головного мозга — у 4 % больных. **Обсуждение.** Сравнительный анализ особенностей клинических проявлений НФ1 у больных из Республики Башкортостан с мировыми данными показал достоверно более редкое выявление нейрофибром, узелков Лиша, глиом зрительных нервов, нарушений интеллекта и психологических расстройств. Количество пациентов с НФ1 в республике увеличилось в 2,3 раза за 15 лет и на 35 % за последние 3 года. Более того, 4 больных с плексиформными нейрофибромами получают ингибитор митоген-активируемой протеинкиназы, показавший свою эффективность. **Заключение**. Полученные результаты свидетельствуют о повышении количества зарегистрированных случаев НФ1 за последние годы и необходимости мультидисциплинарного подхода в исследовании пациентов в связи с достоверно низкой частотой регистрации характерных симптомов болезни.

Ключевые слова: *ген NF1, диагностика, лечение, нейрофиброматоз 1-го типа, нейрофибромы, опухоли, частота встречаемости.*

Конфликт интересов

Авторы заявляют, что данная работа, её тема, предмет и содержание не затрагивают конкурирующих интересов

Источники финансирования

Авторы заявляют об отсутствии финансирования при проведении исследования

Соответствие принципам этики

Все пациенты подписывали информационное согласие. Протокол исследования был утвержден на заседании Локального этического комитета (протокол № 5 от 7 декабря 2009 года)

Статья получена 29.11.2024 г.
Одобрена рецензентом 06.02.2025 г.
Принята к публикации 13.03.2025 г.

Для цитирования: Мустафин Р.Н. КЛИНИЧЕСКАЯ ХАРАКТЕРИСТИКА НЕЙРОФИБРОМАТОЗА 1-ГО ТИПА В РЕСПУБЛИКЕ БАШКОРТОСТАН. Архивъ внутренней медицины. 2025; 15(3): 199-205. DOI: 10.20514/2226-6704-2025-15-3-199-205. EDN: HJYYBD

Abstract

Relevance. Neurofibromatosis type 1 (NF1) is a hereditary tumor syndrome occurring with a frequency of 1:3164 of the world's population. The disease is characterized by severe clinical manifestations such as multiple cutaneous and subcutaneous tumors, plexiform neurofibromas, skeletal abnormalities, cognitive disorders and various complications. **The aim of the study.** To determine the frequency of NF1 in the Republic of Bashkortostan and its dynamics, clinical features of NF1 to improve organizational and therapeutic and diagnostic approaches in providing medical care to patients with NF1.

Material and methods. A clinical and epidemiological study of NF1 patients in the Republic of Bashkortostan and a comparative analysis with data for 2009 and 2021 were conducted. **Results.** In the Republic of Bashkortostan, 544 patients with NF1 from 433 families aged 1 to 85 years (average age 30 years and 7 months) were registered, the incidence rate is 1:7407 people. Pigment spots were identified in all patients, cutaneous and subcutaneous neurofibromas in 58 %, plexiform neurofibromas in 7 %, scoliosis in 17.4 %. Learning difficulties were identified in 14 %, epilepsy in 3.7 %, hydrocephalus in 4 %, optic nerve gliomas in 6 %, and brain tumors in 4 % of NF1 patients from the republic. **Discussion.** A comparative analysis of the characteristics of NF1 in patients from the Republic of Bashkortostan with global data showed a significantly rarer detection of neurofibromas, Lisch nodules, optic nerve gliomas, intellectual disabilities and psychological disorders. The number of patients with NF1 in the republic has increased by 2.3 times in 15 years and by 35 % in the last 3 years. Moreover, 4 patients with plexiform neurofibromas are receiving a mitogen-activated protein kinase inhibitor, which has proven its effectiveness. **Conclusion**. The obtained results indicate an increase in the number of registered cases of NF1 in recent years, but the need for a multidisciplinary approach in the study of patients due to the reliably low frequency of registration of characteristic symptoms of the disease.

Keywords: *NF1 gene, diagnosis, treatment, neurofibromatosis type 1, neurofibromas, tumors, incidence.*

Conflict of interests
The authors declare no conflict of interests

Sources of funding
The authors declare no funding for this study

Conformity with the principles of ethics
All patients signed an informed consent. The study protocol was approved at a meeting of the Local Ethics Committee (protocol No. 5 dated December 7, 2009)

Article received on 29.11.2024
Reviewer approved 06.02.2025
Accepted for publication on 13.03.2025

For citation: Mustafin R.N. Clinical Characteristics of Neurofibromatosis Type 1 in the Republic of Bashkortostan. The Russian Archives of Internal Medicine. 2025; 15(3): 199-205. DOI: 10.20514/2226-6704-2025-15-3-199-205. EDN: HJYYBD

GTP — guanosine triphosphate, NF1 — neurofibromatosis, type 1, RB — Republic of Bashkortostan, CALM — café-au-lait macules, GCP — Good Clinical Practice, GRD — GAP-related domain, MPNST — malignant peripheral nerves sheath tumour, NIH — National Institutes of Health

Introduction

Neurofibromatosis, type 1 (NF1) is one of the most common hereditary tumour syndromes with autosomal dominant mode of inheritance, the global incidence of which is 1 : 3,164 people (the value varies between 1 : 2,132 and 1 : 4,712 depending on the country) [1]. This condition is driven by heterozygous mutations in *NF1* tumour suppressor gene, which encodes neurofibromin, GTP-activating protein, comprising 2,818 amino acids and containing a domain, downregulating the activity of Ras protooncogenes, called GRD (GAP-related domain) [2]. Approximately a half of all NF1 cases are sporadic due to new mutations in gametal cells in parents (80 % are found in spermatozoa) [3].

NF1 manifests with specific café-au-lait pigmented spots (CALM, café-au-lait macules) measuring over 5 mm in diameter in pre-puberty and over 15 mm in post-puberty (99 %), or inguinal or axillary freckles, iris hamartomas (Lisch nodules), cutaneous and subcutaneous neurofibromas, optic nerve gliomas and plexiform neurofibromas, as well as typical bone abnormalities (sphenolateral bone dysplasia, cortex thinning and/or long bone pseudoarthrosis). Where two or more of these signs are present, clinical NF1 is diagnosed as per the guidelines of the National Institutes of Health (NIH). Where NF1 is confirmed in close relatives, one sign of the disease is enough [4]. NF1 is associated with complete penetration, therefore molecular genetic verification is not mandatory, and the condition is diagnosed on the basis of the above criteria in 90 % of cases in patients under 7 years old and in 100 % of cases in patients under 19 years old [3].

According to global references, CALM is observed in 96.5 % of patients with NF1, while inguinal or axillary freckles are recorded in 90 % of cases. Cutaneous and/or subcutaneous neurofibromas are diagnosed in over 99 %, iris hamartomas — in 70 %, plexiform neurofibromas — in a half of NF1 patients [4]. The incidence of optic nerve gliomas in this disease is 27 %, brain tumours — 10 %, dropsy of brain — 7.7 % [5]. Malignant peripheral nerves sheath tumours (MPNST) are very rare and aggressive neoplasms in general population, while they are observed in 13 % of NF1 cases. Usually, these tumours are a result of canceration of existing plexiform neurofibromas [6].

Cognitive disorders in NF1 patients are diffuse and can be observed throughout their lives [3]. According to meta-analysis results, convulsive disorder is recorded in 8.1 % of NF1 patients (of which: generalised tonic-clonic epilepsy — 16.8 %, focal fits — 54.2 %; with one or two anticonvulsants, absence of seizures was observed in 68.5 %; median age: 3.5 to 12 years old) [7]. Impaired mental capacity, resulting in learning difficulties, is diagnosed in 40 % of NF1 cases; the mean IQ value is 85–90. Autism spectrum disorders are observed in 25–30 % of NF1 patients, while attention deficit/hyperactivity disorder is recorded in 40 % [3].

NF1 patients have locomotor disorders. According to a meta-analysis, approximately 26.6 % of NF1 patients have scoliosis. It usually develops in the early childhood and affects the thoracic spine. No reliable correlation between scoliosis and NF1 genotype has been identified. In terms of efficacy and safety, spinal fusion and growing rods demonstrated the best results in scoliosis management in NF1 patients [8]. On the average,

5 % of NF1 patients globally have pseudoarthrosis [4], 24 % of them have short stature [9]. Of interest is the description of the clinical presentation of NF1 in patients in the Republic of Bashkortostan and comparison of the results with the results of academic publications and meta-analyses from various countries, as well as previous data for this region. The results of the analysis can help in identifying the required areas of medical care improvement.

Study Objective

To identify the incidence of NF1 in the Republic of Bashkortostan and its changes, clinical characteristics of NF1 and comparison of results with available global data in order to improve organisational, treatment and diagnostic approaches to the management of NF1 patients.

Materials and Methods

The analysis included data on NF1 patients from the Republic of Bashkortostan (RB) registered with a genetics specialist at the Republican Medical and Genetics Centre with confirmed NF1. All the studies were performed in accordance with the requirements of biomedical ethics and GCP (Good Clinical Practice). We have studied clinical manifestations of NF1 in patients in RB and the comparison of the data with global results, as well as published results of studies conducted in RB in 2009 and 2021. Statistical processing of qualitative binary data was performed using an interactive 2×2 cross table with calculation of relation statistics (Pearson's χ^2) with Yates' correction for continuity developed by V. P. Leonov, as well as analysis of four-fold cross tables; see https://med-statistic.ru/calculators/calchi.html.

Results

In the Republic of Bashkortostan, there are 544 NF1 patients aged 1 to 85 years old (mean age: 30 years 7 months) in 433 families, i. e. 1 : 7,407 people, with uneven area distribution (Figure 1). Despite the fact that these figures differ from the global values more than two times (1 : 3,164 population [1]), if comparing to the 2009 national data (238 NF1 patients in 192 families, incidence: 1 : 17,000 [10]), the number of registered NF1 patient rose 2.3-fold, evidencing higher utilisation of genetics specialist services by patients. Over the past three years vs. the 2021 data (401 patients in 321 families, incidence: 1 : 10,103 [11]), the number of registered NF1 cases increased by 35 % (Figure 2).

In the RB, there are 299 sporadic cases (55 %) and 45 % of hereditary NF1 cases; male-to-female ratio is approximately 1 : 1 (52 % of females and 48 % of males), corresponding to the global statistics [3] and results of previous NF1 studies conducted in the RB [10, 11]. Pigmented spots were observed in all NF1 patients; 314 patients (58 %) had cutaneous or subcutaneous neurofibromas, which is lower than the global value (99 %) [4]. This difference can be explained by the fact that 42 % of patients, who did not present with cutaneous or subcutaneous neurofibromas, had their NF1 diagnosed from the family history (NF1 in either parent). Also, some patients had CALM + plexiform neurofibromas or CALM + optic nerve gliomas without visible cutaneous or subcutaneous neurofibromas, which meets the criteria set forth by the NIH for NF1 diagnosis. Of them, 112 people had focal neurofibromas, whereas the majority of patients (64 %) had multiple neurofibromas. Although the global incidence of MPNST in NF1 patients is 13 % [6], there were no cases of this neoplasm among 544 NF1 patients in the RB. Learning difficulties were diagnosed in 78 patients in the RB (14 %), which also differs from study results in other countries (40 %) [3].

Some NF1 patients in the RB had brain damage; 20 (3.7 %) NF1 patients had epilepsy, 23 (4.23 %) — dropsy of brain, 22 (4 %) — cerebral cysts, 21 (3.86 %) — brain growth, and 34 (6.25 %) — optic nerve gliomas. Lisch nodules were described just in 5 patients (1 %). Scoliosis was diagnosed in 95 NF1 patients (17.4 %), short stature — in 75 (13.8 %), lower-leg bones pseudoarthrosis — in 15 (3 %).

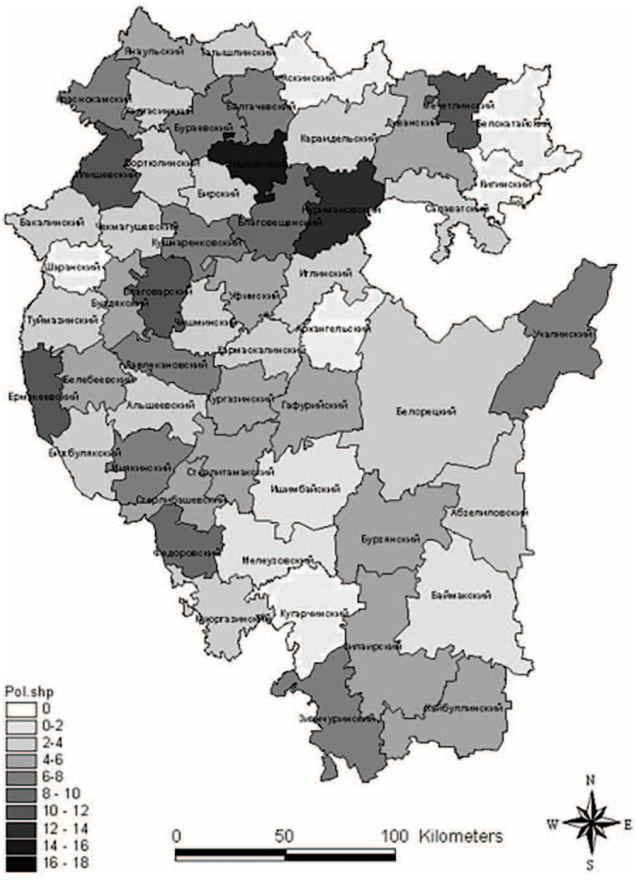

Figure 1. *Distribution map of patients with NF1 in the Republic of Bashkortostan*

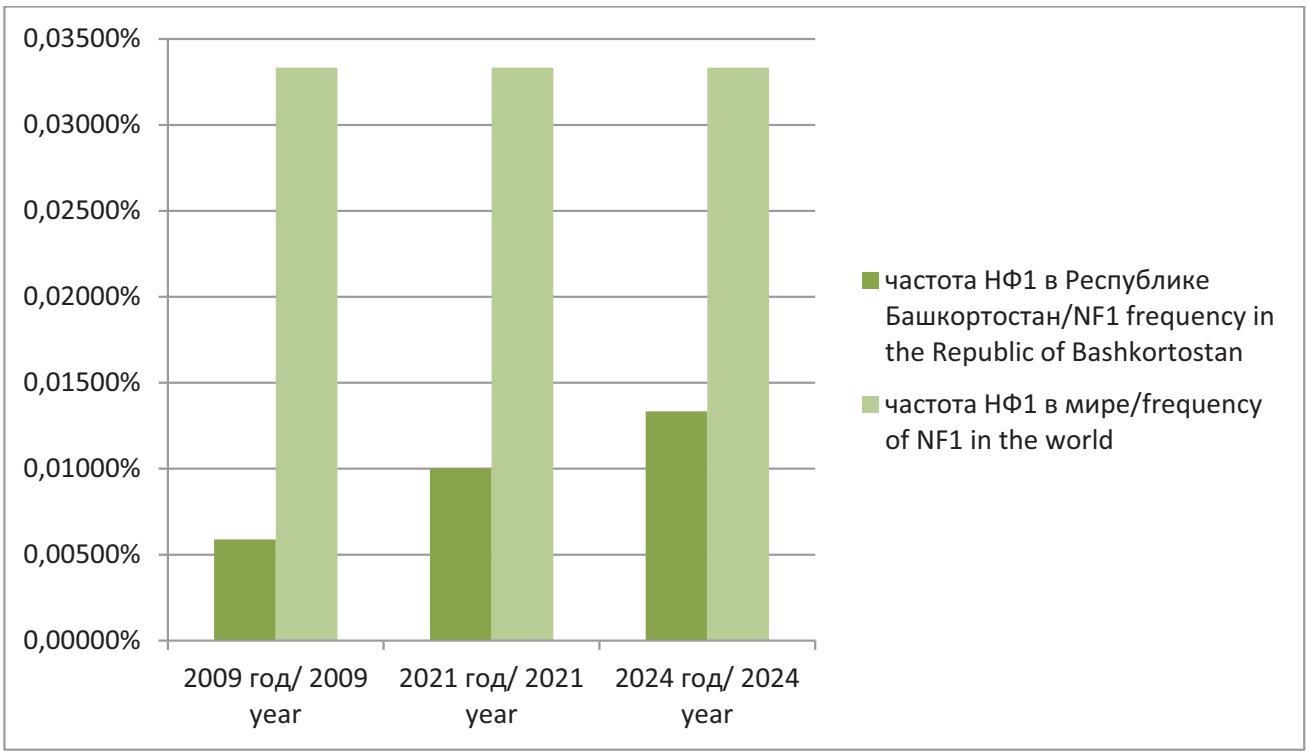

Figure 2. *Scheme of the dynamics of the increase in the frequency of occurrence of NF1 in the Republic of Bashkortostan and in the world*

Plexiform neurofibromas were described in 38 (7 %) NF1 patients in the RB. Four patients are currently undergoing efficient target therapy with mitogenic-activated protein kinase inhibitor (selumetinib [12]) within the Circle of Goodness program. These are a 10-year-old boy (inherited NF1 from his mother, selumetinib 30 mg/day) with facial plexiform neurofibroma; a 6-year-old boy (inherited NF1 from his father, selumetinib 30 mg/day) with oropharynx plexiform neurofibroma; a 12-year-old girl (inherited NF1 from her mother, selumetinib 50 mg/day) with hypopharynx plexiform neurofibroma; and a 6-year-old boy (sporadic case, selumetinib 20 mg/day) with plexiform neurofibroma of his supraclavicular region and mediastinum. With the therapy, the four NF1 patients had improvements over a one-year follow-up period: reduction in the size of plexiform neurofibromas.

Discussion

A comparative analysis of clinical manifestations of NF1 in patients in the Republic of Bashkortostan (Table 1) shows statistically significantly lower incidence of cutaneous and subcutaneous neurofibromas, Lisch nodules, plexiform neurofibromas, optic nerve gliomas, short stature and impaired mental capacity vs. global data [3–6, 9]. These data are likely to be a result of lack of specialised consultations to describe and diagnose the pathology. An analysis of medical records demonstrated that only eight NF1 patients in the RB were consulted by an eye specialist; following consultations, Lisch nodules were diagnosed in 63 %, which is also less than the global data [4], however, the difference is not statistically significant ($\chi^2 = 808$; $p = 0.369$). According to the data from medical records, oncologists consulted 168 (31 %) NF1 patients, mainly those with severe signs of disease, e.g., recorded plexiform neurofibromas, optic nerve gliomas, brain tumours, because these patients require a special approach and antitumour management. There are no data on consultations by surgeons, psychiatrists and psychologists in patient medical records, and such consultations need to be included into examinations of NF1 patients. More reliable pathology identification requires a thorough examination, consultation by an eye specialist, and NF1 signs, patient height and weight should be recorded in medical records; questionnaires should be used to identify any mental impairment.

Also, absence of MPNST, autism spectrum disorders and attention deficit disorder in NF1 patients in the RB is statistically different. It shows the need for whole-body MRI and consultation by a cancer specialist to diagnose MPNST, and consultation by a psychiatrist and psychologist to diagnose mental disorders. The incidence of CALM, brain tumours, dropsy of brain, epilepsy and skeleton abnormalities correlates with the data presented by other authors [4, 5, 7, 8].

Table 1. *Comparative characteristics of neurofibromatosis type 1 features in patients from the Republic of Bashkortostan with world data*

Clinical features	Frequency of occurrence in NF1-patients from RB in %	Frequency of occurrence in patients worldwide in % [author]	χ2 test; p-value at 1 degree of freedom
cutaneous and subcutaneous neurofibromas	58 %	99 % [4]	$\chi^2 = 49,8$; $p<0,001$
Lisch nodules	1 %	70 % [4]	$\chi^2 = 103,9$; $p<0,001$
plexiform neurofibromas	7 %	50 % [4]	$\chi^2 = 45,37$; $p<0,001$
MPNST	0 %	13 % [6]	$\chi^2 = 13,9$; $p<0,001$
optic nerve gliomas	6,25 %	27 % [5]	$\chi^2 = 16,004$; $p<0,001$
brain tumor	3,86 %	10 % [5]	$\chi^2 = 2,765$; $p = 0,097$
hydrocephalus	4,23 %	7,7 % [5]	$\chi^2 = 1,418$; $p = 0,234$
epilepsy	3,7 %	8,1 % [7]	$\chi^2 = 1,418$; $p = 0,234$
scoliosis	17,4 %	26,6 % [8]	$\chi^2 = 2,914$; $p = 0,088$
short stature	13,8 %	24 % [9]	$\chi^2 = 3,25$; $p = 0,072$
pseudoarthrosis	3 %	5 % [4]	$\chi^2 = 0,521$; $p = 0,471$
learning difficulties	14 %	40 % [3]	$\chi^2 = 27,022$; $p<0,001$
autism spectrum disorders	0 %	28 % [3]	$\chi^2 = 32,558$; $p<0,001$
attention deficit hyperactivity disorder	0 %	40 % [3]	$\chi^2 = 50$; $p<0,001$

Table 2. *Comparative analysis of clinical manifestations of NF1 in male and female patients from the Republic of Bashkortostan*

Clinical features	Frequency of occurrence in male NF1-patients with from RB, n=259	Frequency of occurrence in female NF1-patients with from RB, n=285	χ2 test; p-value at 1 degree of freedom
neurofibromas	149 (58 %)	165 (58 %)	$\chi^2 = 0,007$; $p = 0,932$
Lisch nodules	3 (1,16 %)	2 (0,7 %)	$\chi^2 = 0,311$; $p = 0,578$
plexiform neurofibromas	18 (7 %)	20 (7 %)	$\chi^2 = 0,001$; $p = 0,976$
optic nerve gliomas	19 (7,34 %)	15 (5,3 %)	$\chi^2 = 0,995$; $p = 0,319$
brain tumor	12 (4,6 %)	9 (3,1 %)	$\chi^2 = 0,796$; $p = 0,373$
hydrocephalus	14 (5,4 %)	9 (3,1 %)	$\chi^2 = 1,693$; $p = 0,194$
epilepsy	11 (4,3 %)	9 (3,1 %)	$\chi^2 = 0,455$; $p = 0,501$
scoliosis	47 (18,15 %)	48 (16,8 %)	$\chi^2 = 0,160$; $p = 0,689$
short stature	27 (10,4 %)	48 (16,8 %)	$\chi^2 = 3,480$; $p = 0,063$
pseudoarthrosis	4 (1,54 %)	11 (3,9 %)	$\chi^2 = 2,713$; $p = 0,100$
learning difficulties	46 (17,7 %)	32 (11,23 %)	$\chi^2 = 4,714$; $p = 0,030$

A comparative analysis of recorded clinical manifestations of NF1 in patients in the RB this year vs. 2009 [10] and 2021 [11] did not demonstrate significant changes in the incidence of clinical manifestations of the disease. In order to determine possible impact of sex differences on the incidence of NF1 symptoms, a comparative analysis of clinical signs in male and female patients was performed (Table 2). Significant differences were found only in terms of learning difficulties (learning difficulties are more frequent in male patients).

According to the analysed data from the study of NF1 patients in the RB, there is no information on the presence of autism spectrum disorders, attention deficit/hyperactivity disorder; however, the global incidence of these conditions among patients is 30–60 % and 25–30 %, respectively [3]. It demonstrates the need to refer NF1 patients to psychologists, neurologists and psychiatrists for timely diagnosis and management of neurological and mental disorders. It is even more important, since multiple neurofibromas on patients' bodies (64 % of examined NF1 patients) have mental implications [3] (Figure 3). Medical records of NF1 patients in the RB do not contain any data on mental disorders, such as depression, anxiety or distress; however, scientific references suggest that these conditions are not uncommon among NF1 patients. For instance, clinical depression is diagnosed in 19 % and anxiety disorders are observed in 15 % of NF1 patients [13]. Their diagnosis and management by a psychologist will help improve the quality of patient's life significantly. Given a new therapy of plexiform neurofibromas — mitogenic-activated protein kinase inhibitor (selumetinib), this product should be used more widely, since plexiform neurofibromas were diagnosed in 38 NF1 patients in the RB. Indications for selumetinib therapy currently include documented plexiform neurofibroma, and the condition of use is genetically confirmed NF1 (heterozygous mutation in gene *NF1*) [14]. Efficiency criteria of the medicinal product are tumour reduction, which, according to a meta-analysis [12], was observed in 75.3 %. The majority of adverse reactions to selumetinib were mild; the most common reactions were diarrhoea and vomiting [12].

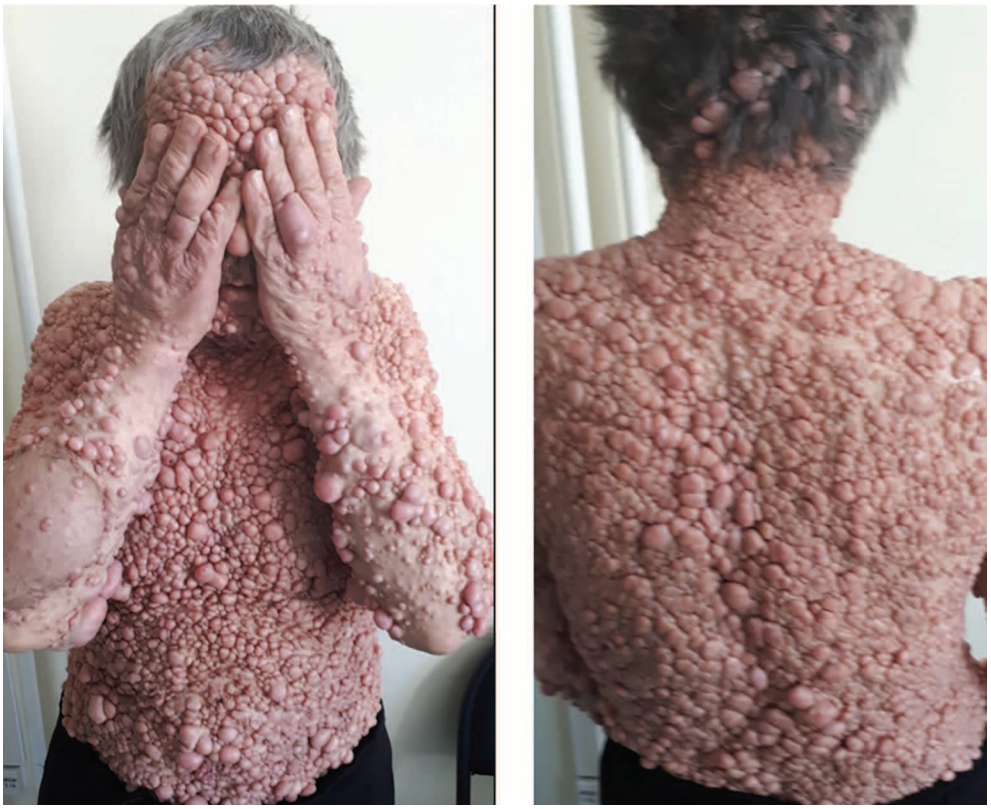

Figure 3. *A patient from the Republic of Bashkortostan with multiple cutaneous and subcutaneous neurofibromas (the author's photo was taken with the consent of the patient and his relatives).*

Conclusion

We have conducted a clinical and epidemiological study of NF1 patients in the Republic of Bashkortostan. As a result, we have identified the incidence of the disease, which was 1 : 7,407, i.e. significantly lower than the global figures (1 : 3,164); however, the incidence is significantly higher than in previous periods. The ration between male and female NF1 patients was 1 : 1, sporadic cases accounted for 55 %. The clinical characteristics of NF1 patients in the Republic of Bashkortostan show comparable incidence of neurofibromas, brain tumours, dropsy of brain, epilepsy, scoliosis, and pseudoarthrosis if compared to the global data. Significantly lower incidence of plexiform neurofibromas, optic nerve gliomas, short stature and impaired mental capacity have been observed in NF1 patients in the Republic of Bashkortostan. It has been established that the incidence of clinical manifestations of the disease in male and female patients is comparable, and men have learning difficulties more often. An analysis of patient examination in the Republic of Bashkortostan shows the need for patient referral to all-body MRI for timely diagnosis of plexiform neurofibromas, because these tumours are an indication for mitogenic-activated protein kinase inhibitor therapy. Since the diagnosis of NF1 is based on NIH-approved clinical criteria, a multidisciplinary approach in disease diagnosis would be advisable. Also, consultations by specialists can help in more precise diagnosis of NF1, since this condition shares clinical presentation with other diseases [15]. For instance, a consultation by an eye specialist can help diagnose Lisch nodules, the presence of which is described just in 1 % of all NF1 patients in the RB. A consultation by a neurosurgeon allows identifying an approach to the management of dropsy of brain, tumours and cerebral cysts. Referral of paediatric NF1 patients to an orthopaedist can ensure early diagnosis and correction of skeleton abnormalities. Resection of multiple cutaneous and subcutaneous neurofibromas is possible in a surgical ward, especially in those using a surgical laser [14]. In order to diagnose and treat autism spectrum disorders, attention deficit/hyperactivity disorder, cognitive deficit and distress caused by numerous psycho-traumatic tumours, it is advisable to refer patients to psychologists and psychiatrists. These measures will significantly improve the quality of diagnosis and management of NF1 patients and make their life better.

Список литературы/ References:

1. Lee T.J., Chopra M., Kim R.H. et al. Incidence and prevalence of neurofibromatosis type 1 and 2: a systematic review and meta-analysis. Orphanet. J. Rare Dis. 2023; 18(1): 292. doi: 10.1186/s13023-023-02911-2.
2. Chai P., Luo Y., Zhou C. et al. Clinical characteristics and mutation Spectrum of NF1 in 12 Chinese families with orbital/periorbital plexiform Neurofibromatosis type 1. BMC Med. Genet. 2019; 20(1): 158. doi: 10.1186/s12881-019-0877-9.
3. Crow A.J.D., Janssen J.M., Marshall C. et al. A systematic review and meta-analysis of intellectual, neuropsychological, and psychoeducational functioning in neurofibromatosis type 1. Am. J. Med. Genet. A. 2022; 188(8): 2277-2292. doi: 10.1002/ajmg.a.62773.

4. Ly K.L., Blakeley J.O. The diagnosis and management of neurofibromatosis type 1. Med Clin North Am 2019;103:1035–54. DOI: 10.1016/j.mcna.2019.07.004.
5. Glombova M., Petrak B., Lisy J. et al. Brain gliomas, hydrocephalus and idiopathic aqueduct stenosis in children with neurofibromatosis type 1. Brain Dev. 2019; 41(8): 678–90. doi: 10.1016/j.braindev.2019.04.003.
6. Lim Z., Gu T.Y., Tai B.C., Puhaindran M.E. Survival outcomes of malignant peripheral nerve sheath tumors (MPNSTs) with and without neurofibromatosis type I (NF1): a meta-analysis. World J. Surg. Oncol. 2024; 22(1): 14. doi: 10.1186/s12957-023-03296-z.
7. Wu F., Ji X., Shen M. et al. Prevalence, clinical characteristics and outcomes of seizures in neurofibromatosis type 1: A systematic review and single arm meta-analysis. Epilepsy Res. 2024; 208: 107476. doi: 10.1016/j.eplepsyres.2024.107476.
8. Wang D., Zhang B.H., Wen X. et al. Clinical features and surgical treatments of scoliosis in neurofibromatosis type 1: a systemic review and meta-analysis. Eur Spine J. 2024; 33(7): 2646-2665. doi: 10.1007/s00586-024-08194-w.
9. Virdis R., Street M.E., Bandello M.A. et al. Growth and pubertal disorders in neurofibromatosis type 1. J Pediatr Endocrinol Metab. 2003; 16 (2): 289–92.
10. Мустафин Р.Н., Бермишева М.А., Хуснутдинова Э.К. Клинико-эпидемиологическое исследование нейрофиброматоза 1 типа в Республике Башкортостан. Якутский медицинский журнал. 2009; 2(26): 23–25.
Mustafin R.N., Bermisheva M.A., Khusnutdinova E.K. Clinical and epidemiological study of neurofibromatosis type 1 in the Republic of Bashkortostan. Yakut Medical Journal. 2009; 2(26): 23-25 [in Russian].
11. Мустафин Р.Н., Валиев Р.Р., Бермишева М.А., Хуснутдинова Э.К. Анализ особенностей нейрофиброматоза 1 типа в Республике Башкортостан. Гены и клетки. 2021; 16(3): 16-21.
Mustafin R.N., Valiev R.R., Bermisheva M.A., Khusnutdinova E.K. Analysis of the features of neurofibromatosis type 1 in the republic of Bashkortostan. Genes and Cells. 2021; 16(3): 16-21 [in Russian]. doi: 10.23868/202110007.
12. Han Y, Li B, Yu X, Liu J, Zhao W, Zhang D, Zhang J. Efficacy and safety of selumetinib in patients with neurofibromatosis type 1 and inoperable plexiform neurofibromas: a systematic review and meta-analysis. J Neurol. 2024 May;271(5):2379-2389. doi: 10.1007/s00415-024-12301-8.
13. Doser K., Andersen E.W., Kenborg L. et al. Clinical characteristics and quality of life, depression, and anxiety in adults with neurofibromatosis type 1: A nationwide study. Am J Med Genet A. 2020; 182(7): 1704-1715. doi: 10.1002/ajmg.a.61627.
14. Мустафин Р.Н. Возможности диагностики и лечения нейрофиброматоза 1-го типа в России. Сибирский онкологический журнал. 2023;22(3):119-124.
Mustafin R.N. Prospects for diagnostics and treatment of neurofibromatosis type 1 in Russia. Siberian Journal of Oncology. 2023; 22(3):119-124 [in Russian]. doi: 10.21294/1814-4861-2023-22-3-119-124.
15. Мустафин Р.Н. Клинические маски нейрофиброматоза 1-го типа. Архив внутренней медицины. 2022. Т. 12. № 2 (64). С. 93-103.
Mustafin R.N. Clinical Masks of Neurofibromatosis Type 1. The Russian Archives of Internal Medicine. 2022; 12(2): 93-103 [in Russian]. doi: 10.20514/2226-6704-2021-12-2-93-103.

Информация об авторах

Мустафин Рустам Наилевич — к.б.н., доцент кафедры медицинской генетики и фундаментальной медицины Федерального государственного бюджетного образовательного учреждения высшего образования «Башкирский государственный медицинский университет» Министерства здравоохранения Российской Федерации (ФГБОУ ВО БГМУ Минздрава России), Уфа, e-mail: ruji79@mail.ru, ORCID ID: http://orcid.org/0000-0002-4091-382X.

Information about the authors

Rustam N. Mustafin — PhD, associate professor of the department of Medical Genetics and Fundamental Medicine of the Federal State Budgetary Educational Institution of Higher Education «Bashkir State Medical University» of the Ministry of Health of the Russian Federation, Ufa, e-mail: ruji79@mail.ru, ORCID ID: http://orcid.org/0000-0002-4091-382X.

Автор, ответственный за переписку / Corresponding author