Clinico-Epidemiological and Molecular Genetic Study of Lumbar-Limb forms of Progressive Muscular Dystrophy in the Republic of Dagestan

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ABSTRACT

For the first time in the Republic of Dagestan (RD) a comprehensive clinical - epidemiological and molecular - genetic research of limb girdle forms of progressive muscular dystrophies (LGPMD) was conducted. LG forms of PMD: 2A type, 2B type and distal type Miyoshi were identified. The prevalence of LGPMD in RD populations was determined.

LGPMD clinical polymorphism in patients living in the mountain, foothill and lowland regions of RD was studied and practical diagnostic algorithm for neurologists was made. Mutation which causes the development of LLPMD family forms was identified.

Keywords: progressive muscular dystrophy, limb girdle form, DNA diagnostics.

INTRODUCTION

Lap - extremity progressive muscular dystrophy (LLPMD) - a group of clinically and genetically heterogeneous polymorphous diseases characterized by a primary lesion of the pelvic and shoulder girdles , progressive course , the increase in activity of the enzyme creatine phosphokinase (CPK) in the blood plasma , primary muscle lesion in electroneuromyographic character study (EMG) [3]. Frequency of all LLPMD in different populations varies from 5 to 70 patients per 1 million population [1].

The Republic of Dagestan (RD) with a population of 2 million 946 thousand people, is characterized by a predominance of rural population living mainly in the highlands, where the preserved isolates with high levels of inbreeding.

MATERIALS AND METHODS

We selected and examined patients with LLPMD according magazines neurological hospitals , clinics , national urban and regional MSCE , medical unit , Republican Genetic counseling , magazines Advisory receiving the Department of neurology of the Dagestan State Medical Academy , as well as according to the register of inherited neuromuscular diseases " Neyroregistr Dagestan". The diagnosis based on clinical exhibited - genealogical research electroneuromyographic examination, biochemical analysis of the level of activity of CK in the blood plasma, a biopsy of the affected muscles and confirms the results of molecular genetic analysis.

RESULTS

The study identified 51 patients us in 32 families with AR mode of inheritance, living in 13 districts and 3 cities of the Republic of Dagestan, in a ratio of 1:1 for men and women. Prevalence PC action in different areas of the Republic of Dagestan ranges from 0.4 to 38.7 per 100,000 population. Based on clinical and genealogical, laboratory and instrumental data were three groups of patients: 1 - LLPMD 2A, 2 - LLPMD 2B and 3 - LLPMD Miyoshi distal type.

In our study, the most common AR pathology residents in mountainous areas, compared to foothill and lowland areas. Burdened correlates with the level of inbreeding: the higher the level of inbreeding, the higher overburdenness [4].

Conducted clinical and genealogical research allowed to allocate 2A, 2B and distal type Miyoshi.

2A LLPMD type was detected in 33 patients in 19 families, representing 64 % of all LLPMD. The ratio of male to female ratio was 1:1. Prevalence of 1.09 per 100 thousand of population. Age debut ranges from 5 to 24 years. The greatest number of patients with age onset of the disease in the first decade of life. In cities revealed 8 patients. It should be noted that the families of these patients are immigrants from high-altitude areas. Intra- analysis of patients from the same family revealed phenotypic polymorphism, which is expressed in the time of the first clinical signs of disease, the severity of the dynamics and movement disorders. Closely related to marriage burdened families was 63 %. Search for mutations in exons 4, 5, 10, 11, 12, 20, 21, 22 calpain gene, (the most frequent among the Western European population) [2] carried out in 15% of patients who did not give a positive result.

2B tip in our study is 20 % of the AR variants LLPMD in RD and identified 10 patients in 6 families, male to female ratio of 3:2. Age onset of the disease from 15 to 21 years. Prevalence in the population RD - 0.34 to 100 thousand people. Typical signs of the disease were debut with weakness in the proximal leg and right hand, with a primary lesion anterior muscle groups with psevdogipertrofie calf muscle in 5% of patients, moderate increase in CPK.

Win Miyoshi distal type from all forms of autosomal LL PMD was 16%. LLPMD Miyoshi distal type was detected in 8 patients in four families in the ratio of 1:2 for men and women, age 11-21 years old debut. The clinical picture prevailed atrophy of the posterior group of muscles distal parts of the legs and forearm muscles, Achilles tendon retraction , 11 patients with clinical variant type 2B and Miyoshi during molecular - genetic studies revealed a mutation in the gene DYSF, with replacement p.Val67Asp., mapped to locus of chromosome 2r13 .

In our epidemiological study in the Dagestan population identified mountain isolate population 2909 people, where accumulated genetic load LLPMD 2B and Miyoshi distal type and identified 15 patients in 8 families. The prevalence of this isolate was 5.1 per 1 thousand of people.

CONCLUSION

First held in RD clinical - genealogical and molecular genetic study of patients with LLPMD distal type 2B and distal type Miyoshi. The data obtained allow to carry out medical examinations active burden families and plan volume Genetic counseling in RD. Carried out molecular genetic studies in patients disferlinopatiyami allow residents to develop screening

research mountain isolates, identifying hereditary pathology at the early stages and carriage, conduct prenatal diagnosis.

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