Autosomal dominant spinocerebellar ataxias (SCA) are phenotypically and genotypically heterogeneous group of disorders. Some of the clinical features have some specific values for predicting a gene defect. However the clinical diagnosis of subtypes of SCAs is complicated by the salient overlap of some of phenotypes between genetic subtypes. Thus genotypic diagnosis is of importance.

Our knowledge of the molecular mechanisms SCAs is rapidly growing. Several identified mutations correspond to expansions of repeated trinucleotides (CAG repeats in SCA1, SCA2, Machado-Joseph disease (MJD)/SCA3, SCA6, SCA7, SCA17, and dentato-rubral-pallido-typanic atrophy (DRPLA) and CTG repeats in SCA8). A pentanucleotide repeat expansion is associated with SCA10. Missense mutations have also been found recently. Anticipation is a main feature of SCAs, due to instability of expanded alleles. It is estimated that extensive genetic testing leads to the identification of the causative gene in about 60-75% of cases. As on today molecular genetic studies have identified about twenty-seven subtypes. Current molecular classification corresponds to the order of gene description.

India is an ethnically and religiously diverse population. The ethnic diversity may have a bearing on the prevalence of SCA subtypes. In this issue of the journal Rengaraj et al report a high prevalence of SCA1 in an ethnic Tamil Vanniyakula Kshatriyar community. The most common type of SCA reported in India is SCA2. The populations in these studies were of mixed ethnicity. Of the 124 families reviewed by Chakravarty and Mukherjee, 47 (38%) families belonged to SCA2. Most of the patients with SCA12 reported were from India and it seems SCA2 is typically an Indian disease (Dr K K Sinha, Indian Academy of Neurology Oratin, 2005). SCA12 accounted for 25 (9%) of the 212 families of autosomal dominant cerebellar ataxia studied. However this needs to be confirmed by other studies. MJD/SCA3 is the common type of SCA worldwide whereas the reported prevalence of MJD/SCA3 from India is very low. Of the 212 families studied by Srivastava et al MJD/SCA3 mutation was seen in 6 (2.8%) pedigrees. However the reported prevalence of MJD/SCA3 was high in ethnic Bengalees in West Bengal. Of the 19 families with autosomal dominant SCA studied in West Bengal till 2001, MJD/SCA3 mutation was seen in 7 (37%) families. In the patients with MJD/SCA3 studied by Chakravarty and Mukherjee many did not have any extrapyramidal features or ophthalmoplegias, MJD/SCA3 showing racially different expressivity has been described in several families of African origin. The phenotype ranged from ataxia with parkinsonian signs to a syndrome clinically almost indistinguishable from idiopathic, L-dopa-responsive Parkinson’s disease. These parkinsonian phenotypes are rare in those of European descent. The observed low prevalence of MJD/SCA3 in India could be because of the low prevalence of large normal alleles that might act as the reservoir for the expanded alleles. MJD/SCA3 mutation in Indian populations had the same origin as found worldwide.

There is an urgent need to do genetic studies of SCAs and genotypic-phenotypic correlation in different ethnic population in India to resolve some of the Genotypic testing even though expensive allows precise classification of genotypic subtype thus allows genetic counseling and predictive testing. It also allows genotype-phenotype correlation, study of natural history and prognosis of specific subtypes of SCA. The development of relevant animal models of SCAs may bring hope for effective therapies in human to resolve some of these issues.

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