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ORIGINAL ARTICLE

Satisfaction from surgical treatment and its influence on the wellbeing of patients with Recklinghausen disease – preliminary report

Authors' Contribution:
A – Study Design
B – Data Collection
C – Statistical Analysis
D – Manuscript Preparation
E – Literature Search
F – Funds Collection

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ABSTRACT:

Background: Neurofibromatosis type 1 (NF-1) is one of the most common autosomal dominant disorders. Multiple benign dermal neurofibromas, café au lait spots, axillary and inguinal freckling are the hallmarks of NF-1.

Aim: The aim of this paper is to verify if surgical treatment performed in patients with NF-1 is satisfactory to them and to describe demographic factors characteristic for patients with Recklinghausen disease.

Methods: A special questionnaire was prepared for the study, which contained 45 questions. Seventeen patients with neurofibromatosis type 1 agreed to fill in the questionnaire aged from 22 to 61 years.

Results: Surgical treatment in patients was started between 6 and 45 years of age. All patients declared their will to continue surgical treatment. After treatment patients felt more comfortable, more self-confident and sociable. The first symptoms of neurofibromatosis were seen at about 13 years of life in most patients. All women who gave birth noticed progression of the disease during pregnancy.

Conclusions: Performed surgical treatment raises life comfort and increases self-confidence in patients with neurofibromatosis type 1. Due to visible skin changes in neurofibromas it is worth referring patients to Plastic Surgery Departments. Doctors dealing with patients with NF-1 should inform them about the potential heredity of the disease and that puberty and pregnancy intensify the process of skin neurofibroma development.

KEYWORDS: neurofibromatosis type 1, satisfaction, self-confidence, surgical treatment

ABBREVIATIONS

NF-1 – neurofibromatoza type 1

BACKGROUND

Neurofibromatosis type 1 (NF-1) was first described in 1882 by Friedrich Daniel von Recklinghausen [1]. He was a German pathologist and he introduced the term neurofibromatosis to medicine [1]. Until today, two names of the condition, i.e. neurofibromatosis type 1 and von Recklinghausen's disease, are used interchangeably.

NF-1 is one of the most common autosomal dominant disorders with an incidence of approximately one in 3000 live births regardless of the ethnicity, race and gender [2, 3]. Approximately 50% of mutations found in patients with Recklinghausen's disease are de novo ones [4]. Gene penetrance in this condition is 100% but clinical manifestations vary widely between patients [3]. People with NF-1, even with the same mutation, or even from the same family, may have extremely distinct medical signs of the disease, which may complicate genetic counseling [3, 4]. This suggests the significant role of modifier genes or epigenetic factors that are responsible for such a wide variability of NF-1 [5].

The development of neurofibromatosis type 1 is a consequence of inactivation of the NF-1 gene. This gene, located on chromosome 17, is characterized by one of the greatest frequencies of spontaneous mutation in the whole human genome [6]. Its product, a cytoplasmic protein called neurofibromin, is a tumor suppressor, with expression detected in various cells, mainly in melanocytes, neurons, Schwann cells and glial cells [6]. Due to its antitumor function, inactivation of the NF-1 protein leads to the growth of several neoplasms, mainly of the skin and central nervous system [6].

Multiple benign dermal neurofibromas, café au lait spots, axillary and inguinal freckling are the hallmarks of NF-1 [2]. Most characteristic are neurofibromas which occur in almost all NF-1 patients at some point of lifetime [7]. Although neurofibromas are benign tumors, they can be disfiguring and can cause cosmetic problems, while plexiform neurofibromas may progress to malignant peripheral nerve sheath tumors [7, 8]. When describing the progression of the disease various scales can be used. One of most popular is the Ablon scale in which the visibility of skin lesions is divided into three degrees [9].

The aim of this paper is to verify if surgical treatment performed in patients with NF-1 is satisfactory to them and to describe demographic factors characteristic for patients with Recklinghausen's disease.

METHODS

Our Department has 39 patients with Recklinghausen's disease under its care. In this group there are 25 women and 14 men. A special questionnaire was prepared for this study. It contained 45 questions. In the first part there were questions about

demographic issues (sex, age, place of living, place of origin, education, occupation). In the second part there were questions concerning neurofibromatosis (the age of the first symptom appearance, course of the disease, progression of the disease in the Ablon scale, undertaken treatment, number of performed surgeries, access to treatment funding by the Polish health care system, patients' satisfaction from performed operations).

The questionnaire was filled in by patients who presented to our Clinic for a control examination or for the next operation. The protocol of the study was approved by the ethics review board of the Medical University of Lodz, and the study was conducted according to the Declaration of Helsinki principles.

RESULTS

Seventeen patients agreed to fill in the questionnaire (11 women and 6 men) aged from 22 to 61 years (mean age 38.7 years). More than a half of the respondents (58.8%) were from the cities, while the rest (41.2%) from the country. Currently, most patients live in the cities (76.5%), while the rest (23.5%) in the country. Higher education was declared by 35.3% of the respondents, secondary – 23.5%, professional – 35.3%, primary – 5.9%. More than a half of patients are married (58.8%), 29.4% of the respondents are single, one woman is divorced (5.9%) and one woman is a widow (5.9%). More than a half of the individuals (52.9%) are manual workers, 23.5% are white-collar workers, 11.8% have their own business, one man is still learning (5.9%), and one woman is on pension (5.9%).

The first symptoms of neurofibromatosis were noticed at about 13 years of life in most patients, some had neurofibromas since birth, and the rest had their tumors developed over the course of 30 years. All women who gave birth (6 respondents) noticed progression of the disease during pregnancy. Nine people (52.9%) declared that their Recklinghausen's disease is familial (the same symptoms were present in parents, siblings or children), 8 respondents (47.1%) had no family history of NF-1. In 15 patients (88.2%) there were more skin tumors than café au lait spots; only in one person (5.9%) an opposite tendency was observed, and in one woman (5.9%) the quantity of tumors and spots was almost equal.

The majority of neurofibromas in our patients were present on the skin of the abdomen, back and face, less of them were observed on the scalp, chest and upper and lower limbs. Most of the patients suffered from NF-1 only, one person had additionally hypertension, thyroid hypofunction, uterus myoma and esophageal reflux. These patients take medications according to the primary care physicians' recommendations. Additionally, 5 persons were diagnosed with a visual defect: – 2 with cardiac defect and one with scoliosis. Surgical treatment in patients was started between the age of 6 and 45 years (mean age 24.2 years). Almost half of the patients (47.1%) had been operated on less than 10 times, but 17.6% had more than 21 surgeries. Almost all of the respondents (94.1%) are satisfied with the performed surgical treatment; only one person (5.9%) did not have any opinion on this issue. However, it should be pointed out that this patient was after the first operation. All patients declared their will to continue surgical treatment. One-third of patients (35.3%) with NF-1 think that access to medical care is easy, but just a little less of them (29.4%) have an opposite belief, the rest (35.3%) did not have any opinion on this topic.

According to the patients, before surgeries they felt less comfortable (52.9%), less self-confident (5.9%) and less sociable (11.8%). The rest of the respondents (29.4%) did not refer to any of these conditions.

After surgical treatment 64.6% of patients declared that they were more comfortable, 11.8% were more self-confident and 11.8% more sociable. Only 2 persons (11.8%) did not refer to the above-mentioned terms.

Most of the patients (76.5%) had a moderate form of the disease according to the Ablon scale, the rest (23.5%) had a severe type of NF-1.

DISCUSSION

Neurofibromatosis type 1 is a multisystem disease with a complex phenotype [4]. It is characterized by the number of distinguishable features, most of which are unfortunately visible and can cause an esthetic problem. To assess the visibility of the disease, the Ablon scale can be used. It has three grades: mild, moderate and severe [9]. The degrees are based on the appearance of the person fully dressed and how readily the physical symptoms could be perceived in impersonal interaction [10]. Grade 1 in the Ablon scale indicates a mild case: essentially no tumors visible outside of normal clothing areas; gait and posture appear unremarkable when casually observed. Grade 2 indicates a moderate case: some tumors appear on the neck, face, and hands, and mild scoliosis or other skeletal features are present but without a noticeable limp. Grade 3 indicates a severe case: numerous tumors appear on the face; optic glioma (tumor) affects sight; severe scoliosis or skeletal features are present causing a noticeable limp [9]. Souza et al. performed a study in a group of 183 patients with NF-1 [11]. More than one-half of the patients presented moderate and severe levels of NF-1 [11]. Bicudo et al. in their research on the group of 15 patients revealed that 3 persons presented a mild form of the disease, 8 – moderate and 2 – severe [3]. In our group we had 13 patients with a moderate neurofibromatosis type 1 and 4 with a severe grade. It can be concluded that Recklinghausen's disease is more frequent and severe then it is usually thought to be.

Type 1 neurofibromatosis is inherited in an autosomal dominant manner, however in about 50% of patients de novo mutations are detected [4]. In the study by Hummelvoll and Antonsen, 7 patients had a familial background of NF-1 and 8 had no such background [12]. In other research, performed by Bicudo et al., 9 patients presented familial inheritance of the disease, 3 had new mutations and in one person the etiology was unknown [3]. Similar results were obtained in our group of patients: 9 of them had a familial background of the disease while 8 not. The literature indicates that cutaneous neurofibromas usually appear around puberty, increase with age and undergo periods of rapid growth in puberty and pregnancy [13]. In 50% of patients with NF-1 the clinical symptoms of the disease become apparent below the first year of life and in 97% before the age of 8 [4]. Dugoff and Sujansky examined a large group of pregnant women with von Recklinghausen's disease. The authors reported that sixty-four of one hundred and five women reported growth of new neurofibromas during pregnancy and fifty-five noted enlargement of the existing neurofibromas [14]. In our group, a majority of patients had their neurofibromas revealed during

puberty at about 13 year of age. All women who had children noticed changes in the size of their neurofibromas and growth of new ones during the period of pregnancy. The patients diagnosed with neurofibromatosis type 1 should be informed that this condition has unpredicted course, many new skin tumors can develop during puberty and during pregnancy (which is very characteristic). Doctors who make the diagnosis of NF-1 and treat such patients should be always informed about its genetic basis and probability of disease inheritance.

The fundamental method of treatment in patients with neurofibromatosis type 1 is surgical removal of skin tumors. It is usually performed in stages because it is almost impossible to remove all neurofibromas during a single operation [15]. It should be emphasized that such surgeries are not cosmetic procedures, but they restore normal appearance in this congenital neoplastic disease [16]. The majority of our patients are satisfied with the performed treatment although it is divided into multiple stages. All of them plan to perform such surgeries in the future. Surgical treatment is funded by the Polish health care system and that is why patients with Recklinghausen's disease can be referred to surgical clinics. As in many cases neurofibromas occur in the face area or in the visible parts of the body, it is indicated to refer such patients to Plastic Surgery Departments in order for them to achieve the best aesthetic results of operations.

This study is not free from limitations. Only 17 persons from 39 with NF-1 agreed to participate in it (43.6%) so our data form preliminary report. Further research is needed to confirm our conclusions. We will try to encourage more patients with Recklinghausen's disease to fill in the questionnaire and every new patient with NF-1 will be asked to complete it after the third surgery.

CONCLUSIONS

1. So far, the performed surgical treatment raised the quality of life and increased the self-confidence of patients with neurofibromatosis type 1;

2. Due to the visibility of neurofibromas it is worth to refer patients to the Plastic Surgery Departments;

3. Doctors dealing with patients with NF-1 should inform them about its e heredity and that puberty and pregnancy intensify the process of skin neurofibroma development.

Tab. I. Questionnaire.

QUESTIONNAIRE
Gender:
a/ F
b/ M
Age ... /years/
Area of residence:
a/ rural
b/ urban, below 20,000 inhabitants
c/ urban, from 21,000 to 50,000 inhabitants
d/ urban, from 51,000 to 100,000 inhabitants
b/ urban, above 20,000 inhabitants
Area of origin:
a/ rural
b/ urban, below 20,000 inhabitants
c/ urban, from 21,000 to 50,000 inhabitants
d/ urban, from 51,000 to 100,000 inhabitants
b/ urban, above 20,000 inhabitants
Educational background:
a/ elementary
b/ vocational
c/ secondary
d/ incomplete higher
e/ higher
Current marital status:
a/ single
b/ married/in partnership
c/ divorced
d/ widowed
Current occupation:
a/ own business
b/ physical worker
c/ intellectual worker
d/ public official
e/ university student
f/ school student
g/ retired/pensioner
h/ unemployed
I observed the first symptoms of the disease at the age of ..... / years/
Is anyone in your family suffering from Recklinghausen's disease/ having similar symptoms/?
a/ yes
b/ no
c/ I don't know
If yes, provide the degree of kinship .....

QUESTIONNAIRE
The lesions are present in greatest numbers within your:
a/ face
b/ scalp
c/ neck
d/ neckline
e/ abdomen
f/ back
g/ buttocks
h/ arms and forearms
i/ hands
j/ thighs and lower legs
k/ feet
Please indicate 3 areas, with number 1 corresponding to the most affected area and number 3 corresponding to the least affected area.
Apart from Recklinghausen's disease, I suffer from:
a/ arterial hypertension
b/ hypothyroidism
c/ hyperthyroidism
d/ diabetes
e/ depression
f/ ischemic heart disease
g/ kidney stone disease
h/ other .....
I am permanently taking medications:
a/ yes
b/ no
If yes, provide details .....
I was diagnosed with other defects:
a/ yes
b/ no
If yes, provide details .....
I first received surgical treatment at the age of ..... /please enter age in years/
The number of my surgical treatments received to date is within the range of /please specify/:
a/ 1 to 5
b/ 6 to 10
c/ 11 to 15
d/ 16 to 20
e/ above 21
Please mark all the answers that apply to you, numbering them in the most-relevant to least-relevant order.
Before starting surgical treatment:
a/ I was socially withdrawn
b/ I was feeling less comfortable
c/ I was less confident
d/ I used to meet friends less often
e/ none of the above
f/ other .....

QUESTIONNAIRE
I am satisfied with my surgical treatment:
a/ yes, definitely
b/ yes, somewhat
c/ I don't know
d/ rather not
e/ definitely not
I intend to continue with my surgical treatment:
a/ yes, definitely
b/ yes, probably
c/ I don't know
d/ rather not
e/ definitely not
In my opinion, it is difficult to get access to National Health Fund-reimbursed treatment of Recklinghausen's disease:
a/ yes, definitely
b/ yes, somewhat
c/ I don't know
d/ rather not
e/ definitely not
Suffering from Recklinghausen's disease, I feel "different":
a/ yes, definitely
b/ yes, probably
c/ I don't know
d/ rather not
e/ definitely not
I used to have problems with learning at school:
a/ yes, definitely
b/ yes, somewhat
c/ I don't know
d/ rather not
e/ definitely not
In my opinion, my school grades were poorer than those of my peers:
a/ yes, definitely
b/ yes, somewhat
c/ I don't know
d/ rather not
e/ definitely not
I had to repeat a year:
a/ yes
b/ no
I have a narrow circle of friends:
a/ yes, definitely
b/ yes, somewhat
c/ I don't know
d/ rather not
e/ definitely not
If yes: I believe this is related to my disease
a/ yes, definitely

QUESTIONNAIRE
b/ yes, somewhat
c/ I don't know
d/ rather not
e/ definitely not
I believe I was hurt by nature
a/ yes, definitely
b/ yes, somewhat
c/ I don't know
d/ rather not
e/ definitely not
I have problems with establishing social contacts
a/ yes, definitely
b/ yes, somewhat
c/ I don't know
d/ rather not
e/ definitely not
I believe that due to my suffering from Recklinghausen's disease I experience more failures than healthy individuals:
a/ yes, definitely
b/ yes, somewhat
c/ I don't know
d/ rather not
e/ definitely not
I consider myself to be an attractive life partner:
a/ yes, definitely
b/ yes, somewhat
c/ I don't know
d/ rather not
e/ definitely not
I have problems with memorizing things:
a/ yes, definitely
b/ yes, somewhat
c/ I don't know
d/ rather not
e/ definitely not
I have problems with focusing on things:
a/ yes, definitely
b/ yes, somewhat
c/ I don't know
d/ rather not
e/ definitely not
I am observant:
a/ yes, definitely
b/ yes, somewhat
c/ I don't know
d/ rather not
e/ definitely not

QUESTIONNAIRE

My disease is a cause of additional worries:

a/ yes, definitely

b/ yes, somewhat

c/ I don't know

d/ rather not

e/ definitely not

Please mark all the answers that apply to you, numbering them in the most-relevant to least-relevant order.

Following the surgical:

a/ I feel I am a more sociable person

b/ I feel more comfortable

c/ I am more confident

d/ I meet friends more often

e/ none of the above

f/ other .....

I am an aggressive person:

a/ yes, definitely

b/ yes, somewhat

c/ I don't know

d/ rather not

e/ definitely not

I believe other people are prejudiced against me because of my disease:

a/ yes, definitely

b/ yes, somewhat

c/ I don't know

d/ rather not

e/ definitely not

I have heard opinions that my disease might be "contagious":

a/ yes, definitely

b/ yes, somewhat

c/ I don't know

d/ rather not

e/ definitely not

I have withdrawn from certain social activity because of Recklinghausen's disease:

a/ yes, definitely

b/ yes, somewhat

c/ I don't know

d/ rather not

e/ definitely not

If yes, provide details on the activity you have withdrawn from ...

.....

QUESTIONNAIRE

I have had difficulty finding a job because of Recklinghausen's disease:

a/ yes, definitely

b/ yes, somewhat

c/ I don't know

d/ rather not

e/ definitely not

I have lost a job because of Recklinghausen's disease:

a/ yes, definitely

b/ yes, somewhat

c/ I don't know

d/ rather not

e/ definitely not

Do you have children?

a/ yes

b/ no

Do you think about having children?

a/ yes

b/ no

c/ I don't know

Are you afraid your children might inherit Recklinghausen's disease?

a/ yes, definitely

b/ yes, somewhat

c/ I don't know

d/ rather not

e/ definitely not

Have you ever received psychological counseling?

a/ yes

b/ no

If yes, provide details on the reason for counseling

.....

Disease grading /Ablon's scale/:

a/ mild — no tumors are visible outside of normal clothing areas; gait and posture appear unremarkable

b/ moderate — some tumors appear on the neck, face, and hands; mild scoliosis is present

c/ severe — numerous tumors appear on the face; scoliosis is present; neurofibroma causing visual disturbances.

REFERENCES

1. von Recklinghausen F.D.: Über die multiplen Fibrome der Haut und ihre Beziehung zu den multiplen Neuromen. Festschrift für Rudolf Virchow (Berlin), 1882.
2. Langenbruch A.K., Augustin M., Granström S., Kluwe L., Mautner V.F.: Clinical and healthcare status of patients with neurofibromatosis type 1. Br J Dermatol, 2011; 165(1): 225–227.
3. Bicudo N.P., de Menezes Neto B.F., da Silva de Avó L.R., Germano C.M., Melo D.G.: Quality of Life in Adults with Neurofibromatosis 1 in Brazil. J Genet Couns, 2016; 25(5): 1063–1074.
4. Abramowicz A, Gos M.: Neurofibromin in neurofibromatosis type 1 – mutations in NF1 gene as a cause of disease. Dev Period Med., 2014; 18(3): 402–411.
5. Ferner R.E.: Neurofibromatosis 1. Eur J Hum Genet, 2007; 15(2): 131–138.
6. Bikowska-Opalach B., Jackowska T.: Neurofibromatosis type 1 – description of clinical features and molecular mechanism of the disease. Med Wieku Rozwoj, 2013; 17(4): 334–340.
7. Rosenbaum T., Wimmer K.: Neurofibromatosis type 1 (NF1) and associated tumors. Klin Padiatr, 2014; 226(6–7): 309–315.
8. Crawford H.A., Barton B., Wilson M.J., Berman Y., McKelvey-Martin V.J. et al.: The Impact of Neurofibromatosis Type 1 on the Health and Wellbeing of Australian Adults. J Genet Couns, 2015; 24(6): 931–944.
9. Ablon J.: Gender response to neurofibromatosis 1. Soc Sci Med., 1996; 42(1): 99–109.
10. Wolkenstein P., Zeller J., Revuz J., Ecosse E., Leplège A.: Quality-of-life impairment in neurofibromatosis type 1: a cross-sectional study of 128 cases. Arch Dermatol, 2001; 137(11): 1421–1425.
11. Souza J.F., Toledo L.L., Ferreira M.C., Rodrigues L.O., Rezende N.A.: Neurofibromatosis type 1: more frequent and severe then usually thought. Rev Assoc Med Bras, 2009; 55(4): 394–399.
12. Hummelvoll G., Antonsen K.M.: Young adults' experience of living with neurofibromatosis type 1. J Genet Couns, 2013; 22(2): 188–199.
13. Cannon A., Chen M.J., Li P., Boyd K.P., Theos A. et al.: Cutaneous neurofibromas in Neurofibromatosis type I: a quantitative natural history study. Orphanet J Rare Dis, 2018; 13(1): 31–37.
14. Dugoff L., Sujansky E.: Neurofibromatosis type 1 and pregnancy. Am J Med Genet, 1996; 66(1): 7–10.
15. Acartürk T.O., Yiğenoğlu B., Pekedis O.: Excision and „transcutaneous" lift in patients with neurofibromatosis of the fronto-temporo-orbital and auricular regions. J Craniofac Surg, 2009; 20(3): 771–774.
16. Taylor L.A., Lewis V.L. Jr.: Neurofibromatosis Type 1: Review of Cutaneous and Subcutaneous Tumor Treatment on Quality of Life. Plast Reconstr Surg Glob Open, 2019; 7(1): e1982.

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