EPIDEMIOLOGICAL ANALYSIS OF
BOVINE SPONGIFORM ENCEPHALOPATHY (BSE)

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Summary: Bovine spongiform encephalopathy (BSE) in cattle, scrapie in sheep and goats, chronic wasting disease (CWD) in cervids, and Creutzfeldt-Jakob disease (CJD) in humans are known as prion diseases or transmissible spongiform encephalopathies (TSE), which cause neurodegenerative disorders. BSE was first reported in the United Kingdom (UK) in 1987, following which over 180,000 cases have been reported to date. BSE cases have been detected mainly in Europe. However, prevalence of BSE was recently confirmed in countries outside Europe, such as Israel, Japan, United States of America (USA), and Canada. BSE has become a worldwide issue that has affected the international trade of cattle, beef, and beef products. Adopting control or preventive measures against BSE based on risk assessment is recommended in all the countries. The World organisation for Animal Health (OIE) provides guidelines for risk assessment which is included in the Terrestrial Animal Health Code (the Terrestrial Code). In this paper, the factors that may influence BSE risk are reviewed.

1. ETIOLOGY OF BSE

An abnormal isoform of the prion protein (PrPSc) accumulates in animals affected by BSE. This is generated by a posttranslational modification of the cellular isoform of the prion protein (PrPC) and consists of the causative agent, namely, a prion [1]. This theory is supported by recent evidence demonstrating that an in vitro form of the prion protein (PrP) can be transformed and is infectious in mice [2]. Detection of PrPSc, including differentiation of this isoform from PrPC, is therefore crucial for the diagnosis of prion diseases. The conversion of PrPC to PrPSc is the central event in prion propagation but the mechanism leading to this conformational change has not been completely understood.

PrPC is a glycoprotein with a molecular mass of 33–37 kDa, containing two N-linked sugar chains, and is attached to the cell membrane by a glycosyl phosphatidylinositol (GPI) anchor. Although the nature of PrPSc remains obscure, PrPSc consists of a larger number of β-sheets and a considerably lower α-helical content as compared to PrPC, despite the fact that both comprise identical amino acid sequences. Hence, PrPSc is relatively resistant to protease digestion, is easily aggregated into amyloid fibrils, and exhibits the property of insolubility. The resistance to protease is widely accepted as the physicochemical characteristic of PrPSc that distinguishes PrPSc from PrPC.

PrPSc is the only known disease-specific marker of TSEs. A single prion strain was believed to cause BSE but many strains are identified in scrapie based on the differences in the duration of the incubation period and the lesion profile of the brain in infected animals. However, the possibility of the natural occurrence of phenotypic variation in BSE or a novel expression of TSE in cattle has been reported from Japan [3], Italy [4], and France [5]. A western blot analysis revealed that all these atypical types of BSE showed glycoform profiles that differed from that of PrPSc. In particular, the immunohistochemistry of brain samples from cases reported in Italy showed different distribution patterns of PrPSc in the brain. To verify the presence of these novel strains of BSE, these phenotype features of atypical BSE need to be confirmed by transmission studies using animals.

2. ROUTE OF INFECTION

The origin of BSE remains unknown, but meat and bone meal (MBM) derived from infected cattle is considered to be a major vehicle of BSE infectivity [6]. Since this agent is highly resistant to heat treatment, rendering processes for the production of MBM from carcasses were not adequate for complete inactivation of the infectivity. MBM has frequently been used as the protein source in concentrates of cattle. Therefore, the BSE agents that were derived from infected animals were recycled through the use of these feeds.
In addition to the use of MBM as a food additive for cattle concentrates, the contamination of cattle feed with MBM from other feeds at feed manufacturing plants (cross contamination) exposed the cattle to MBM. The cases of BSE infection that occurred in UK and other European countries after the ruminant-ruminant or mammalian – ruminant feed ban is considered to occur via this route of exposure.

Another possible route of exposure is the tallow (animal fat), which is also a rendering product from carcasses, and it is suspected to be a source of infection if it contains animal protein derived from infected animals. However, this route of infection was never confirmed. The OIE Terrestrial Animal Health Code states that protein-free tallow, which contains less than 0.15% of insoluble impurities, can be traded without any BSE-related condition.

The possibility of TSE transmission via blood was suggested to occur during blood transfusion experiments conducted on sheep and epidemiological investigations conducted in humans [7, 8]. In animals, transmission via this route is not possible because blood transfusion between animals is uncommon. There is no direct evidence of horizontal transmission of BSE among cattle or from environmental contamination and true maternal transmission has not been established.

3. CONTROL STRATEGY

Since the linkage between variant CJD and BSE was suggested, control measures against BSE have been taken from the viewpoint of both animal and public health. The ban on the use of ruminant protein for ruminant feeds is one of the most important measures for controlling BSE. This measure will enable the termination of the infection cycle among cattle population. Pigs and chickens are either not susceptible or less susceptible to BSE under field conditions. Therefore, principally, the removal of ruminant protein from ruminant feed may be adequate to avoid further infection. However, considering possible cross-contamination of cattle feed that includes MBM at feed plants, the European Union (EU) and Japan adopted a total ban on the use of mammalian protein in feeds for all mammals.

Monitoring of the feed production is one of the most crucial factors in the implementation of the feed ban.

Removal of specified risk materials (SRM); brain, spinal cord, etc. at abattoirs is usually undertaken for protecting humans from exposure to BSE prion in BSE-affected countries. In order to prevent the BSE prions from entering the human food chain, many affected countries reviewed and regulated methods of slaughtering, splitting carcasses, removal of SRM, etc. at abattoirs. The incineration of removed SRM also guarantees preventing of accidental or illegal exposure to cattle.

When a BSE case is encountered, the infected animal must be destroyed completely. The animals that are suspected to have consumed the same feed until one year of age should also be destroyed. However, due to the poor records maintained by some farms, identification of these animals is sometimes difficult. Therefore, a cattle identification system was introduced in some countries to reinforce the ability of tracing the source of infected cattle. Due to the long incubation period of BSE, the effectiveness of the control measures cannot be determined immediately. Therefore, surveillance is necessary to ascertain the BSE status of a country.

4. DIAGNOSIS OF BSE

a) Clinical features of BSE

BSE has a slowly progressive and invariably fatal course. It is characterised by a long incubation period in the affected animals and the absence of a detectable immunological response in the host. The clinical features of BSE are characterised by (1) apprehension, behavioural changes, fear, increased startle response, or depression; (2) hyper reactivity or hyperreflexia to touch, to sound, and to light; (3) ataxia of gait, including hypermetria and paresis, resulting in falling; (4) adventitial movements such as muscle fasciculations, tremor, and myoclonus; (5) autonomic dysfunction, including, reduced rumination, bradycardia, and cardiac arrhythmia; and (6) loss of body weight and deterioration in general health condition, and reduction in milk yield. These clinical features can also arise due to other central nervous system disorders and are not evident until the terminal stage of the illness. Therefore, diagnosis of BSE based on clinical signs is difficult. Laboratory tests are required, particularly to detect infected animals in the preclinical stage.

b) Laboratory diagnosis of BSE

Currently, performing an ante mortem diagnosis is difficult, and the available BSE diagnostic tests are all postmortem procedures. PrPSc accumulates in the central nervous systems and brain samples should therefore be collected as soon as possible after death.
BSE has been diagnosed using histopathology, immunohistochemistry (IHC), and biochemical analyses (western blot and ELISA). With the exception of histological examination, all these tests aim at detecting PrPSc as proteinase K (PK)-resistant PrP [9, 10]. Recently, a new technique has been introduced for BSE diagnosis, and it aims to detect PrPSc on the basis of a conformational change in the PrP molecule [11]. However, none of the available BSE tests can detect the infected cattle in the early stage of the incubation period.

5. SURVEILLANCE OF BSE

The aims of surveillance are as follows: (1) monitoring the evolution of BSE, (2) monitoring the effectiveness of a feed ban and/or other risk mitigation measures, (3) supporting a claimed BSE status, and (4) gaining or regaining a more favourable BSE status. OIE states that the following four subpopulations of cattle have been identified for surveillance purposes: (1) cattle over 30 months of age displaying behavioural or clinical signs consistent with BSE; (2) cattle over 30 months of age that are non-ambulatory, recumbent, and unable to rise or to walk without assistance, and cattle over 30 months of age sent for emergency slaughter or condemned at ante mortem inspection; (3) cattle over 30 months of age that are found dead on the farm (fallen stock); and (4) cattle over 36 months of age at routine slaughter.

In view of the long incubation period of BSE, a certain proportion of infected cattle are believed to die before the clinical onset of the disease. Unlike other infectious diseases, the incidence rate of BSE is very low. These features create difficulties in designing an efficient BSE surveillance programme. The surveillance programme should consider the diagnostic limitations, the disease characteristics and the age structure of the cattle population in each country. BSE surveillance consists of passive surveillance based on the notification of suspected cases, and active surveillance targeting the fallen stock and healthy slaughtered cattle. Most of the BSE-affected countries conducted both types of surveillance.

6. CONCLUSION

The livestock production system which varies from country to country influences the risk of occurrence of BSE. Countries that import cattle or MBM from other countries possibly have a risk of BSE introduction in the domestic cattle population. Therefore, necessary measures should be adopted on the basis of risk assessment, even if no outbreak is confirmed. In addition, it should be recognised that surveillance is another important measure for the eradication of BSE from the region, considering the fact that BSE was detected by active surveillance. It is obvious that appropriate diagnostic and sampling procedures are required to achieve a technically sound surveillance system. In countries with limited resources on these technical issues, international cooperation would contribute to the establishment of reasonable countermeasures against BSE. Of late, trade relations between the countries in the region have been strengthened. Hence, coping with animal diseases, such as BSE, should be dealt with at an international level, and this will be beneficial for all the countries in the region.

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