HEREDITARY SPASTIC PARAPLEGIA IN RUSSIA: EPIDEMIOLOGICAL, CLINICAL AND MOLECULAR ASPECTS

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Data on ***HSP epidemiology*** were obtained in field studies carried out since 1985 in Russian and Central Asian regions, total population ≈ 2 m and 0.5 m correspondingly. In most of Russian populations minimum HSP prevalence is 1–3 per 10^5, only Kirov region in European Russia north-east showed a significantly higher value of 7.2 per 10^5 though not due to an accumulation of one form. Average proportions of autosomal dominant (AD) and autosomal recessive (AR) HSP are about equal. HSP contribution to the structure of hereditary nervous disorders is about 10%. Striking distinctions were seen in inbred Uzbek and Tajik populations with large-size families where HSP presented a wide spectrum of AR complicated forms, mostly unique. In one of Uzbekistan regions HSP prevalence was as high as 12.9 per 10^5 though also not due to some particular form. Unfortunately, these studies were carried out mostly in 'pre-molecular' era, and the cases were not attributed genetically. In our everyday practice in genetic counseling department we also meet ***rare and unique HSP*** phenotypes, such as AD HSP with torsion dystonia in four members of a three-generation family, probably AD early-onset HSP with ophthalmoparesis, AR early onset HSP with dysarthria and amyotrophy. Our experience of HSP ***molecular studies*** is still modest and limited to SPG4, yet it is the only one in Russia. A search of *SPAST* mutations by routine methods was carried out in a sample of 26 unrelated families with AD HSP, in 6 of which (23%) mutations were detected; three of them, Arg431Stop, Gln280Arg FsX9 and Asn386Ser, were reported previously; three others, Asp555Tyr, Thr369Thr and Asn184Thr were novel. Later on SSCP-negative samples were tested by MLPA (Dr. Christian Beetz, Uniklinikum IKCL-FZL, Jena, Germany), in two cases large deletions were detected – a deletion of the whole *SPAST* gene and a deletion of 11 exons. With these findings the proportion of SPG4 among AD HSP is 30-35% which does not contradict to world results. In a large family linked to SPG4 locus both SSCP and MLPA failed to detect a mutation.
Most of SPG4 patients had typical clinical features. Rare features were: very early or very late onset in few patients, epilepsy in one patient, early incontinence surpassing spasticity in all affected members of a family. SPG3 diagnostics was also begun with no findings yet.
Molecular studies of HSP in Russia should be developed and expanded, we hope, international contacts will facilitate the task.