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Practical Application of *microRNA* Markers in the Diagnosis of Multiple Sclerosis in the Realm of Routine Clinical Neurology

Introduction

Multiple sclerosis (MS) is a disease that is characterized by loss of myelin (demyelinization).[1] In MS, demyelinization usually affects white matter in the brain, but sometimes it extends into the gray matter. When myelin is damaged, nerve fiber conduction is faulty or absent, and nerve cell death may occur. Impaired bodily functions or altered sensations associated with those demyelinated nerve fibers give rise to the symptoms of MS, which range from numbness to paralysis and blindness. People with MS experience attacks of symptoms that may last days, months, or longer. For many patients, the disease is progressive and leads to disablement, although some cases enter long, perhaps even permanent, remission. The cause of MS is unknown.[1]

General epidemiological factors

MS is not contagious or directly inherited; epidemiologists have identified factors in the distribution of MS around the world that may eventually help determine what causes the disease.[1]

MS is thought to affect >2.3 million people worldwide. The factors associated with MS are gender, genetics, age, geography, and ethnic background.[1]

Age factors

Most people are diagnosed between the ages of 20 and 50 years, although MS can occur in young children and significantly older adults.[1]

Gender factors

MS is at least two to three times more common in women than in men, suggesting that hormones. Recent MS studies have suggested that the female to male ratio may be as high as 4 to 1.[1]

Ethnic factors

MS is more common in Caucasians of northern European ancestry.[1] Rates of occurrence may differ significantly among groups living in the same geographic area regardless of distance from the equator.[1]

Geographic factors

In general, MS is more common in areas farthest from the equator.[1] The MS prevalence rates may differ signiifically among groups living in the same geographic area regardless of distance from the equator. Some environmental trigger in genetically susceptible individuals.

Diagnosis of multiple sclerosis

No single test can diagnose MS. The medical history, neurologic examination, and laboratory tests help physicians rule out other diseases and confirm the MS diagnosis.[1] "Improvement in neuroimaging techniques such as positron emission tomography or magnetic resonance imaging (MRI) carries a promise for better diagnosis and prognostic predictions."[1]

In order to make a diagnosis of MS, the physician must find evidence of damage in at least two separate areas of the central nervous system (CNS), which includes the brain, spinal cord, and optic nerves and (a) find evidence that the damage occurred at different points in time and (b) rule out all other possible diagnoses.[1]

MS is now being more frequently diagnosed in India due to two important factors, namely (a) increase in the number of practicing neurologists and (b) availability of MRI.[2] The cases of MS in India display the same clinical features and outcome as those cases seen in the Western countries.[2]

Molecular Markers

In recent years, newly emerging highly specific molecular markers called "*microRNAs*" had appeared in the research literature, which are found both in the peripheral blood and the cerebrospinal fluid in the realm of such neurological diseases as amyotrophic lateral sclerosis, Alzheimer's disease, Parkinson's disease, Huntington's disease, and MS.[3-10]

What makes these microRNA (miRNA) markers so potentially useful in clinical neurology is that they are seen very early on long before the appearance of symptoms and other confirmatory conventional indicators of pathology.[3-10]

What are microRNAs

"A miRNA is a small noncoding RNA molecule (containing about 22 nucleotides) found in plants, animals, and some viruses, which functions in RNA silencing and posttranscriptional regulation of gene expression.[4] While the majority of miRNAs are located within the cell, some miRNAs, commonly known as circulating miRNAs or extracellular miRNAs, have also been found in extracellular environment, including various biological fluids and cell culture media."[4]

"Extracellular miRNAs in serum, plasma, saliva, and urine have recently been shown to be associated with various pathological conditions including cancer."

In a recent article that appeared in the journal "Neurology," Reed *et al*. noted that miRNAs were prodromal biomarkers for Huntington's disease.[8]

microRNA molecular markers found in multiple sclerosis patients

A minimally invasive blood-based specimen type is what is needed in the quest for early detection of a potential MS scenario.

Vesicles known as exosomes contain RNA, DNA, and proteins.[11] These structures can cross the blood–brain barrier.[11] These exosomes are secreted from a broad variety of cell types which include the cells of the CNS.[11]

Ebrahimkhani *et al*. hypothesized that serum exosomal miRNAs could therefore provide the means for a useful blood-based assay for MS disease detection and monitoring.[11] These investigators therefore utilized exosome-associated miRNAs derived from 25 serum samples from MS patients.[11]

Ebrahimkhani *et al*. found nine miRNAs (miR-15b-5p, miR-23a-3p, miR-223-3p, miR-374a-5p, miR-30b-5p, miR-433-3p, miR-485-3p, miR-342-3p, and miR-432-5p)[11] This important discovery allowed these investigators to distinguish relapsing-remitting disease from progressive disease. Eight out of the nine miRNAs were validated in an independent group (n = 11) of progressive MS cases.[11]

The investigation of Ebrahimkhani *et al*. was the first demonstration that miRNAs associated with circulating exosomes are informative biomarkers not only in the diagnosis of MS, but in predicting disease subtype with a high degree of accuracy.[11]

Conclusion

The recent advancements in the field of miRNA research now have provided clinical neurologists with technologies that will make possible both a diagnosis of MS and also enable a prediction of disease subtype.

The detection of MS using miRNA molecular markers is now at hand to be utilized in the realm of clinical neurology!!

The ability to also utilize minimally invasive blood-based specimen types for applications involving early detection of a potential MS scenario has provided additional rational for using miRNA markers in the practice of clinical neurology!!

Thus, the time has now arrived for clinical neurologists to intensely apply these miRNAs on a routine basis for early detection of MS.

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