American Journal of Medicine and Medical Sciences 2024, 14(9): 2253-2255
DOI: 10.5923/j.ajmms.20241409.27

Genealogical Analysis of Pedigree and Study of Heredity in Infantile Cerebral Palsy

Nabieva Nozima Abdurakhimovna

Bukhara State Medical Institute, Bukhara, Uzbekistan

Abstract Cerebral palsy (CP) is a disorder of the nervous system characterized by abnormal muscle tone and movement. The role of heredity in the development of CP is recognized as significant. The study shows an increased risk of epilepsy in families with CP, up to 90%. The genealogical method is used to study heredity and the spread of pathologies in families. **Objective of the study:** To study the inheritance of neurological traits and epilepsy in families with CP, to identify inheritance patterns. **Methods:** Genealogical analysis of 255 families with CP, including groups with and without epilepsy, a control group of 50 healthy children. **Results:** Autosomal recessive and X-linked inheritance patterns were found in both groups. Epilepsy is more often observed in the group with epilepsy. In 44.7% of cases, epilepsy is symptomatic. **Conclusion:** Genetic factors play a role in the pathogenesis of cerebral palsy and epilepsy, autosomal recessive inheritance prevails.

Keywords Cerebral palsy, Hereditary diseases, General population, Geneological method, Symptomatic epilepsy

1. Introduction

Cerebral palsy (CP) is a developmental disorder of the nervous system characterized by abnormalities of muscle tone, movements, and motor skills. Most researchers do not deny the role of the hereditary factor in the development of CP, but consider it a predisposing factor. It has been established that the risk of developing epilepsy in families with syndromic identity is 3-4%, which is 2.4 times higher than in the general population, and in CP the incidence of SE is 18-90% [1-3].

Hereditary diseases develop as a result of a mutant gene in a family from generation to generation. The task of the genealogical method is to study the nature of the spread of hereditary traits in the family being studied. In clinical genetics, the genealogical method is used to identify patterns of distribution of hereditary diseases. [4]

Genealogical analysis of pedigrees is the most accessible method for studying human heredity and variability for a practicing physician. The essence of the method is to study any disease or pathological feature in generations of people who are related. [5] The geneological method can determine the following: whether the disease being studied is hereditary. If it is, the type of inheritance is determined. Consequently, there is a possibility that a sick child may be born in the family.

The aim of the study is to study the nature of the distribution of neurological signs and epilepsy in the family of a proband with cerebral palsy and symptomatic epilepsy, to identify patterns of their inheritance.

Received: Aug. 7, 2024; Accepted: Sep. 5, 2024; Published: Sep. 18, 2024
Published online at http://journal.sapub.org/ajmms

2. Materials and Methods of the Study

We examined 255 first-degree related families (parents, siblings) of children with cerebral palsy using the genealogical method: Group 1 - 102 children with cerebral palsy complicated by SE, Group 2 - 153 patients with cerebral palsy without SE. The control group - 50 healthy children without any hereditary pathologies. All children were of the same age, 3-14 years. The following were accepted as hereditary traits: neurological deficit occurring in cerebral palsy and epilepsy in families. The medical history was collected for both parents by cross-questioning, and in some cases - grandparents. After compiling the pedigree, we graphically depicted the family tree. We used standard symbols accepted in genealogical research (Fig. 1).

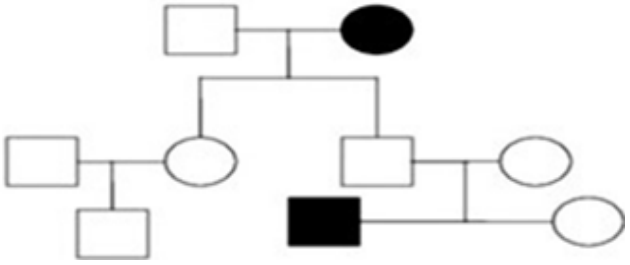

Figure 1. Autosomal recessive type of inheritance

We carried out the genealogical research in two stages:

I – study of the prevalence of a trait or disease in a particular family and compilation of a family tree;

II - pedigree analysis.

A proband is a patient whose pedigree is compiled. In our studies, the proband was a patient with cerebral palsy with

and without SE.

We carried out the genealogical method based on two criteria:

1st – the prevalence of any neurological deficit in the family under study;

2nd - the presence of epilepsy in the studied family.

We carried out our genealogical research in two stages:

I - collecting information about the family and compiling a pedigree, which begins with the proband.

II - pedigree analysis.

The proband is considered to be the person under study, for whom the pedigree is compiled. In our study, the proband was a patient with cerebral palsy with and without SE. For the pedigree, we collected information on the presence of neurological deficit and epilepsy in 3 generations of the patient's family. We analyzed both signs of the variant separately (Table 1 and Table 2).

3. Results of the Study and Their Discussion

The results of the study of neurological deficit showed that in both groups there were mainly two types of heredity: autosomal recessive and recessive, linked by the X-chromosome.

Pathological signs in the recessive, X- linked type of inheritance were relatively rare, not in all generations. Neurological deficit was detected mainly in men, women were ill rarely and only when their father was ill. This explains the fact that in the general group of children with cerebral palsy, boys - 155 (60.8%) are more susceptible to pathology than girls - 100 (39.2%).

Autosomal recessive inheritance pattern for neurological deficit was observed in both groups, but with greater reliability - in the group of patients with cerebral palsy without SE. In 112 (43.9%) patients out of the total, the inheritance pattern could not be determined. It is likely that neurological deficit in the form of cerebral palsy in these cases developed against the background of other non-hereditary factors.

Example. Proband - patient R, 10 years old. Diagnosis: cerebral palsy. Spastic diplegia, spastic lower paraparesis. Oligophrenia in the stage of mild debility. The trait of neurological deficit among the patient's relatives is assessed as autosomal recessive. Genotypes of parents, father: mother - aa , father - AA or Aa; parents are phenotypically "healthy", genotypes of the sick son Aa , daughter may be heterozygous.

In the autosomal recessive inheritance pattern, the disease was not identified in every generation, but phenotypically “healthy” family members were carriers of the recessive gene.

There are different opinions about the cause of epilepsy development in cerebral palsy. Some researchers believe that epilepsy occurs as a result of organic damage to the brain in cerebral palsy. But then it is unclear why sometimes there are no convulsive paroxysms with total damage? Others point out that hereditary predisposition is important in the development of epilepsy.

We studied the families of probands - patients with cerebral palsy in both groups for the presence of epilepsy among relatives (Table 2).

We established the presence of epilepsy in the families of probands in both groups with each type of heredity. Significantly more frequent cases of heredity for epilepsy were established in the group of patients with cerebral palsy with SE of the recessive type linked to the X chromosome. Epilepsy in a large number of children - 114 (44.7%) from the total group of cerebral palsy could not be established by the genealogical method. It is possible that in these cases epilepsy was not hereditary, but was symptomatic, i.e. a complication of the main disease - cerebral palsy (Fig. 2).

Example. Patient A, 7 years old. Diagnosis: cerebral palsy. Double hemiplegia, spastic tetraparesis with predominant damage to both hands. Symptomatic epilepsy. Oligophrenia in the imbecile stage. This type is considered as recessive, X-linked inheritance. From the genotype of the first generation daughters - XA and XA, it can be concluded that they are both phenotypically "healthy".

Genotypes of the second generation children: daughters XA, XA and XA, sons – XAU. XAU, XAU and XAU. The genotype of the proband we are studying is XaY.

Table 1. The nature of the distribution of heredity for neurological deficit in cerebral palsy, people (%)

Type of inheritance	Cerebral palsy with SE	Cerebral palsy without SE	t	R
Autosomal recessive	31 (30.4)	61 (39.9)	23.8	p< 0.001
X- linked recessive	29 (28.4)	22 (14.4)	25.7	p< 0.001
Unspecified	42 (41.2)	70 (45.7)	33.9	p< 0.001
Total	102 (100)	153 (100)		

Table 2. The nature of the distribution of heredity for epilepsy in cerebral palsy, people (%)

Type of inheritance	Cerebral palsy with SE	Cerebral palsy without SE	t	R
Autosomal recessive	30 (29.4)	35 (22.9)	15.9	p< 0.001
X- linked recessive	45 (44.1)	30 (19.6)	25.9	p< 0.001
Unspecified	26 (25.5)	88 (57.5)	6.5	p< 0.001
Total	102 (100)	153 (100)		

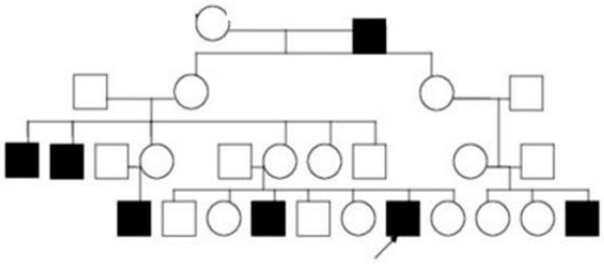

Figure 2. Recessive, X-linked inheritance

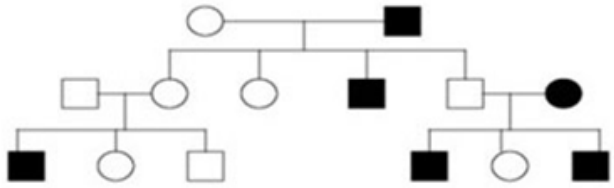

Figure 3. Recessive, X-linked inheritance

Example. Proband, patient III, 14 years old. Diagnosis: cerebral palsy. Hyperkinetic form. Mild mental retardation. Proband's genotype is XAXa. The epileptic trait is sex-linked, localized in the X chromosome and is recessive (Xa). Father's mother is XAXa, father is XAУ. Genotypes of the first generation: daughters XAXa, sons XAУ, XAУ. Genotypes of the children of the second generation: daughter - XAXa, sons - XAУ (Fig. 3).

Epilepsy, as a pathological sign with recessive, X-linked inheritance, was relatively rare, not in all generations. The disease was found mainly in men. It was found that their fathers were usually healthy, and their grandfathers on the maternal side were sick. Daughters were rarely sick and were sick only when their father was sick.

4. Conclusions

Thus, The presence of confirmed cases of association of gene mutations with the development of the cerebral palsy phenotype (in the form of a neurological defect) indicates the involvement of genetic factors in the pathogenesis of cerebral palsy and epilepsy. Autosomal recessive type of inheritance for neurological deficit was established in both groups with high reliability (more than a third of patients) in the group without SE. Slightly more cases (by 4.2%) of heredity for epilepsy were established in the group of patients with SE by the recessive type linked by the X chromosome. In a large number of children - 114 (44.7%) of the total indicator of the cerebral palsy group It was not possible to establish the type of inheritance using the genealogical method. It is possible that in these cases epilepsy was not hereditary, but was symptomatic, i.e. a complication of the underlying disease - cerebral palsy.

REFERENCES

[1] Janzing A. M. et al. Clinical characteristics suggestive of a genetic cause in cerebral palsy: A systematic review // Pediatric neurology. – 2024.

[2] Klebe S., Stevanin G., Depienne C. Clinical and genetic heterogeneity in hereditary spastic paraplegias: from SPG1 to SPG72 and still counting // Revue neurologique. – 2015. – Т. 171. – №. 6-7. – С. 505-530.

[3] Shakoor N. Study of hereditary disorders in Potohar region and high throughput SNP genotyping of a family with intellectual disability: дис. – Quaid i Azam University, Islamabad, 2020.

[4] Erickson R. P. The importance of de novo mutations for pediatric neurological disease—it is not all in utero or birth trauma // Mutation Research/Reviews in Mutation Research. – 2016. – Т. 767. – С. 42-58.

[5] Rauf N. Descriptive epidemiology of hereditary and congenital anomalies in Sialkot district, Punjab Pakistan: дис. – Quaid i Azam University, Islamabad, 2021.