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Bleeding disorders in calves identical to Bovine Neonatal Pancytopenia (BNP) NOT associated with PregSure® vaccination of the dam

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We wish to highlight the occurrence of a bleeding disorder in calves clinically and histopathologically indistinguishable from Bovine Neonatal Pancytopenia (BNP) where there is no possibility of ingestion of colostrum derived from PregSure®-vaccinated cattle.

BNP was first recognised as a clinicopathological entity in Europe in 2007 (Bastian and others 2011) and the United Kingdom in 2009 (Penny and others 2009), defined as a haemorrhagic disease occurring in calves less than 28 days of age and involving bone marrow lesions of trilineage hypoplasia (severe depletion of all three main haematopoietic cell lineages) (Lambton and others 2012). It has been diagnosed in calves of many breeds between one and four weeks of age, and a strong association has been demonstrated with vaccination of the dam with the Bovine Viral Diarrhoea virus (BVDV) vaccine PregSure® (Lambton and others 2012; Sauter-Louis and others 2012). Field and experimental data strongly suggest the pathogenesis involves colostral alloantibody-mediated destruction of haematopoietic progenitor cells in bone marrow. This results in cytopenias including thrombocytopenia, and hence bleeding.

BNP is still being diagnosed despite the withdrawal of the vaccine in 2010, both in calves born to PregSure® vaccinated cows which have previously had affected calves, but also in calves born to cows which previously raised healthy calves post vaccination (SACCVS 2016). The mechanism for this delayed presentation is unknown, though increasing alloantibody titre in subsequent pregnancies may be involved (Bell and others 2013), and calves from previous gestations may have been sub-clinically affected as demonstrated by (Bell and others 2014). A genetic component relating to the sire of the calf has been identified (Krappmann and others 2011), and a genetic predisposition in some cows to produce higher quantities of alloantibody following vaccination has been postulated as one of the risk factors (Benedictus and others 2014).

However cases identical to BNP were identified prior to the introduction of PregSure®, including calves in Canada (Ammann and others 1996), and in Germany in 1989 and 1991 in a retrospective study (Friedrich and others 2011). Scottish Agricultural Colleges Consulting Veterinary Services (SAC C VS) recently reported a case where the use of PregSure® could not be confirmed in a purchased cow (SACCVS 2016).

Here, we report a case meeting the case definition of BNP where **there was no use of PregSure® vaccine in the dam, and no possibility of ingestion of colostrum from another dam that had been vaccinated with PregSure®**. One of the authors (KB) is the owner of the dam and affected calf.

A previously thriving, fourteen day old British White cross Hereford female calf (from a twelve year closed herd of 5 suckler cows, 3 calves and 3 yearling heifers) was found dead at grass in August 2016. Skin petechiation, frank bleeding from the skin of the head and neck, widespread ecchymoses and petechiation on the thymus, heart and abdominal organs, and blood clots distending the distal small intestine were observed during on-farm post-mortem examination (Figures 1-3).

BNP was suspected, and sternum was submitted for histological examination to the Animal and Plant Health Agency (APHA) which identified trilineage hypoplasia characteristic of BNP.

Prior to this, in 2013, a ten day old calf born to the same British White dam and by the same Hereford sire was found dead and necropsied on farm. Extensive haemorrhage was also seen in this calf including intestinal bleeding, but histological examination of the bone marrow was not carried out.

Yearly clostridial vaccination with Bravoxin 10™of the dam was then undertaken (at that time the death was presumed to be due to clostridial disease) but no other vaccination had been practiced. The following year a healthy calf (sired by a Ruby Red Devon) was raised without incident, but the dam apparently resorbed a confirmed pregnancy in 2015. She had previously raised four healthy calves in the period 2009 to 2012.

In summary, one calf with features of BNP and a second probable case of BNP were born to the same dam and by the same sire in this small closed herd in which no animal had ever been vaccinated against BVDV. The dam was home bred, had never been vaccinated against BVDV (she had been vaccinated against clostridial disease since the death of the first calf) and had never been off the farm.

The presence of trilineage hypoplasia rules out bleeding due to thrombocytopenia associated with BVDV-infection, and bleeding associated with bacterial septicaemias. The history ruled out other possible causes of trilineage hypoplasia such as acute bracken toxicity (no access in this case), and tricothecene mycotoxicosis (associated with feeding of mouldy foodstuffs).

The cause of disease indistinguishable from BNP in this calf was not determined, though a hereditary predisposition was suspected given two calves out of the same dam and sire had shown a bleeding disorder. One possible reason for sporadic cases like this is that the same colostral alloantibody responsible for BNP (low levels of which are boosted by vaccination with PregSure®) is involved (Bell and others 2013). Evidence has been presented for a familial component to the development of PregSure® linked BNP (Krappmann and others 2011).

Given that the vaccine was withdrawn in 2010 (and notwithstanding the continuing cases in calves from dams which have previously had normal calves), it is inevitable diagnoses of BNP associated with PregSure® vaccination will fall and eventually cease (Veterinary Investigation Diagnosis Analysis data (VIDA) shows a fall from a peak of 249 cases in 2012 to 78 cases in 2015).

Despite that downward trend we believe that deaths due to haemorrhagic anaemia with trilineage bone marrow hypoplasia (BNP) will continue to occur in young calves born to dams with no history of PregSure® vaccination. If necropsy of young calves with haemorrhagic diathesis is undertaken, a longitudinal section of two anterior sternebrae (with bone marrow) should be fixed in 10% formalin for histological evaluation of possible BNP, along with additional fixed and fresh samples as appropriate to investigate the other main differential diagnoses including BVDV infection and septicaemias.

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Figure 1: Petechiation on the skin around the anus

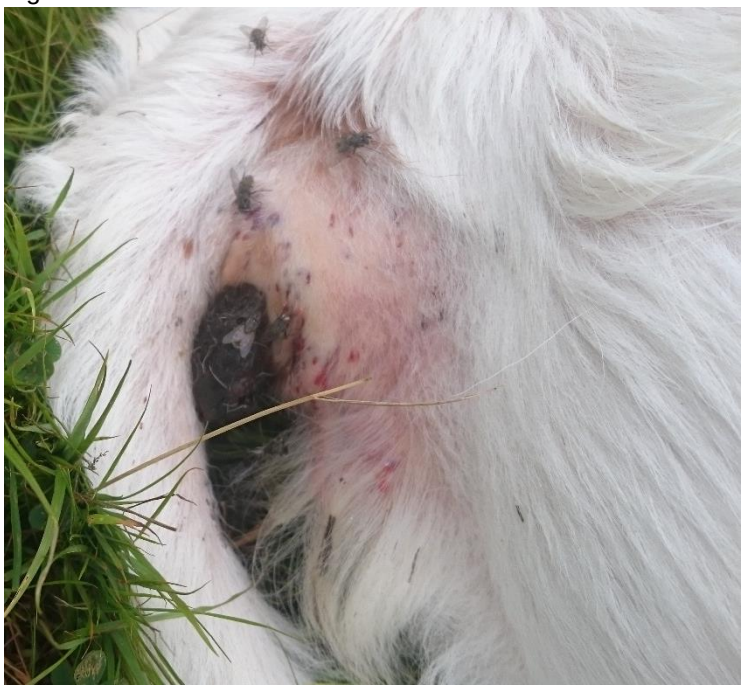


Figure 2: Extensive petechiation/haemorrhage on the thymus and heart

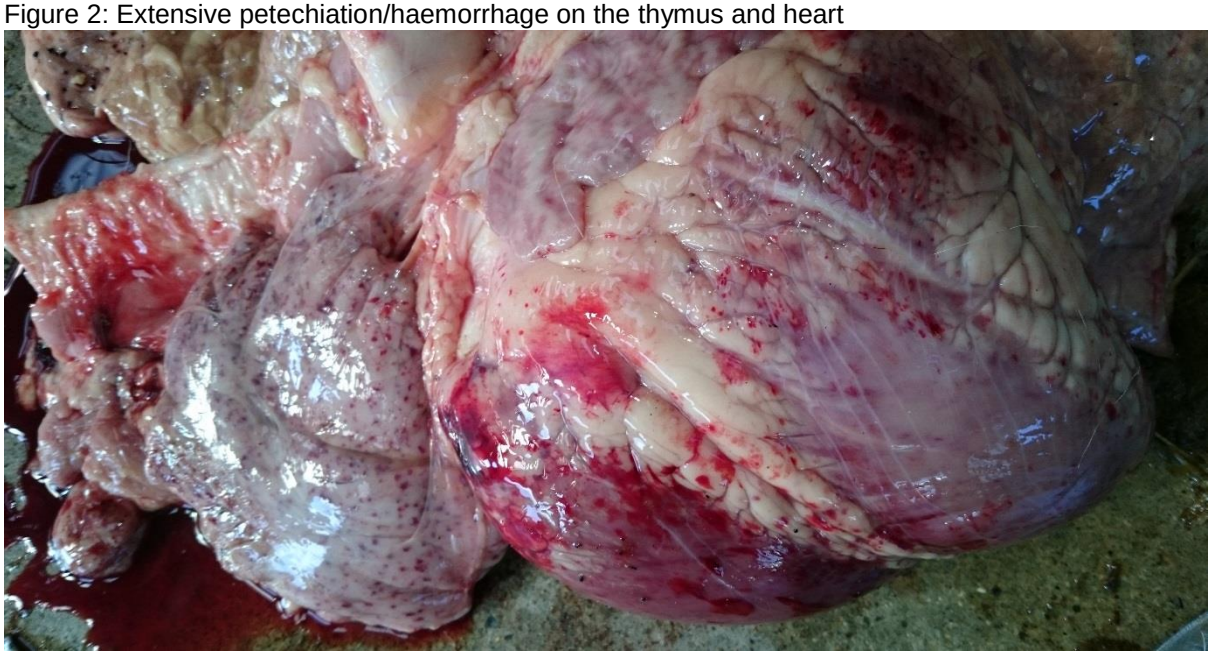
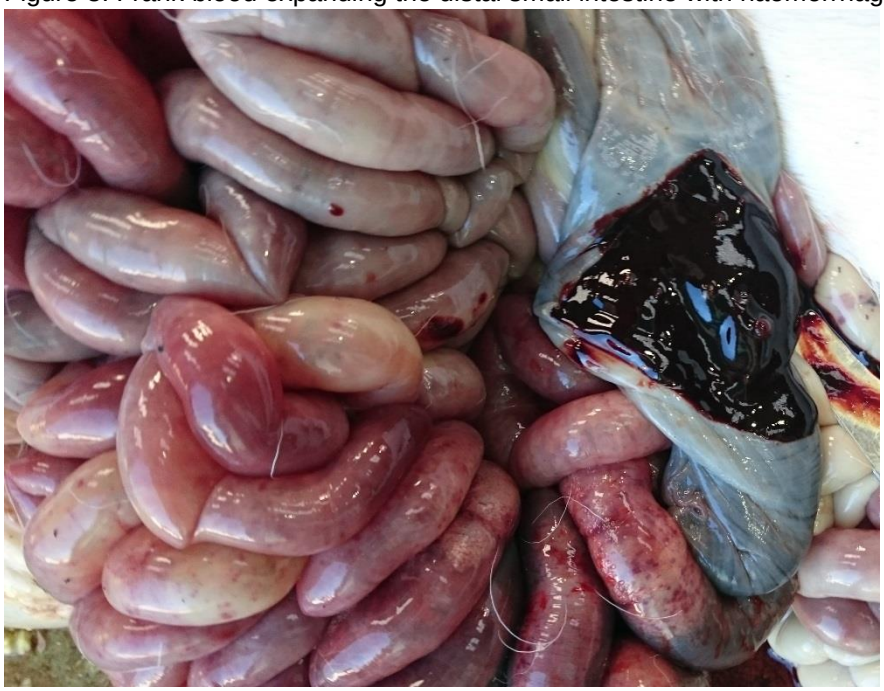


Figure 3: Frank blood expanding the distal small intestine with haemorrhages on the serosa



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