Prions in dentistry: A need to be concerned and known

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ABSTRACT
Prion diseases were first discovered by Stanley B. Prusiner who defined prions as infectious, transmissible proteinaceous particles that lack nucleic acid and are composed exclusively of a modified isoform of the noninfectious cellular prion protein (PrPC). These are incurable neurodegenerative conditions affecting both animals and humans. They may be sporadic, infectious or inherited in origin. Human prion diseases include Creutzfeldt–Jakob disease (CJD), Gerstmann–Straussler–Scheinker disease, Kuru and Fatal familial insomnia. Prions resist the conventional sterilization procedures and hence the dentists must be aware of such diseases so as to opt standard methods of infection control and decontamination for such infectious agents. This review article divulge the dentists with a brief overview of the characteristics of prions, the risk of transmission and the implications for infection control in dentist.

Key words: Prion, prion protein, transmissible spongiform encephalopathies

INTRODUCTION

Prion diseases also known as transmissible spongiform encephalopathies (TSEs) are degenerative disorders of the nervous system caused by transmissible particles that contain a pathogenic isoform of the prion protein, a normal constituent of cell membranes. Stanley B. Prusiner discovered and defined prions as infectious, transmissible proteinaceous particles that lack nucleic acid and are composed exclusively of a modified isoform of the noninfectious cellular prion protein (PrPC). Prusiner distinguished these infectious particles from viruses or viroids and finally designated it as a prion protein (PrP) for which he was later awarded the Nobel Prize in Physiology or Medicine in 1997.

Prion diseases are incurable neurodegenerative conditions affecting both animals and humans. They may be sporadic, infectious or inherited in origin. Human prion diseases include Creutzfeldt–Jakob disease (CJD), Gerstmann–Straussler–Scheinker disease, Kuru and Fatal familial insomnia. Although the risk of transmission of these diseases through dental procedures is quite inquisitive and unclear, the theoretical possibility of transmission through contaminated dental instruments should be kept in mind.

This article reviews a new understanding about hitherto unreported phenomenon about prions and divulges the dentists with a brief overview of the characteristics of prions, the risk of transmission and the implications for infection control in dentistry.
of acetylcholine receptors. The PrP is expressed in most adult tissues but is found at the highest levels in the central nervous system (CNS) and immune systems.\textsuperscript{[2,4]}

The disease-associated isoform, referred to as PrPSc (Prion protein in Scrapie) is found only in infected brains as aggregated material, is partially resistant to protease treatment and insoluble in detergents. This mutated PrPSc gives rise to TSEs, including bovine spongiform encephalopathy (BSE) in cattle, scrapie in sheep and goats and CJD in humans. These diseases are characterized by vacuolization of the gray matter, and these vacuoles are located in the neutrophils between the nerve cell bodies.\textsuperscript{[2,4]}

**PRION HYPOTHESIS**

Gibbons\textsuperscript{[9]} in 1993 using X-ray crystallography studies on prions suggested that even if nucleic acids are present in association with PrP, this would be at a size too small to encode phenotypic diversity, further strengthening the protein-only “prion hypothesis.” The “Prion Hypothesis” suggests that an abnormal conformer (PrPSc) of the PrPc is capable of inducing PrPc to undergo a change of conformation into PrPSc. An alternative hypothesis was proposed by Weissmann in 1991.\textsuperscript{[10]} This hypothesis suggests that the protein component of a prion designated the apo-prion can cause disease by itself but that a small host-derived nucleic acid designated the co-prion can associate with it. The combination of both (the holo prion) can then give rise to a host modified strain of disease.

**HUMAN PRION DISEASES**

Human prion diseases include CJD, Gerstmann–Straussler–Scheinker disease, Kuru and Fatal familial insomnia. CJD is actually a group of diseases divided into sporadic CJD (sCJD), inherited (Gerstmann–Sträussler–Scheinker syndrome and fatal familial insomnia) and acquired (iatrogenic, kuru, variant CJD [vCJD]) forms. The onset, duration and clinical signs and symptoms of each disease are illustrated in Table 1.

Sporadic cases of CJD occur spontaneously, without any apparent reason. The mean age of patients with sCJD is 68 years. The mortality rate is 85% within 1 year and the diagnosis is best ascertained during the final stages of the disease, at or near the time of death. The disease is characterized by progressive dementia, ataxia, myoclonus, cortical blindness, akinnesia and speech loss, followed by death within 4 months.\textsuperscript{[2,11,12]}

Gerstmann–Sträussler–Scheinker syndrome and fatal familial insomnia are both very rare, with an annual incidence of 1/10 million to 100 million people. They occur in people with an apparent hereditary predisposition. There is lack of coordination leading to ataxia, dysarthria and nystagmus and death occurs after 1–10 years.\textsuperscript{[2,15]}

Table 1: Clinical signs and symptoms of prions diseases

| Human prion disease          | Age of onset | Duration of disease | Clinical signs and symptoms of disease                                      |
|------------------------------|--------------|---------------------|---------------------------------------------------------------------------|
| Creutzfeldt–Jakob disease    | 60-69        | 3-6                 | Early: Lapses in memory, mood swings (similar to depression), lack of interest, social withdrawal and unsteadiness Late: Blurred vision, sudden jerking movements and rigidity in the limbs, slurred speech, difficulty swallowing, progressive mental deterioration and immobility |
| Variant Creutzfeldt–Jakob disease | 20-29       | 9-35                | Early: Mostly depression, unusual sensory signs, such as “stickiness” of the skin Late: Unsteadiness, difficulty in walking and involuntary movements as the illness progresses, complete immobility and muteness |
| Kuru                         | >20          | 6-36                | Early: Cerebellar syndrome; communication difficulties due to severe dysarthria Late: Progression to total incapacitation and death in final stages |

**vCJD** is indeed a new disease and is associated with the intake of BSE-contaminated beef and beef products. The disease is usually characterized by depression, delirium, hallucinations, paresthesia and dysesthesia followed by dementia and akinnesia. The duration of illness is more prolonged in these cases. Deposition of amyloid plaques in the lymphatic tissues throughout the body is a prominent feature.\textsuperscript{[2,11]}

Kuru, first described in 1950s, an acquired human TSE, geographically restricted to the Okapa area of the Eastern Highlands of Papua New Guinea. It resulted from cannibalism specifically the consumption of deceased relatives' tissues as a form of respect. It affected predominately women and children who consumed deceased relatives as a mark of respect. The mean incubation period was estimated to be about 12 years.\textsuperscript{[11]} The disease is characterized by ataxia, tremors, dysarthria and death.\textsuperscript{[2,13,14]} Finally, cannibalism was banned in 1956 which resulted in decreased incidence of this disease.\textsuperscript{[2]}

Iatrogenic transmission of CJD occurs as a result of cross-contamination, neurosurgery, dura mater transplantation, corneal grafting and injection of pituitary hormones obtained from human cadavers. This type of prion disease is important to dentists due to the risk of cross-contamination after the use of infected dental instruments. The incubation period is variable ranging from 2 to 35 years. The clinical features are similar to sporadic form, but cerebellar motor symptoms are predominant in this type.\textsuperscript{[2,6]}
ORAL MANIFESTATIONS OF PRION DISEASES

Dysphagia (difficulty in swallowing) and dysarthria (poor articulation of speech), paresthesia (tingling, prickling or numbness), orofacial dysesthesia (abnormal sensations in the absence of stimulation) and in one case loss of taste and smell have been reported in the literature. A significant level of infectivity in the trigeminal ganglia and in the gingival and pulpal tissues of scrapie-affected hamsters after intraperitoneal inoculation, suggesting possible transmission from the CNS through trigeminal nerves toward the oral cavity is also documented.[2,15]

PRIONS AND DENTISTRY

Prions are highly resistant to inactivation and can survive autoclaving even at high temperatures; therefore, dentists and members of their dental teams should be aware of the precautions and principles of appropriate infection control to minimize iatrogenic transmission of prions.[6] There is no evidence to show that TSE is transmissible from one person to other by normal social contact, sexual contact or airborne droplets. So far no studies have shown evidence of transmission of sCJD by blood components or plasma products. To date, there are no reported definite or suspected cases of human TSEs arising from dental procedures. However, the enigmatic mechanisms postulated for the transfer of CJD via dental instruments were accidental abrasion of lingual tonsil during dental procedures and contact of dental instruments with pulp tissue. As dental pulp originates from richly innervated neural crest cells, it is theoretically possible that the dental pulp of individuals infected with CJD may be infectious.[2]

INFECTION CONTROL IN DENTISTRY

There is no risk of transmission of TSE to health care workers including medical doctors and dentists through clinical contact or noninvasive clinical investigative procedure. In 2005, a total of 24 cases of sCJD have been reported in health care workers.[16] The general infection control practices recommended by the national dental associations are sufficient. However, when certain invasive interventions are performed on patients who are at risk, it is essential to implement proper infection control to reduce the possibility of transmission of TSEs via dental instruments.

The participants in the WHO Consultation on Infection Control Guidelines for TSEs suggested that single-use items and equipment such as disposable needles and anesthetic cartridges represented the safest method for minimizing the risk of prions.[17,18]

A study conducted by Bourvis et al.[19] showed that the risk of sCJD transmission is higher because of the reuse of endodontic instruments in the absence of effective prion decontamination procedures. Achieving appropriate decontamination of endodontic instruments intended for reuse is extremely difficult. Therefore, there is a possibility that these decontaminated instruments that were in contact with dental pulpal tissue may transfer the PrPs from the infected patients to other patients.[20]

In 2001, the Fédération Dentaire Internationale announced a policy statement regarding the prevention of TSEs in dentistry, suggesting universal precautions, complete medical history of the patient, family history of prion diseases, travel history to know about the possible exposure during visits to endemic areas like United Kingdom and appropriate continuing education for dentists about the control of cross-infection in dental practice. For at-risk patients, referral to specialist clinics or hospitals and incineration of all instruments and extracted teeth were recommended. It was suggested that animal-derived graft materials should not be used in oral or periodontal surgery unless the safety of the product has been certified. Moreover, caution should be exercised in the use of heterologous human graft materials.

A recent communication in 2007 titled “Advise for dentists on re-use of endodontic instruments and variant Creutzfeldt-Jakob Disease” issued by the UK Department of Health has advised dentists to ensure single use of endodontic reamers and files as a precaution to reduce any potential risk of transmission of vCJD as endodontic files used in the treatment of pulp cavity contain blood and peripheral nerves known to carry the PrPs and their intricate surface topography enable to trap the proteins. For heat-resistant dental instruments, they suggested thoroughly cleaning and steam autoclaving the instruments at 134°C for 18 min.[21]

Patients with confirmed prion disease should be scheduled at the end of the day to permit more extensive cleaning and decontamination. It is preferable to avoid activating water lines because of the risk of retraction of prions in oral fluids. Moreover, a stand-alone suction unit with the disposable reservoir, rather than the suction component of the dental unit and a disposable bowl instead of the dental unit spittoon should be used. To avoid environmental contamination, dental equipment should be adequately shielded using disposable, impermeable cover sheets.

CONCLUSION

Recently, there has been an increase in scientific and public awareness about prion disease. The precise nature and structure of prion and the risk of transmission of prion disease through dental treatment points to the importance of maintaining optimal standards of infection control and decontamination for infectious agents, including prions. In addition, the dental professionals should have up-to-date knowledge about transmission, diagnosis, infection control and decontamination procedures regarding prion diseases.
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