CLINICAL MANIFESTATIONS OF NEUROFIBROMATOSIS TYPE 1

Anna M.Dąbrowska[1], Agnieszka Zwolak[1,2], Maria Kurowska[1], Jerzy S.Tarach[1]

[1]Department of Endocrinology, [2]Department of Internal Medicine in Nursing, Medical University, Lublin, Poland

Introduction

NEUROFIBROMATOSIS TYPE 1 (NF1; von Recklinghausen's disease), a disease first described by pathologist- Friederich Daniel von Recklinghausen in 1882, is an **autosomal disorder** with a penetrance of almost 100% and without sex or racial predilection. Its **prevalence** is estimated to be **1 in 3 000 births**.

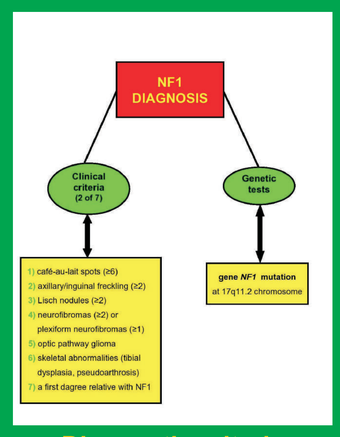
NF 1 is caused by dominant loss-of-function **mutation of the tumour-suppressor gene *NF1***, located at the 17q11.2 chromosome, encoding **neurofibromin** - a protein expressed in neurons, Schwann cells, oligodendrocytes and leukocytes and taking part in some intracellular processes.

NF1 may affect **various organs** and patients are at increased risk of developing **many neoplasms**.
The **CLINICAL MANIFESTATIONS** of the disease **may differ significantly**- from mild lesions to several complications and function impairment, even in members of one family.

Material and Methods

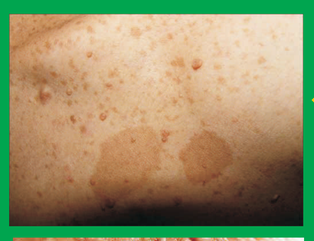
We **analyzed retrospectively SEVEN CASES of patients with NF1 (4 females and 3 males)** aged 19-52 who were treated at the **Department of Endocrinology** between 2003 and 2013.

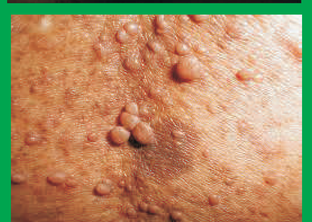
In the studied subjects, **the diagnosis was made** based on **CLINICAL SYMPTOMS** and **confirmed by genetic tests.** **Four patients** (3 women and 1 man) were diagnosed **in childhood.** In **three cases** (1 woman and 2 men) the diagnosis was made **in adolescence.**



Diagnostic criteria for neurofibromatosis type 1.

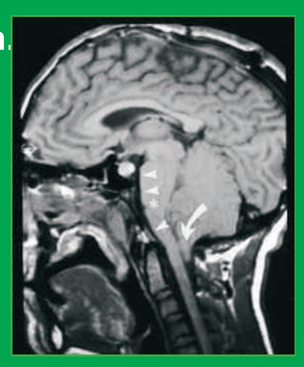
Results

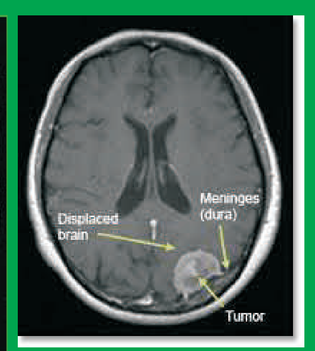




Five patients had a positive family history of NF1, two cases represented spontaneous mutation.

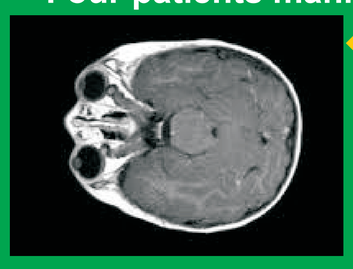
All of analyzed subjects presented NEUROCUTANEOUS MANIFESTATIONS of the disease such as café-au-lait spots and neurofibromas on the body.



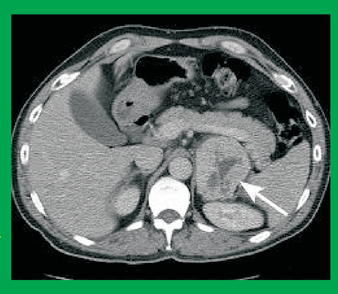


NEUROLOGICAL DISORDERS such as: epilepsy- in 2 patients and Arnold-Chiari malformation - in 1 man have been observed.
Benign brain neoplasms developed in two persons.

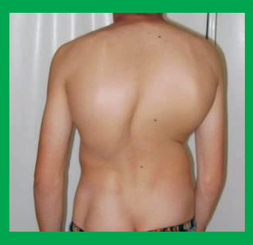
Four patients manifested COGNITIVE IMPAIRMENT.



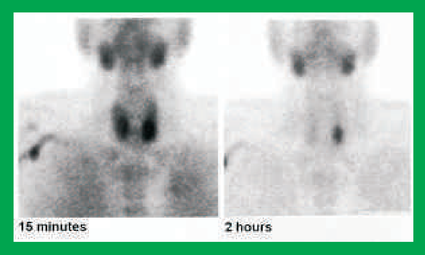
OPTIC GLIOMAS appeared in two cases: one man had a surgery and received radiotherapy due to optic chiasma astrocytoma; left eye blindness, as a complication of the management, has been occurred and one woman was operated because of bilateral optic gliomas; without complications.



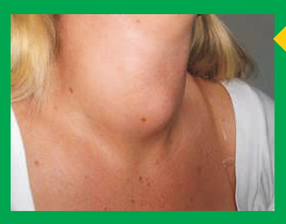
MANY NEOPLASMS developed in other organs: leiomyomas in the uterus- in 2 woman, pheochromocytoma (without clinical symptoms)- in 1 man, nodule in the apex of the left lung - in 1 case, non-functioning pituitary adenoma- in 1 woman, parathyroid adenoma with primary hyperparathyroidism - in 1 patient.



Moreover, we observed the SKELETAL MANIFESTATIONS of NF1 such as: scoliosis - in 1 man and short stature- in 6 cases.

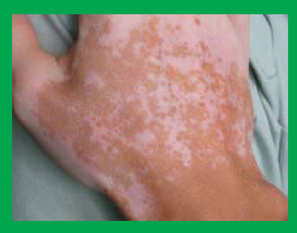


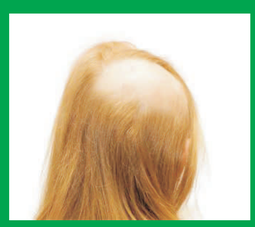
Most of analyzed subjects suffered from THYROID DISORDERS, including: hypothyroidism due to Hashimoto's disease - 4 patients and toxic nodular goiter - 1 woman.



Other AUTOIMMUNOLOGICAL DISORDERS such as: - vitiligo - in 2 cases and alopecia areata - in 1 woman have also been found.

In one man we have noted the VASCULAR MANIFESTATION of NF1.
He has been operated, after birth, due to coarctacion of the abdominal aorta.





The clinical manifestations of NF1 in the analyzed group of patients.

CLINICAL SYMPTOMS OF NEUROFIBROMATOSIS TYPE 1	NUMBER OF PATIENTS	% OF CASES (total- 7 cases)
Neurocutaneous manifestations		
• café-au-lait spots	7	100%
• soft tissue cutaneous nodules (neurofibromas)	7	100%
Endocrine and autoimmunological disorders		
• Hashimoto's disease	4	57%
• toxic nodular goiter	1	14%
• parathyroid adenoma	1	14%
• pituitary adenoma	1	14%
• pheochromocytoma	1	14%
• vitiligo	2	29%
• alopecia areata	1	14%

CLINICAL SYMPTOMS OF NEUROFIBROMATOSIS TYPE 1	NUMBER OF PATIENTS	% OF CASES (total- 7 cases)
Neurological and vision disorders		
• optic glioma	2	29%
• epilepsy	2	29%
• Arnold-Chiari malformation	1	14%
• benign brain neoplasm	2	29%
• cognitive impairment	4	57%
Other neoplasms		
• nodule in the lung	1	14%
• leiomyomas in the uterus	2	29%
Skeletal manifestations		
• short stature	6	86%
• scoliosis	1	14%
Vascular manifestations		
• coarctation of the aorta	1	14%

Conclusions

1) Variety of clinical symptoms causes that NF1 still remains **diagnostic and management challenge** for many physicians. Therefore, **multidisciplinary approach** is needed to optimize patients' diagnosis and treatment.

2) From an **endocrine point of view**, the most common pathology in the studied group of patients was **hypothyroidism** due to **Hashimoto's disease**. Hence, we suggest that in each newly diagnosed subjects with NF1, a screening test of this disease should be performed.