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PATHOLOGY RELATED WITH "NOVEL" EMERGING INFECTIOUS AGENTS IN LIVESTOCK

Stelian BĂRĂITĂREANU, Doina DANEŞ

University of Agronomic Sciences and Veterinary Medicine of Bucharest,
Faculty of Veterinary Medicine, 105 Splaiul Independentei, 050097, Bucharest 5, Romania
Tel: +40214011122, stelian.baraitareanu@gmail.com, danes.doina@gmail.com

Corresponding author email: stelian.baraitareanu@gmail.com

Abstract

Emergence of "novel" infectious agents with or without zoonotic potential continues to occur in livestock. Such events have many causes, some natural and a lot off are associate with human interference upon microorganisms or their environment. Animal world is hosting many more pathogens than those who are subject of current surveillance and/or diagnostic: some of them are endemic in limited ecosystems, and are usually defined as exotic pathogens by European countries (e.g., Hendra virus, Nipah virus, Akabane virus); others are not associated with collective or individual known pathology in them natural hosts (asymptomatic carriers) but can produce or can be involved in diseases of other domestic animals or humans (e.g. Hanta virus, Crimea-Congo hemorrhagic fever virus), or are just new discovered pathogens (e.g., Schmallenberg virus). It is difficult to accomplish, but it would be highly useful to investigate if these organisms, introduced in different populations other than the originating one, could generate pathology. Would be useful to map the distribution of these newly discovered agents whose potential pathogen is still unevaluated or even appear devoid of pathogenicity, to estimate their emerging potential in the case of contact with unusual hosts. The large number of pathogens, which are not subject to official notification, makes difficult their active surveillance by specific laboratory testing methods; the cost-effectiveness of active surveillance systems could not be accepted for the animal disease surveillance and the prompt reporting. However, the passive surveillance and the risk analysis (exposure assessment and risk characterization) can be perform using conventional or participatory epidemiology if the specialist or farmers are trained to identify the pathology that can be produced by these new pathogens. The aim of this review was to describe the main clinic pathological features generated in livestock by "novel" infectious agents: Schmallenberg virus, Hendra virus, Menangle virus, Nipah virus and Usutu virus. In our opinion, once emerged a new microorganism it is advisable to make investigation in similar ecosystems to check his presence.

Key words: *Schmallenberg virus, Hendra virus, Menangle virus, Nipah virus, Usutu virus.*

INTRODUCTION

Animal world is hosting many more pathogens than those who are subject of current surveillance and/or diagnostic. Diseases previously considered with limited ecosystem level of dissemination, today experience an expansion towards the territories previously classified as unsuitable for their pathogens and/or vectors. Hendra virus, Nipah virus or Akabane virus are usually defined as exotic pathogens in European countries, but the risk of intercontinental and/or transcontinental dissemination must be considered in the context of increased trade and tourism with countries from Southeast Asia and Australia. Other viruses, such as Hanta virus or Crimeea - Congo hemorrhagic fever virus are not associated with collective or individual known pathology in them natural hosts but can produce or can be involved in diseases of other domestic animals or humans; the expansion risk of this viruses in new territories need to be considerate both, into wild and domestic animals. Emerging infectious agents, such as Schmallenberg, can lead to major problems in the context of their discovery performed long time after the virus spread to susceptible livestock, active investigation proving that a large number of them have been already infected.

Schmallenberg virus (SBV) has been first documented in Germany and The Netherlands where, in 2011, farmers and veterinarians reported an unidentified disease in dairy cattle with a short period of clear clinical signs, including fever, decreased milk production, and diarrhea (Hoffmann et al., 2011). The SBV name is after the city of Schmallenberg, located in North Rhine-Westphalia, Germany, the place of origin of the first samples used at Friedrich-

Loëffler Institute (Germany) in a metagenomic approach for detection of viral RNA (Hoffmann et al., 2011, Doceul et al., 2013). Up to this, Germany (2011), The Netherlands (2011), Belgium (2011), United Kingdom (2012), France (2012), Luxembourg (2012), Italy (2012), Spain (2012), Denmark (2012), Switzerland (2012), Austria (2012), Poland (2012), Sweden (2012), Finland (2012), Ireland (2012) , Norway (2012), Czech Republic (2012), Estonia (2013), Slovenia (2013) (Doceul et al., 2013; De Regge et al., 2014), reported SBV in cattle, sheep, goat, bisons, several *Culicoides* species and biting midges. In Romania, we started in September 2013, at the Faculty of Veterinary Medicine of Bucharest, a preliminary serological screening of SBV and Simbu group viruses. We carried out the investigation on serum samples collected from cattle and sheep breeded in South and South-East counties using a commercial ELISA kit (IDEXX, Switzerland); our preliminary results revealed the prevalence of positive samples and suggest the SBV circulation in cattle and sheep populations from southern Romania (personal unpublished data). The public health does not seem endangered or at risk related to Schmallenberg. Shamonda virus, close related virus to SBV, is considered nonpathogenic for humans and it is supposed that SBV is also with low risk for human being (Hoffmann et al., 2011).

Hendra virus (HeV) has been documented for the first time in Queensland, Australia, in 1994 (Murray et al., 1995). Until today is still considered a rare emerging disease that is reported only in Australia, were is an endemic disease. The HeV name is from the suburb of Hendra - Brisbane, Australia, where it was described the first outbreak of illness in horses. This outbreak involved also two human cases, the horse keepers in the large racing stable. Pteropid bats are the wildlife reservoir of HeV in Australia (Smith et al., 2011). In the HeV infection the public health risk is high, exposed people at high levels of viruses can develop clinical signs and many of them die (http://access.health.qld.gov.au/hid/InfectionsandParasites/ViralInfections/hendraVirusInfection_fs.asp).

Menangle virus (MeV) has been documented in New South Wales, Australia for the first time, 1997, in stillborn piglets at a large commercial piggery (Philbey et al., 1998). MeV was reported only in Australia. Flying foxes are likely reservoir of MeV (Philbey et al., 1998). MeV exhibit professional risk for piggeries workers, through occupational exposure to infected pigs. Humans develop influenza-like illnesses with serological conversion to MeV (Chant et al., 1998).

Nipah virus (NiV) emerged first time in Malaysia, in 1998, producing febrile encephalitis among pig farmers and respiratory and neurological disease in pigs (Mohd et al., 2000).

The virus was first isolated from a sick human originating the village Sungai Nipah (State of Negeri Sembilan, Malaysia), giving the virus name NiV. NiV outbreaks were reported in Malaysia, Singapore, Bangladesh and India. NiV has a high risk for public health. NiV can cross the species barrier causing fatal disease in humans and in several mammalian hosts.

In 1959 USUV has been first documented in South Africa, (McIntosh, 1985). The USUV is the name of a river in Swaziland, county where the virus was originally isolated from mosquitoes (Woodall, 1964). In Europe, it was first identified in wild birds from Tuscany (Italy), in 1996, (Weissenböck et al., 2013). Since 2001, several outbreaks of disease have been reported in wild and captive birds in Austria, Hungary, Switzerland, Spain, Italy, United Kingdom and Germany (Becker et al., 2012). USUV is considered a zoonotic pathogen.

It is difficult to accomplish, but it would be highly useful to investigate if these organisms, introduced in different populations other than the originating one, could generate pathology.

Would be useful to map the distribution of these newly discovered agents whose potential pathogen is still unevaluated or even appear devoid of pathogenicity, to estimate their emerging potential in the case of contact with unusual hosts.

SCHMALLENBERG VIRUS INFECTIONS

The livestock animals involved in outbreaks of Schmallenberg virus were cattle, sheep and goats. The infection has not been reported in horses, dogs or humans (Doceul et al., 2013).

In adult cows the clinical signs include loss of appetite, hyperthermia, diarrhea and reduction with up to 50% in milk production. In 9-month old calves the sings can be fever and mucous diarrhea (Hoffmann et al., 2011). In younger calf the clinical sings and lesions can be severe: central nervous system lesions generate severe dysfunctions of the cerebral cortex, basal ganglia and mesencephalon, severe porencephaly or hydranencephaly, cerebral and cerebellar hypoplasia are frequent (Garigliany et al., 2012; Hahn et al., 2012). Infection of fetuses from infected cattle can produce atypical malformations leading to intra-uterine death or death closely after birth. Atypical fetuses malformations are classified in two disorder groups: neuromusculoskeletal disorder (e.g. arthrogryposis, severe torticollis, ankylosis, kyphosis, lordosis scoliosis, brachygnathia inferior) and neurological disorders (e.g. amaurosis, ataxia, behavioral abnormalities) (Herder et al., 2012).

The clinical course of SBV infection appears to be influenced by the animal's age. While the symptoms usually disappear within a few days in adult bovines, the newborns with neurological disorders, depending on the severity of the lesions, will die in few hours or few days after birth (Doceul et al., 2013).

Clinical and sessional features of SBV infection in sheep and goats seem to be much mildly (Doceul et al., 2013). The reports of SBV infection in sheep and goats consist in abortions and birth of malformed lambs and kids with crooked neck, hyrocephalus and stiff joints (van den Brom et al., 2012; Doceul et al., 2013).

In the central nervous system of animals with neurological signs, histological exams revealed the following lesions: lymphohistiocytic meningoencephalitis and poliomyelitis, astrogliosis, microgliosis and glial nodules in the mesencephalon and hippocampus (Doceul et al., 2013). Calves and lambs can have myofibrillar hypoplasia of skeletal muscles (Doceul et al., 2013).

HENDRA VIRUS INFECTIONS

The livestock animals involved in outbreaks of Hendra virus are horses. In horses, the incubation period is 5-16 days. Exhibited clinical signs belong to the respiratory syndrome and neurological syndrome, but HeV can cause a widely range of clinical signs in horses, due to the virus endothelial tropism, that for the clinical features will be related with the most affected organ system by the endothelial damage. Disease start in acute-onset fever (>40°C) and respiratory troubles design is define by respiratory distress with labored breathing and copious frothy nasal discharge, which is initially clear, thereafter progress to white or bloody stain. Neurologic signs are progressive ataxia, altered consciousness (aimless walking in a dazed state) and apparent loss of vision, muscle twitching, lethargy, circling and dull demeanor, urinary incontinence, recumbence, weakness and collapse in 75% of cases. Other clinical signs are tachycardia, facial edema, anorexia, congested mucous membranes and colic-like symptoms (Bewg, 2012).

Post mortem examination can reveal in respiratory disease the following gross lesions: oedema and congestion of the lungs, dilatation of the sub pleural lymphatic, airways filled with thick froth blood-tinged fluids, increased pleural and pericardial fluids, congestion of lymph nodes, hemorrhages in various organs, and slight jaundice. The gross lesions in neurologic disease are non-suppurative meningitis or meningo-encephalitis.

Histological the respiratory disease show acute interstitial pneumonia, serofibrinous alveolar edema, hemorrhage, thrombosis of capillaries, necrosis of alveolar walls, and alveolar macrophages. In neurologic disease was reported the following microscopic lesions: perivascular cuffing, neuronal degeneration and focal gliosis. In pulmonary capillaries and arterioles, lymph nodes, spleen, heart, stomach, kidneys and brain can be seen characteristic large endothelial syncytial cells. In lungs, heart, kidneys, spleen, lymph nodes, meninges, alimentary tract, skeletal muscle and bladder can be seen the fibrinoid degeneration of small blood vessels (Bewg, 2012).

MENANGLE VIRUS INFECTIONS

The livestock animals involved in outbreaks of MeV are swines. The infection is producing reduction of the farrowing rate, reduction of the number of live piglet births per litter, fetal

deaths at a different gestation stages, occasionally abortions with mummified, autolyzed, stillborn and live piglets and congenital abnormalities (e.g. arthrogryposis, brachygnathia, kyphosis) (Philbey et al., 1998). Post mortem examination can reveal absence of part or all of the brain and spinal cord, malacia and nonsuppurative inflammation of the brains and spinal cords, nonsuppurative myocarditis and hepatitis (Philbey et al., 1998).

NIPAH VIRUS INFECTIONS

The livestock animals involved in outbreaks of NiV are pigs which develop a marked respiratory and neurological syndrome, occasionally with sudden death in sows and boars. Horses and goats can fall infected after exposure to infected pigs. In pigs the disease produced by infection with NiV is named "porcine respiratory and neurological syndrome", "porcine respiratory and encephalitis syndrome", "barking pig syndrome" or "one mile cough" (Mohd Nor et al., 2000). Usually, the infection is asymptomatic or very subtle and the symptomatic pigs have clinical patterns according to age: respiratory syndrome in porkers and neurological syndrome in sows. The incubation period in pigs is 1-2 weeks.

Piglets aged before four weeks express the following signs: breathing with open mouth, weakness, tremor and twitches. Rate of mortality in suckling pigs is ≈40%.

Weaned piglets and fattening pigs (1 to 6 months of age) develop acute hyperthermia (> 39.9°C), tachypnea, laboured respiration and loud barking cough, which can result in haemoptysis. Also, weaned piglets and fattening pigs can reveal the following neurological signs in association with respiratory syndrome: trembling, twitches, spasms, myoclonus, weakness, spastic paresis, lameness, uncoordinated gait, pain of hind quarters. Rate of infection in weaned piglets and fattening pigs is 100%, but mortality is 1-5%.

Boars and sows can develop acute hyperthermia (>39.9°C) and the following neurological signs: agitation, head pressing, seizures, tetanic contractions, nystagmus, mouth champing, pharyngeal muscle paralysis associated with frothy salivation, inability to swallow and tongue hanging out of the mouth. Also, Boars and sows can reveal the following respiratory signs in association with neurological syndrome: labored breathing, hypersalivation, serous to mucopurulent or bloody nasal discharge and early abortion of pregnant sows (Mohd Nor et al., 2000).

Post mortem examination can reveal in respiratory disease the following gross lesions: consolidation, emphysema, petechial to ecchymotic haemorrhages, distension of the interlobular septa, bronchi and trachea filled with a serous to bloody frothy fluid. The microscopic lesions have been hemorrhagic interstitial pneumonia, syncytialisation of endothelial cells in lung blood vessels, vasculitis with fibrinoid necrosis, haemorrhages, thrombosis and mononuclear infiltration. In neurological disease the main gross lesions are congestion and oedema. The microscopic lesions described in neurological disease are: vasculitis with fibrinoid necrosis, haemorrhages, mononuclear infiltration sometimes associated with thrombosis, and nonsuppurative meningitis with gliosis.

Also, post mortem examination revealed congestion of kidney tissue with generalised vasculitis, fibrinoid necrosis, haemorrhages, and infiltration of mononuclear cells sometimes associated with thrombosis.

USUTU VIRUS INFECTIONS

The livestock animals weren't involved in outbreaks of Usutu virus, but the risk of interspecific transmission need to be considered because members of this virus group (Japanese encephalitis virus group) are pathogenic for human beings, inducing febrile illnesses, meningitis or encephalitis (Vazquez et al., 2011). Also, experimental infection of suckling mice causes depression, disorientation, paraplegia, paralysis and coma associated with widespread neuronal and glial apoptosis especially in the brain stem and demyelination (Weissenbock et al., 2004). Clinical and/or lesional reports associated with natural USUV infections were described mainly in European wild birds (Buchebner et al., 2013).

Clinical signs recorded in birds were associated with a central nervous system disease (depression, incoordination, seizures) and

peracute death (Steinmetz et al, 2011; Höfle et al., 2013). The birds have poor body condition, moderate to poor nutritional status, greenish urate-soiled feathers around the cloaca and ruffled plumage (Steinmetz et al, 2011; Höfle et al., 2013; Buchebner et al., 2013).

Post mortem examination can reveal absence of subcutaneous or visceral fat deposits, partial atrophy of pectoral muscle, marked splenomegaly, a mild hepatomegaly, and pulmonary hyperemia (Steinmetz et al, 2011; Höfle et al., 2013). Also, birds with severe generalized congestion could be seen (Höfle et al., 2013).

In the central nervous system histological lesions could be very discrete and comprised neuronal necrosis, leucocytolysis in and around blood vessels (Steinmetz et al., 2011) or severe congestion, neuronal and Purkinje cell necrosis, gliosis, satellitosis, neuronophagia, and endothelial cell swelling and vasculitis (Höfle et al., 2013). Also, it were described multiorgan congestion, necrosis of renal tubular epithelium, moderate hemosiderosis in the liver and spleen (Höfle et al., 2013) and miliary liver necrosis (Steinmetz et al., 2011).

DISCUTION

Increasing number of emerging and reemerging pathogens, which are not every time subjected to official notification, makes difficult their active surveillance by specific laboratory testing methods.

Before detection of Schmallenberg virus in blood samples collected on a dairy cows farm near the city of Schmallenberg (North Rhine-Westphalia, Germany) in October 2011, all classical endemic and emerging viruses, such as pestiviruses, bovine herpesvirus type 1, foot-and-mouth disease virus, bluetongue virus, epizootic hemorrhagic disease virus, Rift Valley fever virus, and bovine ephemeral fever virus were excluded (Hoffmann et al., 2012). In view of these data, would be helpful in the near future to include the SBV in the group of endemic and emerging viruses that are part of active surveillance programs of cattle, goat and sheep.

Since their emergence in Australia and Asia, Hendra virus and Nipah virus continuously present a hazard to humans and livestock (Clayton et al., 2013). In the affected areas, the Bat-borne Paramyxoviruses - Hendra virus, Menangle virus and Nipah virus - can be associated for surveillance activities with others diseases/viruses. It could be associated with the survey of other paramyxoviruses currently monitored (e.g. Newcastle disease, rinderpest-cattle plague, contagious caprine pleuropneumonia, peste des petits ruminants, canine distemper virus) or with others major viral diseases with similar natural host (e.g. variants of the rabies virus associated with bats). The choice of association will be determined up to the available tools or, better, up to epidemiological status of the area.

Even if, for instance, USUV seems do not pose an imminent threat to zoo and wild bird populations in Europe, Buchebner et al. (2013) strongly suggested following the combined WNV and USUV surveillance activities in the affected areas. Moreover, Vazquez et al. (2011) conclude "*In Europe the risk exists that potential emerging infectious diseases, such as those caused by WNV or USUV, will not be recognized in time* (despite) *by existing surveillance infrastructures of the various European countries*".

The cost-effectiveness of active surveillance systems could not support all animal disease surveillance and the prompt reporting. However, the passive surveillance and the risk analysis (exposure assessment and risk characterization) can be perform by using conventional or participatory epidemiology if the specialist or farmers are trained to identify the pathology that can be produced by these new pathogens (Bewg S., 2012).

CONCLUSION

Once emerged, a new microorganism it is advisable to investigate the similar ecosystems in order to check his presence. The active surveillance of such events opens the request for multiplex detection tools, continuous training of field workers and flexibility of the policy and decisional structures.

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