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GENETIC COUNSELING – AN APPROACH FOR SOLVING DIAGNOSTIC PROBLEMS IN CLINICAL PRACTICE

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ABSTRACT

The authors report five clinical cases in which the geneticist in the genetic counseling has come across family history and pedigree data for a certain type of inheritance of the disease in the concrete family and that has been the reason for changing the clinical diagnosis.

In the first case report the primary diagnosis of tu cerebri was changed to Marfan syndrome. In the second case report the diagnosis of idiopathic osteoporosis was changed to osteogenesis imperfecta, an autosomal dominant form. In the third case report the diagnosis of Friedreich ataxia was denied and clinical thinking was focused on autosomal dominant forms of neurodegenerative entities. In the fourth case report the diagnosis of Duchenne muscular dystrophy (X-recessive disease) was not confirmed and further tests were directed to eventually finding autosomal dominant forms of progressive muscular dystrophies. In fifth case report the primary diagnosis of 'diversions in the endocrine status' was not confirmed because an autosomal dominant anhydrotic ectodermal dysplasia was found out. It was pointed out that geneticist's efforts in these and other similar cases contributed to a more precise diagnosis or even changed the primary diagnosis. This optimized the work in the clinical settings and made the prevention of some hereditary diseases possible.

Key words: genetic counseling, clinical diagnosis, hereditary diseases, Varna

Genetic counseling has as a main task to evaluate the genetic risk and make prognosis only in cases with defined clinical diagnosis. In their practical work, counselors may come across cases in which the initial clinical diagnosis does not correlate with the family data, or is even contradictory. The intervention of the genetic counselor in these cases may help making the clinical diagnosis more precise or even change it, which consequently will help solving the medical problems of the patient and his family.

In this paper we report on patients whose primary clinical diagnosis has been changed with the participation and contribution of the genetic counselor.

Case report No 1. The patient, 11 years old girl, taller for her age, thin, with arachnodactily and abnormal refraction, has clinical diagnosis of tu cerebri. Occasionally seen by a geneticist, she was invited to visit the genetic counseling. Patient's typical clinical features were found in four relatives in four consecutive generations of the pedigree (mother, grandmother and grand-grandfather). Clinical diagnosis was transformed to Marfan syndrome (6), a hereditary disease with autosomal dominant (AD) transmission in the generations (Fig. 1).

Case report No 2. The patient, 18 years old boy, with clinical diagnosis of osteoporosis proved by osteodensitometry and not responsible to applied therapy, with peculiar x-ray image, is referred to genetic counseling. Direct and thorough gathering of family history and clinical data of the relatives found out the presence of micro symptoms of osteogenesis imperfecta (3) in patient's mother and confirmed the clinical diagnosis of the proband to be AD variant of this entity (Fig. 2).

Case report No 3. The patient, 37 years old male with clinical diagnosis of Friedreich ataxia, is referred to genetic counseling for evaluation of the genetic risk for his close relatives. Pedigree analysis found out family members in three consecutive generations with history and medical reports for 'rough involuntary movements'. The clinical thinking has never discussed these findings to be one joint diagnosis. Genetic evaluation of the family members was done for the first time. Patient's father, aged 64, had difficulties in movement as a result of the expressed generalized choreiform hyperkinesias and verbal contact was very limited because of speech and memory disturbances and dementia. The onset of the symptoms has been at the age of 57. The rest of the family members with history of the disease were either deceased, or in a very bad condition, so that it was not possible to evaluate them in the genetic counseling. The finding of similar clinical manifestation, course

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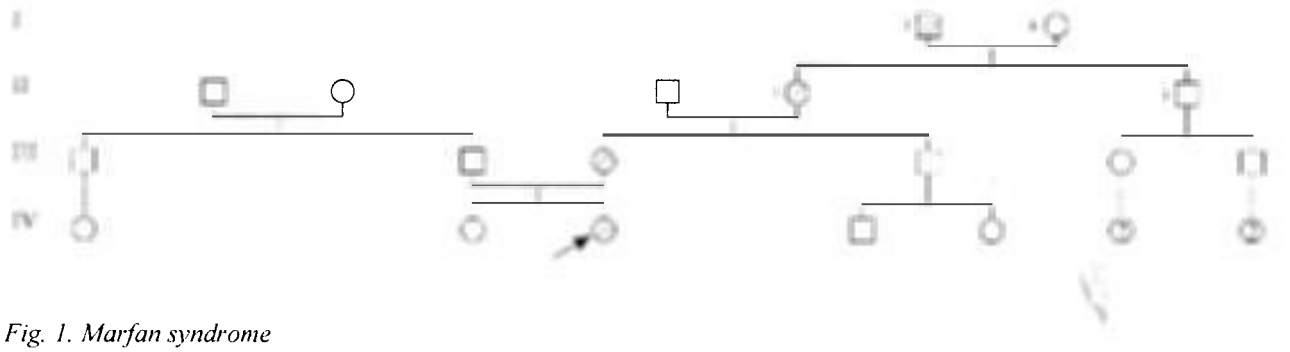

Fig. 1. Marfan syndrome

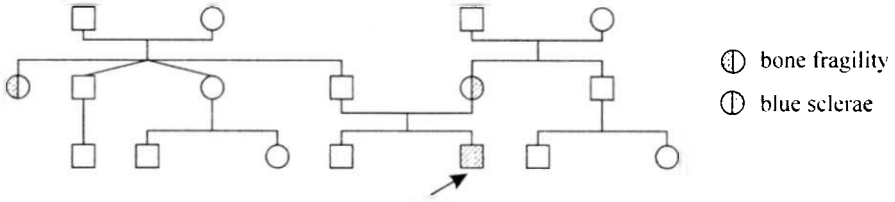

Fig. 2. Osteogenesis imperfecta

and outcome of the disease in different family members in three consecutive generations denied the clinical diagnosis of Friedreich ataxia (4,5) and turned clinical thinking to a probable neurodegenerative condition with AD inheritance (Fig. 3).

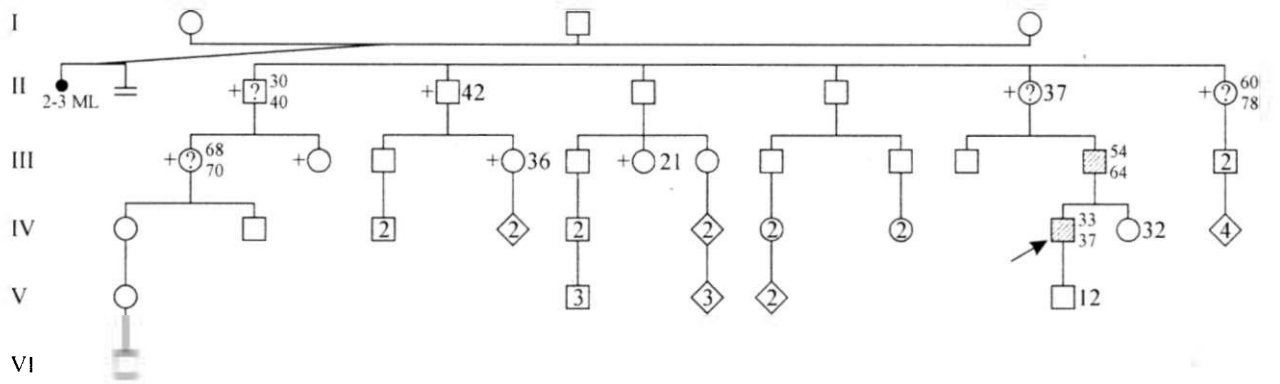

Fig. 3. Autosomal-dominant hereditary neurodegenerative disease

Case report No 4. The patient, 23 years old female with discrete EMG and biopsy findings, is referred to genetic counseling with clinical diagnosis of Duchenne muscular dystrophy. Four other members of the family had the same diagnosis based on clinical, laboratory, EMG and pathomorphologic findings. In three of them, proband's brother, uncle and cousin on father's site of the proband's mother, the disease had been manifested as progressive muscular dystrophy with lethal outcome before 20 years of age. In the fourth member, 43 year-old proband's mother, the medical examinations revealed a moderate muscular degenerative disease accepted to result from the heterozygosity of X-recessive mutant gene. These specific pedigree data were the reason to deny recessive inheritance and to look for a possibility for a progressive muscular dystrophy dominantly transmitted in the generations (7) (Fig. 4).

Case report No 5. The patient, 36 years old female, referred to the genetic counseling with 'diversions in the endocrine status' was found to have anhydrotic ectodermal dysplasia, a manifested hypofunction of the sweat, sebaceous and mucous glands, hypotrichosis and anodontia. Clinico-genetical analysis proved AD, phenotypically variable up to incomplete penetrance, rare form of anhydrotic ectodermal dysplasia (1,2) expressed in five consecutive generations of the concrete family (Fig. 5).

With these case reports we want to point out geneticist's contributions to solving the clinical and prognostic problems in the patients with hereditary diseases and their relatives, namely:

In the first patient the serious clinical diagnosis of brain neoplasm was denied and a hereditary disease was proved needing prevention of cardiovascular complications as a substantial part of the clinical symptoms of the disease.

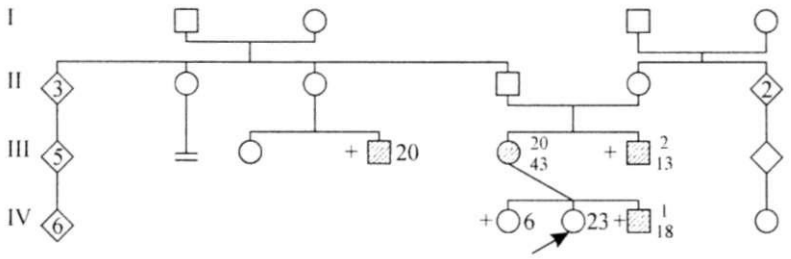

Fig. 4. Muscular dystrophy

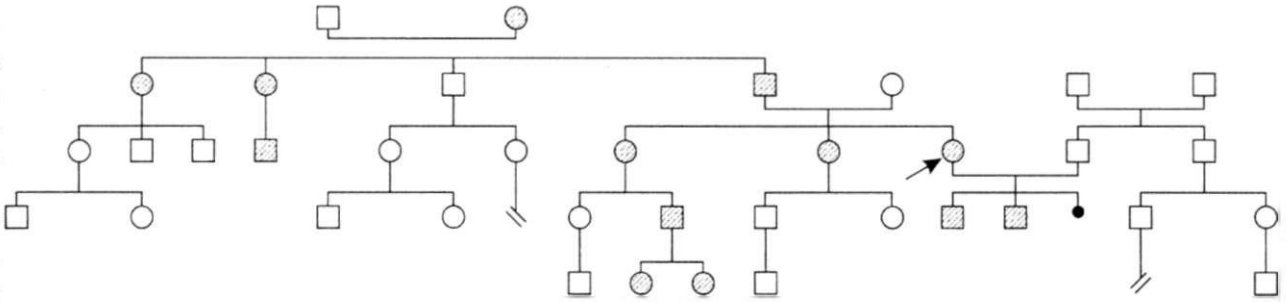

Fig. 5. Anhydrotic ectodermal dysplasia

In the second patient suggesting the diagnosis of imperfect osteogenesis we gave the patient the right to be discharged from the army for medical reasons and he was given advices for sparing life-style and exact professional orientation. Thus the forthcoming disability could be postponed for years. Together with the prevention for the patient himself, the genetic counseling determined the genetic risk for his offspring as well.

In the third patient it became possible to give real genetic prognosis for the offspring and perspectives for etiologic DNA diagnostics.

In the fourth patient the necessity of new molecular genetic tests was evaluated in a view to prenatal prevention of the hereditary disease.

In the fifth patient the exact diagnosis eliminated the necessity of carrying expensive tests and directed the treatment of the patient in the right way.

These case reports are not occasional events in the practice of the genetic counseling. That is why we consider genetic counseling not only a method for genetic prognosis, but also an approach for solving diagnostic problems in different clinical entities.

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