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Update on Schmallenberg virus infections in small ruminants☆

M. Ganter*, R. Eibach, C. Helmer

Clinic for Swine and Small Ruminants, University of Veterinary Medicine Hannover Foundation, Germany

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ABSTRACT

In 2011 a new disease occurred in dairy cattle in the border region between the Netherlands and Germany, indicated by fever, reduction in milk yield and in some cases diarrhoea. The German Federal Research Institute for Animal Health detected a new orthobunya virus in blood samples of cows with fever, and named the virus for the localization of the infected cows, Schmallenberg virus. In the lambing season 2011/2012 numerous malformations occurred in lambs and kids in the Netherlands and in the northwestern parts of Germany, due to intra uterine infections of the foetuses mainly during the second month of pregnancy. The virus is transmitted by biting midges of several *Culicoides* spp. Subsequently the infection spread throughout the whole German country, and into several European countries including United Kingdom and Scandinavia. In contrary to cattle there are no clinical signs reported in adult small ruminants, but there are numerous malformations in newborn lambs mainly in form of the arthrogryposis-hydranencephaly syndrome.

1. Introduction

In autumn 2011 a new disease in dairy cattle was presented to the Animal Health Services in North Rhine-Westphalia (Germany) and in the Netherlands, indicated by fever up to 41 °C over a period of 3 days, severe reduction in milk yield of up to 50% in individual cows or of up to 10% on herd level. Animal Health Services of the Netherlands reported severe diarrhoea in these cows (Muskens et al., 2012). Most of those cows recovered after some days (Holsteg, 2012).

2. Detection of Schmallenberg virus

The Animal Health Service of North Rhine-Westphalia informed the Friedrich-Loeffler-Institute (FLI, Federal Research Institute for Animal Health, Germany) and asked for diagnostic aid. Wide ranging virological and serological investigations were performed in order to exclude several classical and new virus diseases of cattle, like Infections with Pestivirus (BVDV), Bovine Herpesvirus 1 (BHV1), Foot and Mouth Disease Virus (FMDV), Bluetongue Virus (BTV), Epzootic haemorrhagic Disease Virus (EHDV), Rift Valley Fever Virus (RVFV) and Bovine Ephemeral Fever Virus (BEFV). Trials to culture the unknown infectious agent on different cell cultures failed. Using a metagenomic approach with next generation sequencing genome sequences of a new virus were found in the pooled blood samples of three sick dairy cows which were housed on a farm close to the city of Schmallenberg, North Rhine-Westphalia, Germany. Due to its place of discovery, the virus was provisionally called “Schmallenberg virus” (SBV) (Hoffmann et al., 2012).

Phylogenetic analysis showed that the virus is part of the Simbu serogroup, genus Orthobunya virus, family Bunyaviridae. Further, already well known members of this group as Shamonda virus, Aino virus and Akabane virus particularly infect ruminants (Hoffmann et al., 2012) and might induce malformations if the embryo or foetus is

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* Corresponding author.
E-mail address: martin.ganter@tiho-hannover.de (M. Ganter).

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transplacentally infected during a vulnerable period of time (Parsonson and McPhee, 1985). Thereafter the virus could be isolated from the blood of a diseased cow by culturing the samples on *Culicoides variipennis* larvae cells followed by passaging the virus on baby hamster kidney-21 cells, where the virus showed a severe cytopathic effect after 5 days (Hoffmann et al., 2012). Investigations of Goller et al. (2012) revealed that SBV belongs to the species Sathuperi virus and might be a possible ancestor of the reassortant Shamonda virus. Other members of the family Bunyaviridae are known to be spread by arthropods (arthropod-borne viruses) and occur in Africa, Asia and Australia. The main vectors of these viruses are biting midges, as *Culicoides* spp. and mosquitoes (Hoffmann et al., 2012).

From December 2011 onwards a high amount of abortions and malformations occurred in the offspring of sheep and goats. First cases of malformations were described in the Netherlands and subsequently in the north-western parts of Germany. The highest number of malformations throughout German small ruminant flocks was reported in January 2012.

3. Animals that can be infected

Up to now Schmallenberg virus was detected in cattle, sheep, and goats. Antibodies against SBV were found in new world camelids, bisons, roe deer, red deer, European fallow deer (Conraths et al. (2013), and mufflons (Anonymous, 2013)).

4. Risk for humans

Investigations in shepherds from flocks with malformations due to SBV revealed no evidence of SBV transmission to humans (Reusken et al., 2012; Ducomble et al., 2012).

5. Transmission

Orthobunyaviruses are mainly transmitted by biting midges of different *Culicoides* spp. Several *Culicoides* spp. (*C. obsoletus* complex, *C. dewulfi*, *C. chiopterus*) were tested positive for SBV, as two RT-PCR studies on the presence of SBV RNA in *Culicoides* spp. revealed, which were performed in Belgium and Denmark in fall 2011. These findings strongly indicate that these *Culicoides* spp. are important natural vectors for SBV (De Regge et al., 2012; Rasmussen et al., 2012).

A direct transmission from animal to animal is considered to be unlikely. A vertical transmission from the ewe/doe to the foetus during gestation is possible and can cause malformations. According to the pathogenesis of Akabane virus in small ruminants (Anonymous, 2012) an infection between day 1 and day 28 of gestation leads to embryonic death, delivery of small lambs/kids, decreased fertility and stillbirth. If the pregnant ewe/doe becomes infected between day 28 and day 56 of pregnancy typical clinical signs of arthrogryposis-hydranencephaly (A-H) syndrome can be observed in newborns. Moreover, symptoms as mummification, abortion and stillbirth might occur. From day 56 of gestation onwards the foetus becomes immunocompetent and is supposed to fight the virus. Nevertheless, losses due to mummification, abortion and stillbirth are still reported in some cases Concluding these facts, an infection of the ewe/doe in the second month of gestations is most dangerous for the foetuses as it can induce malformations.

Besides the intrauterine transmission of SBV from the pregnant doe to her foetuses the Friedrich-Loeffler-Institut (FLI) detected SBV-genome in the semen of bulls with a known SBV-antibody status. If SBV can be transmitted by SBV-positive semen still needs to be investigated more precisely. In some bulls SBV genome was detected in semen despite antibodies were already detectable in the blood samples. Preliminary trials show, that SBV positive semen might be infectious (Anonymous, 2013).

6. Clinical symptoms

Adult cattle show mild symptoms like fever and reduction in milk yield after SBV infection. In some animals diarrhoea is reported (Muskens et al., 2012; Holsteg, 2012). Acute SBV infections occur in summer and autumn when the biting midges are active. Due to the short viraemic period of only 1 to 6 days the animals recover quickly. There are no reports about acute clinical symptoms in adult small ruminants up to now.

Arthrogryposis-hydranencephaly syndrome (A-H S) is the most common symptom of intrauterine SBV infections (Ganter and Köß, 2012; Ganter and Ehlers, 2012; Ganter et al., 2012; van den Brom et al., 2012). Furthermore high numbers of embryonic deaths, abortions and stillbirth were described (van den Brom et al., 2012). Most of the malformed animals are born dead or had to be euthanized shortly after birth. Especially severe arthrogryposis characterized by stiffening of the joints and malposition of the extremities induce severe problems in lambing and necessitates obstetrical aid frequently. In some cases spontaneous or induced ruptures of the uterus are induced during lambing, due to arthrogryposis. In those lambs and kids which are born alive hydranencephaly and other malformations of the brain go along with decreased suckling reflex, central blindness and movement disorders ranging from ataxia to paralysis, or paresis. Rare findings are anasarca and peripheral blindness of alive malformed lambs due to opacity of the lens. Most of the malformed lambs born alive had to be euthanized due to animal welfare reasons. Even if the malformed lambs stay alive they show reduced weight gain during their development.

Twins or triples born together with a malformed lamb/kid often appear clinically normal but there are increasing numbers of personal reports from farmers that many of these lambs first grow normally within the first 6–12 weeks of their live but thereafter their progress comes to a standstill.

7. Pathology and pathogenesis

Pathomorphological findings in malformed lambs revealed different stages of cerebral malformations ranging from hydrocephalus internus, hypoplasia of the cerebellum