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Pathogenesis of Neurodegenerations – Alzheimer's Disease, Parkinson's Disease and Motor Neuron Disease – Relation to Archaeal Mediated Rna Viroids and Amyloidosis

Introduction

Prion proteins have been implicated in neurodegenerations - Alzheimer's disease, Parkinson's disease and motor neuron disease. The beta amyloid in Alzheimer's disease, alpha synuclein in Parkinson's disease, the TAR protein in frontotemporal dementia and copper zinc dismutase in motor neuron disease behaves like prion proteins. Prion diseases are conformational diseases. The abnormal prion protein seeded into the system converts the normal proteins with prion like domains to abnormal configuration. This abnormal protein resists digestion by lysosomal enzymes after its half life is over and results in deposition of amyloid plaques. This produces organ dysfunction. Prion phenomena were initially described for Creutzfeldt Jakob's disease (CJD), but now it is found to be wide spread in chronic disease pathogenesis. Ribonucleoproteins are well known to behave like prion proteins and form amyloid. We have demonstrated actinidic archaea which secretes RNA viroids in neurodegenerations - Alzheimer's disease, Parkinson's disease and motor neuron disease. The RNA viroids can bind with normal proteins with prion like domains eg., superoxide dismutase and produce a ribonucleoprotein resulting in prion phenomena and amyloidogenesis. The actinidic archaeal growth results in increased digoxin synthesis and phenotypic conversion of homo sapiens to homo Neanderthals as reported earlier. The increased actinidic archaeal growth is due to global warming and this results in neanderthalisation. Homo neanderthalis tend to have more of civilizational diseases like neurodegenerations - Alzheimer's disease, Parkinson's disease and motor neuron disease. Actinidic archaeal secreted RNA viroids may play a crucial role in amyloid formation and pathogenesis of these disorders.[1-16]

Materials and Methods

The following groups were included in the study: - neurodegenerations - Alzheimer's disease, Parkinson's disease and motor neuron disease. There were 10 patients in each group and each patient had an age and sex matched healthy control selected randomly from the general population. The blood samples were drawn in the fasting state before treatment was initiated. Plasma from fasting heparinised blood was used and the experimental protocol was as follows (I) Plasma+phosphate buffered saline, (II) same as I+cholesterol substrate, (III) same as II+cerium 0.1 mg/ml, (IV) same as II+ciprofloxacine and doxycycline each in a concentration of 1 mg/ml. Cholesterol substrate was prepared as described by Richmond. Aliquots were withdrawn at zero time immediately after mixing and after incubation at 37 ℃ for 1 hour. The following estimations were carried out:- Cytochrome F420, free RNA, Cytochrome F420 was estimated flourimetrically (excitation wavelength 420 nm and emission wavelength 520 nm). Plasma of control subjects showed increased levels of the above mentioned parameters with after incubation for 1 hour and addition of cholesterol substrate resulted in still further significant increase in these parameters. The plasma of patients showed similar results but the extent of increase was more. The addition of antibiotics to the control plasma caused a decrease in all the parameters while addition of cerium increased their levels. The addition of antibiotics to the patient's plasma caused a decrease in all the parameters while addition of cerium increased their levels but the extent of change was more in patient's sera as compared to controls. The results are expressed in tables 1-2 as percentage change in the parameters after 1 hour incubation as compared to the values at zero time.

Results

The results show that there was increase in cytochrome F420 in neurodegenerations - Alzheimer's disease, Parkinson's disease and motor neuron disease indicating increased archaeal growth. There was also an increase in free RNA indicating self replicating RNA viroids in neurodegenerations - Alzheimer's disease, Parkinson's disease and motor neuron disease. The RNA viroid generation was catalysed by actinides. The RNA viroids can bind with proteins having prion like domains forming ribonucleoproteins. These ribonucleoproteins can give an abnormal conformation to the protein resulting in generation of abnormal prions. The abnormal prions can act as a template to convert normal proteins with normal configuration to abnormal conformation. This can result in amyloidogenesis. The abnormal configured proteins will resist lysosomal digestion and accumulate as amyloid.

Table 1. *Effect of cerium and antibiotics on cytochrome F420.*

Group	CYT F420% (Increase with Cerium)		CYT F420% (Decrease with Doxy+Cipro)	
	Mean	± SD	Mean	± SD
Normal	4.48	0.15	18.24	0.66
PD	23.46	1.87	59.27	8.86
AD	23.12	2.00	56.90	6.94
MND	22.06	1.61	57.81	6.04
F value	306.749		130.054	
P value	< 0.001		< 0.001	

Table 2. *Effect of cerium and antibiotics on free RNA.*

Group	RNA % change (Increase with Cerium)		RNA % change (Decrease with Doxy+Cipro)	
	Mean	**± SD**	**Mean**	**± SD**
Normal	4.37	0.13	18.38	0.48
PD	23.08	1.87	65.09	3.48
AD	23.29	1.92	65.39	3.95
MND	23.11	1.52	66.68	3.97
F value	427.828		654.453	
P value	< 0.001		< 0.001	

Discussion

There was increase in cytochrome F420 indicating archaeal growth. The archaea can synthesize and use cholesterol as a carbon and energy source. The archaeal origin of the self replicating RNA was indicated by antibiotic induced suppression. The study indicates the presence of actinide based archaea with an alternate actinide based enzymes or metalloenzymes in the system as indicated by cerium induced increase in enzyme activities. There was an increase in free RNA indicating self replicating RNA viroids. The actinides modulate RNA folding and catalyse its ribozymal action. Digoxin can cut and paste the viroidal strands by modulating RNA splicing generating RNA viroidal diversity. The viroids are evolutionarily escaped archaeal group I introns which have retrotransposition and self splicing qualities. The RNA viroids can bind with proteins having prion like domains forming ribonucleoproteins. These ribonucleoproteins can give an abnormal conformation to the protein resulting in generation of abnormal prions. The abnormal prions can act as a template to convert normal proteins with normal configuration to abnormal conformation. This can result in amyloidogenesis. The abnormal configured proteins will resist lysosomal digestion and accumulate as amyloid. This can lead to neurodegenerations - Alzheimer's disease, Parkinson's

disease and motor neuron disease.

Amyloidogenesis has been implicated in neurodegenerations - Alzheimer's disease, Parkinson's disease and motor neuron disease. The beta amyloid in Alzheimer's disease, alpha synuclein in Parkinson's disease, the TAR protein in frontotemporal dementia and copper zinc dismutase in motor neuron disease behaves like prion proteins. Prion diseases are conformational diseases.

The RNA viroids generated from actinidic archaea can bind to proteins with prion like domains resulting in generation of ribonucleoproteins. Ribonucleoproteins with abnormal conformation can act as a template for normal proteins with prion like domains to change to abnormal conformation. This results in generation of prion proteins with abnormal conformation resisting lysosomal digestion and generating amyloid. These neurodegenerations - Alzheimer's disease, Parkinson's disease and motor neuron disease are due to actinidic archaeal generated RNA viroid induced prion protein generation and amyloidogenesis. Prion proteins have been implicated in neurodegenerations - Alzheimer's disease, Parkinson's disease and motor neuron disease. The beta amyloid in Alzheimer's disease, alpha synuclein in Parkinson's disease, the TAR protein in frontotemporal dementia and copper zinc dismutase in motor neuron disease behaves like prion proteins. The present study shows that the same prion protein mechanism can operate in neurodegenerations - Alzheimer's disease, Parkinson's disease and motor neuron disease. Sporadic CJD is also induced by actinidic archaea induced RNA viroids. Actinidic archaeal induced RNA viroids generated prions can be transferred between individuals indicating the infective nature of neurodegenerations - Alzheimer's disease, Parkinson's disease and motor neuron disease.

The global warming results in increased growth of actinidic archaea and neanderthalisation of the homo sapien species. The actinidic archaea secreted

viroids can generate ribonucleoproteins by binding to proteins with prion like domains. This generates amyloidogenesis and neurodegenerations - Alzheimer's disease, Parkinson's disease and motor neuron disease. The widespread incidence of these systemic diseases leads to extinction of the neanderthalised species.

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