

Research Article

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Kuru: The Neurodegenerative Disorder; Roles of PrP^C and PrP^{Sc} in infection, Effects in Blocking Neural Synapses and its Comprehensive Observation

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Abstract

Kuru is a rare and neurodegenerative disorder-creating disease that effectively and principally affects Neural Synapses and the Central Nervous System. For this reason, brain cells and tissues started to be damaged and deceased. Microbials step out to act against the dangerous deceased cells of the human brain, and spongiform encephalopathy gets created. Thus, the Axon-Dendron of Neuron that contains the human brain gets blocked. In the mid of 19s, Kuru has been revealed as a complicated and a suspected pandemic creating disease. Although most of the diseases are caused by different types of virus, bacteria, fungus etc., Kuru is the first human transmitted disease that has been caused by a complicated and misfolded protein. Human body also bears protein, but that is a normal and not dangerous protein, and it is regarded as Cellular Prion Protein, also known as PrP^C. That protein donates itself for the betterment of the human body. But the Scrapie Prion Protein also known as PrP^{Sc} is the Prion Protein that causes Kuru Disease and acts against the Brain and Immune System. Actually, Kuru is penetrated through oral intake. The discussion of Alpha-helices and Beta-sheets have been accurately and theoretically revealed from the aspect of Neuroscience in this review paper. Some figures have been added for a better understanding of most relevant and challenging features.

Keywords: Prion-Protein; Neuron; Scrapie; Alpha-helices; Beta-sheets

Abbreviation: PrP^C : Prion Protein (Cellular); PrP^{Sc}: Prion Protein Scrapie

Introduction

Professor Luisetto M et al. introduced that KURU, the first human transmissible spongiform encephalopathies, can be penetrated in humans. And can impact the brain and immune system by the primary process of the oral intake of affected materials by cannibalising. Also revealed that no boundaries of the genome had not been determined and added that the Kuru Disease efficient process works explicitly against the Brain and immune system as well as creates a fatal neurodegenerative disorder [1].

Methods & Materials

- Observation of the risk factors and impacts on the human body caused by KURU represented through the vigour of research articles.

- What are the must to alleviate the criticisms and analysis of pathogenesis?
- References have been referred based on the information collected from reliable and high impact journals, videos of related lectures by prominent professors of the world.

Results & Discussion

Background: Dr Collinge J. recently introduced that possibly, the disease and incubation somehow sign any future epidemic. Besides, oral intake is the principal factor of infection. It is regarded as a prion disease. The appearance of Kuru indicates the assumption of a disease which occurs rarely. Cannibalism can be the wherewithal

to get rid of the prion disease infection [2]. *Dr Collinge, J., et al.* represented that the neurological and genetic analysis on some Kuru infected enlightened one person having Kuru infection in the tonsil biopsy. In the end, this relevance has created a firm belief that it is positively related to oral as a medium of disease [3].

Dr Janbaz, KH., et al. revealed that the incurable and neurodegenerative disorder created by Kuru disease attacks in the brain system. It is a disease caused by prions. Three echelons of Kuru infection - (i) Ambulant Stage, (ii) Sedentary Stage, and the most criticism, and the last stage is considered as (iii) Terminal Stage. The ambulant echelon represents the disorder in operating body organs, and synchronisation in speech can be found while speaking. Then, in the step of Sedentary, jerking in body, bursting out with laughter, and mental disabilities have been analysed. Besides, the infected become unable and cannot do any work without the support of anyone. Finally, in the last stage- Terminal Stage, infected become more incompetent, and other symptoms and orders turn more synchronised. Kuru disease was first identified in the tribal society of Papua New Guinea during the 1950s. As a disease which is rare and transmits positively from one to another, it transferred to several people. And sex variation analysis mentioned that the chance of the women and the children is very high because of cannibalism and getting a heightened touch to the corpses which can be attacked with Kuru [4].

Dr Liberski, PP. introduced that Kuru, the first transmitted prion disease had been manifested from Chimpanzees to humans. It has been considered acting as a neurodegenerative disease. Neurodegenerative disease is regarded as an illness in the human brain that mainly attacks neurons or creates neuron criticism. Neurons combination builds the nervous system- brain and spinal cord. Cannibalism is taken as a medium of infection [5].

Dr Kompoliti, K. mentioned that this very neurodegenerative disease infects the human body by an unconventional medium that acts against DeoxyRiboNucleic Acid and RiboNucleic Acid. And it has been created from the usual precursor protein and Cross Beta Pleated contamination. Since it is a brain system infecting disease, its presence in the very tiny neurons can be observed by only the microscopic system. One of the most common and fearful signs and symptoms alongside the risk factor of this disease is a disorder in regular movements. But soon after, it turns into a high fatal neurological disorder. It means criticism and synchronisation in the brain and the immune system. Consequently, brain and movement-related problems like coma and inabilities in activities are analysed. Women and children are having a high chance to get an infection and can have highly infected brain tissue through the following cannibalism in the regions of Papua New Guinea. Besides, they highly get contact with the Kuru infected- people and even animals. In some areas, ritual-like endocannibalism is a must to be followed by them as their culture, so like their culture, they consume the dead body of Kuru infected or non-infected. And this can be probably

considered as the principal wherewithal transmission although a hypothesis found that people who don't follow cannibalism, can get infected by Kuru Disease [6].

Ferguson-Smith, MA. and his study recently introduced that at the beginning of the disease transmission in 1957, 5%-10% infected patients were found in some regions. His study revealed that negative-fastness in movement, shivering while working had been effectively recognised. Alongside problems had been found while they talk- sometimes get muted and sometimes speak unsteadily. In the critical stage, patients sometimes go into a coma. Death took place within 1year of this disease. For consuming, preparing the fleshes, brains or other tissues of estimated cannibalising material; women do these processes. That's why getting in touch with fluid of the materials, and they have a high chance of infection. And several studies revealed that the percentage of women is more than that of men. Besides, men do not involve themselves in this process. That's a very relevant evidence of this study [7].

Structural Protein Effects

In the 20th century, researchers discovered that any disease could be caused by protein and the protein that causes disease-most often neurodegenerative illness, disorder and other diseases is called Prion Protein; in short PrP. PrP has two effective forms- PrP^C that is called Cellular Prion Protein, and the other one is- PrP^{Sc}, which is called Scrapie Prion Protein [8]. In the chromosome number 20 of the human body, PRNP bears a protein called PrP [9]. PrP^C is the normal protein and also found in heal the human body; it is formed as Alpha-helices form [10]. But because of the amino-acid formation and polypeptides, Alpha-helices of PrP^C transform into PrP^{Sc} and beta sheets from the transforming receptacle named Molten Globule [11]. PrP^{Sc} is an abnormal and unstable phase that plays a role in mutation of PrP. PrP^{Sc} impacts on the standard and cellular prion protein-PrP^C and it turns into PrP^{Sc} and creates a beta-sheet that is abnormal and misfolded/improperly folded [12]. The misfolded or PrP^{Sc} effects on the Central Nervous System and final cause is the failure of activities in the brain [13]. The centrum of the mind is Neuron. Neuron is consistent with axon, dendron, cellular body. Combination of Axon and Dendron features Neural Synapses. Due to the misfolded PrP^{Sc}, Neural Synapses get blocked and heal cells start to be deceased and damaged [14]. Microbials soon begin to kill the damaged cells, and the spongiform phase gets created.

Finally, death occurs by average 1year onset of the disease infection [15] (Figure 1).

In the above-added Figure: 01, two types of Prion Protein- PrP^C and PrP^{Sc} have been introduced by several signs and graphical work. In the figure, the regular phase of Cellular Prion Protein and abnormal phase of Scrapie Prion Protein have been accurately figured out with the accurate analysis and study on Alpha-helices and Beta-sheets. As beta-sheets belonged to an improper phase of protein, it contains a complicated gene-coding cycle that acts for mutation. And be-

ta-sheets containing Scrapie Prion Protein inspire other Alpha Helices normal prion protein. And if the appearance of one PrP^{Sc} is found in the human body, it transforms into many and many heal PrP^C and the brain and immune system get positively affected (Figure 2). A neuron is consistent with a cellular body, axon and dendron. PrP^C or Cellular Prion Protein generally remains in the human body that does not play any dangerous role in the case of disease production.

It has a connectivity to the human brain and its neurons. Cellular Prion Protein moves to the Neurons and the human brain through the Axon and axonal transport. So, axon is considered as the media [16]. Actually, PrP^C plays a role in the comprehensive management and activities of the brain, body and immune system. If there remains any misfolded Prion Protein anyhow, that can cause life hampering disease.

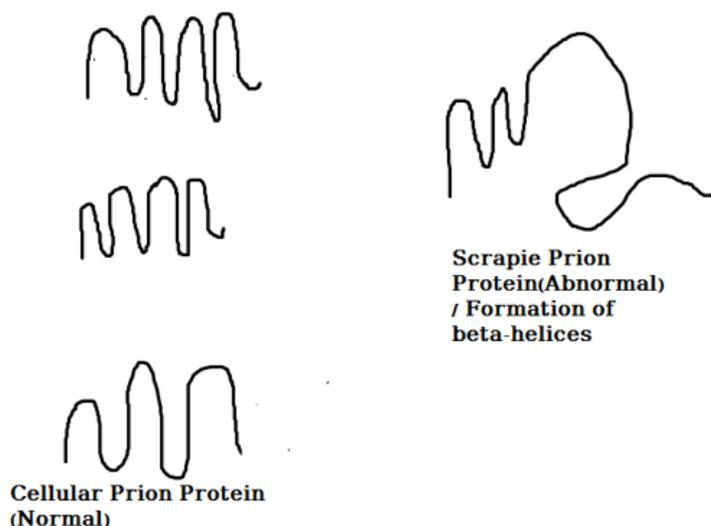


Figure 1:

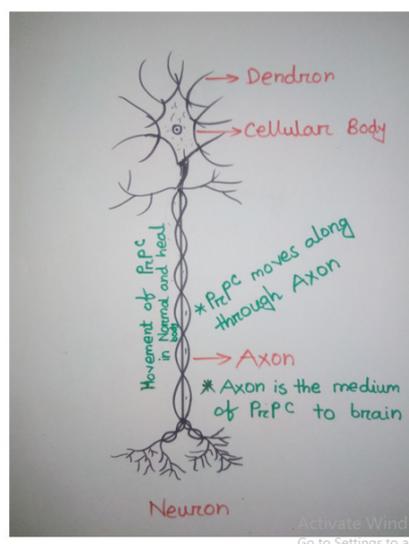


Figure 2: A neuron and the activities of Neuron's parts have been introduced.

Transmission

Kuru is a prion disease that is transmitted by practising cannibalism and consuming affected human brain [17] Or no other natural criticism and complications can be acknowledged as the where-withal of the transmission of the protein-based disease. Principally, improperly appeared protein is the responsible because, through experiment, it has been revealed that the misfolded protein-based PrP^{Sc} blocks the neural synapses. Finally, it impacts the brain and immune system and causes death. Thus, kuru disease occurs and

effects [18]. Besides, PrP^{Sc} contains scrapie and scrapie is positively related to the Transmissible Spongiform Encephalopathies [19]. In the 19 mid's, it was revealed that Kuru is the first human prion disease transmitted to the Chimpanzees. For this reason, it was proved that the principal cause of transmission of Kuru is allowing and practising Cannibalism [20]. Later, cannibalistic people were found having the prion disease. And from then, Kuru started to transmit to humans. Finally, in 2004, when the government of Papua New Guinea and other infected regions headed to avoid the practice, the

cases of Kuru were declined and discarded [21]. Kuru is under the section of Infectious TSE-Transmissible Spongiform Encephalopathies that effectively affects the brain and immune system. TSE is formed from Infectious, Sporadic and Familial features. Besides, Kuru cannot be defined in Sporadic and Familial Sections. As Kuru can be transmitted, it has been remarked under the Infectious TSE or Transmissible Spongiform Encephalopathies. After studies introduced that the patients who were infected in and died of Kuru Disease, they anyhow got contact with the brain and materials got contacted with PRPN. The pathophysiology of Kuru disease is quite unimaginable since it extracts growth hormones and central nervous system [22].

Death and Affected Analyses with Epidemiology

The cases of Kuru features fatality and left untreated for those patients who were infected because there was neither any proper treatment nor any kind of reliable and recommended medication. In the 20th Century, precisely in 1957-1959, frequency of cases of neurodegenerative disease-Kuru was about 2700, and mostly 200 infected died because of the lack of treatment [22]. A study by Alpers, MP, et al. revealed that during 1987-95, 66 people died of being attacked by the neurodegenerative disorder creating Kuru Disease; in which 49 people were in female sex, and the rest 17 were male. Every year, about 3-12 people died from it. Including that in 1987, a one-year-old person and 1991, a 30 years person died from the suspected epidemic creating disease. In one study, the incubation period of the disease and its infection was introduced 30 years and here on this study, ranging to 1995, showed 35 years. The study by Alpers, MP, et al. also introduced that in 1987, overall 12 people died from the Kuru in which eight people were females and 4 were males. People ranging from 50-59 & 30-39 died most- 10(5people+5people=>50-59ages + 30-39ages) in number then in 1987. And 1 death was found below 20, and ranging 20-29, 1 person died. In 1988, 8 people died; 7 were females, and 1 was male. In that year also, people aging 30-39 and 50-59 were mostly infected- 6 people (3+3=>30-39+50-59). In 60-69 and 40-49, 2 deaths were found one by one in every range. In 1989, 11 patients died while female and male in number were respectively 6, 5. But in 1989, ages from 40 to 49 suffered most considering the death- 4 in number. For the people of 30-39 and 50-59 ages, death cases were respectively 3,3. And also in the year, among people aged 60-69, 1 death was caused. In 1990, death cases started to decline, occurring nine deaths; in which seven were female and 2 were male. People ageing from 40 to 49 faced five deaths. 50-59 aged people faced three deaths, and only one death was found in 30-39 aged people. But a flabbergasting feature is that in 1991, there were three deaths and three of them were female. In between 40-49 and 30-39 age, respectively 2 & 1 deaths were revealed. But death cases increased by 1992, causing seven new deaths. Here females and males were consecutively 5 and 2. In 50-59 ages, four deaths and 40-49 ages, three deaths were found. But death cases declined by 1993. Then, overall, four deaths were introduced and all of them from female gender. In age

variation, it has been found that from 50 to 59 age, three people's death were found and one additional death was found from the 40-49 range. Five new deaths were newly started in 1994 in which four were female, and 1 was male. From the age range of 60-69, 1 new death; in 50-59 ages, three new deaths and 40-49 ages, one death were revealed. Seven new deaths were found in 1995. 1, 4, 2 deaths were found respectively in the age ranging of 40-49, 50-59, 60-69 [23].

Symptoms

Like other diseases, Kuru has several complicated and problematic symptoms which indicates the possibility of Kuru. Pain in the body and headache (especially in joint arms) is one of the symptoms in most cases [24]. Serious management complications by improper movement in the human body, problems in activities performing, jerking in Human Body are also the effects and symptoms [25]. Random and unreasonable Laughing and brain working system complications [26] and Coma (in serious and final feature- not always happens) are the impacts on heal human body [27].

Prevention

As Kuru is a prion and rare disease caused from the infected brain tissue and spinal cord fluid [28], it is tough to get the proper medication as while the PrP^C transforms into PrP^{Sc} (misfolded protein), PrP^{Sc} forms the Beta Sheets is the leading causing reason of complications due to its genomic abnormality. It is also a discovery that a disease can be occurred by any protein. So, currently, no medication has been accurately defined [29]. A study by Louisiana State University revealed that Kuru cases were clearly declined by un-following Cannibalism. So, avoiding cannibalism can be the where-withal to prevent it [30].

Conclusion

Kuru has been identified as the first human TSE. It indeed penetrates the human body by oral intake-through practising cannibalism. As for citizens of Papua New Guinea practised cannibalism, the disease has been transmitted by the conduct; proved by experiment. Besides, it is also revealed that Chimpanzees are remarked as the media of transmission to humans. There were three stages- Ambulant, Sedentary and Terminal Stage in the discussion of Pathophysiology. Cellular Prion Protein remains in an ordinary human body that does not affect the human body by any disease. But on the contrary Scrapie (beta-sheet containing and abnormal) Prion Protein is the main reason for Kuru disease. And day by day, it modes Cellular Prion Protein into Scrapie Prion Protein. That finally plays a role in blocking the Neural Synapses, and then the brain gets affected. Later on, the condition of the patient attacked with Kuru gets complicated, and in the terminal stage, people worsen into Coma and then to Death. As currently, no vaccination or medication has been defined, there is no alternative of Prevention in our conducts while prevention is just to prohibit cannibalism. If cannibalism can be banned, the entire world can get rid of a suspected future epidemic.

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Conflict of Interest

No conflict of interest in every sphere.

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