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Prions-Dental Implications

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Abstract

Prions are infectious proteinaceous particle that causes fatal neurodegenerative disease. Prions have recently emerged as challenge to health care workers. Resistance to routine sterilization technique makes this infective protein particle unique and fearsome. Although transmission of prions through dental operative procedures is scarce, its risk cannot be avoided. This article reviews existing knowledge on etiology, pathogenesis, clinical features and dental implication on prion infected disease.

Keywords: Prions; Infective protein particles; CJD; Infectious disease; vCJD

Introduction

Prions are infective proteins lacking a well-defined genetic constitution (DNA/RNA). The word prion was first coined by Stanley Prusiner in 1982 to describe an infectious agent that causes transmissible spongiform encephalopathy. The term prion was derived from the phrase 'Proteinaceous infectious particle' [1]. Initially they were believed to cause fatal zoonotic infections, but later on prions were isolated from brain samples of humans affected by Alzheimer's disease (AD), Huntington's disease (HD), and Parkinson's disease (PD) [2]. Hence prions affect both animals and humans. Prion infected diseases have unique characteristics; they are highly heterogeneous and have varied phenotype [3]. Diagnostic procedures are not sensitive, no therapeutic intervention has shown reliable result, and mode of transmission is not under stood. So prion associated disease is an enigma to the medical field.

History

It was Griffith in 1967 first proposed protein could be infectious, pathogenic and postulated their involvement in scrapie [4]. Scrapie was a zoonotic infection seen among sheep's and goats in European farms which was first reported in the 18th century, were animals scraped of their coats suffering from pruritus, hence the name scrapie4 .Griffiths hypothesis was later proved by Prusiner and co-worker when infectious proteinaceous particles were isolated from infected hamster brain and called the particle prion.

Cellular Prion Protein

The exact physical nature of prion protein is a controversy. It is believed that prion proteins are of 2 types PrP^{c} and PrP^{sc}. PrP^{c} is associated with cell surface protein, they are present in healthy human cell and are soluble, monomeric and protease sensitive [5]. They play role in oxidative stress reduction, signal transduction, apoptosis regulation, binding of copper ions, adhesion of extracellular matrix, formation and maintenance of synapse [6].

PrP^{c} is usually soluble; however insoluble form of PrP^{c} ($IPrP^{c}$) has also been identified in the brains of normal healthy human as well as cultured neuronal cells [7]. This isoform $IPrP^{c}$ binds only to the misfolded PrP^{sc} not to the PrP^{c} and is resistant to proteinase K degradation [8]. PrP^{sc} (protein associated with scrapie) is an isomer of PrP^{c} found in infected brain as aggregated material and are associated with pathogenesis; the molecular phenomenon involved is transition of α-helix rich PrP^{c} to β sheets of PrP^{sc}. βsheet rich structure has better stability and can form aggregates that are capable of forming amyloid fibrils [9]. This protein aggregation is major molecular event accompanying the conversion of PrP^{c} to PrP^{sc}.

Pathogenisis

The true mode of transmission of prion disease is not yet proven. Pathogenesis can be explained in following steps

1) Peripheral Replication

2) Neuroinvasion

3) Neuron degeneration [10]

Peripheral Replication

Various strains of prions show varying cell tropism. Hence the site of peripheral replication may vary, but many strains have shown high titres in the lymphoid tissues like tonsils, Peyer's patches, and spleen before neuroinvasion. Next appears in serous and mucous glands in the oral cavity. It is the heamopiotic cells responsible for the transport of prions from the site of injury to the lyphoreticular system [10].

Neuroinvasion

Mature and follicular dendritic cells located in payer's patches and B lymphocytes are known to cause neuroinvasion of prions. The exact mechanism of neuroinvasion is not well clear and is beyond the scope of this review .However role of complement system and hyper innervation to the secondary lymphoid organ in neuroinvasion has been documented in few studies [10] [Table 1].

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Table 1: Various Human Prion Diseases and clinical manifestation.

NAME OF THE DISEASE	CAUSE	CLINICAL MANIFESTATION
CJD	sporadic	EARLY: Lapses in memory, mood swings, social withdrawal and unsteadiness LATE: Blurred vision, sudden jerking, movements and rigidity in the limbs, slurred speech, difficulty swallowing, progressive mental deterioration [11]
vCJD	Intake of BSE contaminated beef and beef products	Mostly depression, delirium, hallucinations, paraesthesia and dysesthesia [18]
KURU	Cannibalism;consumption of disease relatives tissue.	ataxia, tremors, dysarthria and death [12]
Gerstmann–Sträussler–Scheinker syndrome	Familial (germ line *PRNP* mutation)	ataxia, dysarthria and nystagmus and death occurs after 1-10 years [13]
Fatal Familial Insomnia (FFI)	Familial (germ line *PRNP* mutation)	to ataxia, dysarthria and nystagmus and death occurs after 1-10 years [13]

Table 2: WHO Guidelines.

Incineration	• Use for all disposable instruments, materials and wastes. • Preferred method for all instruments exposed to high infectivity tissues.
Autoclave and chemical methods for heat-resistant instruments	• Immerse in sodium hydroxide (1 N NaOH) and heat in a gravity displacement autoclave at 121°C for 30 min; clean; rinse in water and subject to routine sterilization. • Immerse in NaOH or sodium hypochlorite (20 000 ppm available chlorine) for 1 h; transfer instruments to water; heat in a gravity displacement autoclave at 121°C for 1 h; clean and subject to routine sterilization. • Immerse in NaOH or sodium hypochlorite for 1 h; remove and rinse in water, then transfer to open pan and heat in a gravity displacement (121°C) or porous load (134°C) autoclave for 1 h; clean and subject to routine sterilization. • Immerse in NaOH and boil for 10 min at atmospheric pressure; clean, rinse in water and subject to routine sterilization. • Immerse in sodium hypochlorite (preferred) or NaOH (alternative) at ambient temperature for 1 h; clean; rinse in water and subject to routine sterilization. • Autoclave at 134°C for 18 min (to be used for worst-case scenario; i.e., brain tissue bake-dried on surfaces).
Chemical methods for surfaces and heat-sensitive instruments	• Flood with 2 N NaOH or undiluted sodium hypochlorite; let stand for 1 h; mop up and rinse with water. • For surfaces that cannot tolerate NaOH or hypochlorite, thorough cleaning will remove most infective agents by dilution, and some additional benefit may be derived from the use of one or another of the partially effective methods (chlorine dioxide glutaraldehyde, guanidinium thiocyanate [4 mol/L], iodophors, sodium dichloro-isocyanurate, sodium metaperiodate, urea [6 mol/L]).
Autoclave or chemical methods for dry goods	Small dry goods that can withstand either NaOH or sodium hypochlorite should first be immersed in one or the other solution (as described above) and then heated in a porous load autoclave at ε 121°C for 1 h. • Bulky dry goods or dry goods of any size that cannot withstand exposure to21 NaOH or sodium hypochlorite should be heated in a porous load autoclave at 134°C for 1 h.

Oral Manifestation

Since these are neurodegenerative disorder the oral manifestation reported include- dysphagia, paraesthesia, orofacial dysasthesia, loss of taste more over infectivity to trigeminal ganglion has been documented [14].

Diagnosis

Detection of PrP^{sc} may be advantageous in the diagnosis of prion disease as $PrPs^{c}$ is associated with pathogenesis. Detection of sarogate markers has been documented but these markers are less specific they might show high titre in other neurodegenerative disorder as well. PrP^{sc} proteins are usually identified with Western Blot, ELISA, and Immune Precipitation [15]. Other tests used: EEG, Cranial magnetic resonance imaging, Cerebrospinal fluid test, Tonsilar biopsy, blood test to extract DNA and check for mutation.

Transmission

The risk of transmission of CJD through dental treatment is unclear. A very few cases of disease transmission through blood transfusion have been reported [16] but further studies need to be conducted on it. However, the risk of disease transmission through neuronal tissue following neurological surgery like Dura mater graft, corneal transplant cannot be excluded. Studies also state that long incubation period could be the reason that masks the iatrogenic transmission of the disease [17]. There is no evidence of saliva as an infective agent for prion disease, even though few animal studies have isolated pathogenic prion protein from serous and mucous glands no human studies have been documented [18].

Prions and Dental Implication

Although the occupational risk of transmission of CJD in dentistry is less, on endodontists perspective, pulp tissue which is highly innervated by the nerves the chances of prion protein transmission through endodontic files cannot be completely exempted. One of the most important feature of prions are they are highly resistant to autoclave and other methods of sterilisation and disinfection. Therefor proper infection control has to be followed. All treatment should begin with a detailed case history [19]. Any history of neurological surgery like Dura mater graft, corneal transplant coinciding with neurological symptoms should be subjected to further neurological evaluation prior to the treatment [20].

The CDC guidelines for infection control for treatment of patients with vCJD include

• The dental items that are difficult to clean such as endodontic files, broaches, carbide and diamond burs should be discarded, other dental instrument that are heat resistant should be thoroughly cleaned and steam autoclaved for 134°C for 18 minutes

• Patients with confirmed disease should be scheduled for end of the day to permit more extensive disinfection cleaning and decontamination

• Activation of waterlines should be avoided as there are chances of retraction of prions from the oral fluid.

• Standalone suction unit with disposable reservoir and disposable bowl instead of spittoon should be used.

• All the dental equipment should be shielded with impermeable sheets [11].

Besides these measures given by CDC operator should use all the PPE including face shield, once used all the all the PPE along with disposable used instruments should be quarantined in a leak proof combustible clinical waste container and should be subjected for incineration as soon as possible [21]. In case of re-usable instruments, it should be kept moist as the resistance of prion tissue to get removed increases as it becomes dry [Table 2].

Post Exposure Prophylaxis

• Contamination of unbroken skin with internal body fluids or tissues

Wash with detergent and abundant qualities of warm water, rinse and dry. Exposure to 0.1N NaOH or 1:10 dilution of bleach for 1 minute can be considered for maximum safety.

• Needle sticks or lacerations

Gently encourage bleeding. Wash with warm soup water, rinse, dry and cover with a water proof dressing. Further treatment like suturing should be appropriate to the type of injury. Report the injury according to normal procedures of your hospital or health care facility. Records should be kept for no less than 20 years.

• Splashes into eye or mouth

Irrigate with either saline (eye) or tap water (mouth). Report according to normal procedures for your hospital or health care facility [21].

Conclusion

Till date no case of transmission of prion associated disease through dental treatment has been reported yet. Still it is our responsibility to raise the standards of sterilisation and disinfection protocol to ensure safe and secure dental practice. This review aims to provide an overview of prion, its structure, pathogenesis diagnosis treatment and its relevance in dentistry. Further research should come up for a proper understanding of its transmission diagnosis and treatment.

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