Bleeding Calf Syndrome
November 5, 2009

Overview

A bleeding calf syndrome of unknown cause, resulting in high case fatality rates, has been detected in several European countries. The syndrome, first detected in Germany in 2007, affects calves from two to four weeks of age and has been reported in Belgium, England, France, Germany, Italy, the Netherlands, Scotland, and Wales (ProMED 20091006.3465). The syndrome affects beef and dairy calves of various breeds and crosses.

As of March 2009, more than 100 cases had been reported in Germany (ProMED 20090329.1214). Scotland has reported 40 cases from 20 farms, mostly in beef herds. Thirty-seven cases from 31 farms have been identified in England and Wales, almost exclusively in dairy herds (SAC and Surman). Because blood count changes were detected in asymptomatic calves at affected German farms, researchers concluded in an October 2009 report that the undiagnosed problem may be wider spread than originally thought (Friedrich et al.). Of the asymptomatic calves with blood count changes, some proceeded to develop clinical signs of the bleeding calf syndrome, but others remained clinically asymptomatic.

Syndrome Details

Two published case studies indicate that mortality ranges from 3 to 5 percent of calves born on an affected farm (SAC and Penny). The case fatality rate is reported as approximately 95 percent (Surman). Antimicrobials, clotting agents, and supportive treatment have been relatively unsuccessful. In one case report, two of three calves that received transfusions died in spite of supportive therapy (SAC). In a media report, a farmer indicated that vitamins and blood-clotting agents were not effective (ProMED 20090329.1214).

Clinical signs have been relatively consistent across countries detecting the syndrome:

- Persistent pyrexia, fever reaching 41°C
- Spontaneous hemorrhage from the nares, mouth, rectum, injection or tagging sites.
- Internal hemorrhage and subcutaneous hematoma formation.
- Petechial hemorrhages often present on gums, conjunctiva and pinnae.
- Intestinal bleeding, blood shed with feces.
- Severe secondary infections like diarrhea or pneumonia.
- Death within a few hours to days after first signs observed.

Laboratory findings included:

- Variable severity anemia.
- Severe thrombocytopenia.
- Leucopenia; lymphocytes present, but few, if any, granulocytes.
- Clotting times for prothrombin (PT) and activated partial thromboplastin (APTT) were within normal limits.
- No evidence of bovine viral diarrhea virus (BVDV); calves serological positive only if dam vaccinated.

Histopathology results included:

- Severe bone marrow hypoplasia.
- Severe depletion of hematopoetic precursor cells (consistent with antemortem pancytopenia).
- Widespread hemorrhage.
- Lymphoid depletion.
- Zero or only a few megakaryocytes.

Necropsy findings included:

- Widespread petechial and ecchymotic hemorrhages.
- Intestinal intraluminal hemorrhage. Intestinal bleeding commonly in the form of a cast, suggesting that there was still ability of the blood to clot.
- Massive bleeding of subcutaneous tissue, body cavities, intestines and other organs.
- Bone marrow of jelly-like consistency.

Potential Causes

Bone marrow aplasia, a consistent finding in the bleeding calf syndrome, can be caused by infectious, toxic, genetic, physical or idiopathic factors. Thus, several potential causes of the bleeding calf syndrome have been proposed in the categories of toxic, immunologic, and genetic; bacterial infections were ruled out.

Potential toxic causes of the bleeding calf syndrome include plant toxins, drug toxins, and feed contaminants. Friedrich et al. found no evidence from affected farms or calves of the following toxic causes of blood disorders: furazolidone, chloramphenicol, NSAIDs, sulfonamides, bracken fern, macrocyclic trichothecenes (a class of mycotoxins), or DCVC (S-[1,2-dichlorovinyl]-L-cysteine), extracted with trichlorethylene, appearing in soybean meal.

Another potential cause of the bleeding calf syndrome is an immunologic reaction. Clinical signs observed with the bleeding calf syndrome are compatible with signs of BVD and bluetongue infection. Antibodies developed from BVD vaccine and bluetongue vaccine or from natural exposure could have provoked an autoimmune response. No evidence of live BVDV or bluetongue virus has been detected in affected calves. Autoimmune thrombocytopenia due to colostral antibodies may be unlikely because some calves have been symptomatic prior to consuming colostrum. A circovirus similar to porcine circovirus type 2b (PCV2b) was detected in samples of several of the affected calves in Germany (Kappe et al.).

In Germany, the virologic tests for BVDV and bluetongue have been negative for affected calves; serology for BVDV and bluetongue was positive only when the dam had been vaccinated. No evidence of concurrent BVDV infection was detected in Scottish calves with the bleeding syndrome. Another reason why BVD is unlikely to be the cause of the bleeding calf syndrome is that BVD virus-induced hemorrhagic syndrome is known to be related to the peripheral destruction of thrombocytes, whereas damage of progenitor cells in bone marrow has been observed in the bleeding calf syndrome cases.

Although most reports suggest that the bleeding calf syndrome affects only a few calves on each farm, Wolfgang Klee of the University of Munich indicated that some clusters of approximately 40 affected calves have been detected on individual farms (ProMED 20090329.1214). If an infectious agent is associated with the syndrome, the agent does not appear to be highly contagious, although calves could be infected but remain asymptomatic. Media reports have not indicated if case samples have been tested for viral agents other than BVD and bluetongue. A French veterinarian recently hypothesized that a circovirus, such as chicken anemia virus or porcine circovirus, might have a role in the syndrome (ProMED 20091006.3465). Chicken anemia virus and porcine circovirus are immunosuppressive viruses that cause medullar aplasia and hemorrhagic syndrome in chickens and pigs, respectively.

Although a genetic abnormality has been considered as a cause of the bleeding calf syndrome, it is less likely than an infectious or toxic cause because beef and dairy cattle of various breeds have been affected. Idiopathic abnormalities have been identified as previous causes of bone marrow aplasia in cattle. A report of a Holstein calf in Japan in 2006 with pancytopenia and a bleeding tendency associated with bone marrow aplasia was attributed to a congenital disorder or a drug-induced toxicity (Shimada). A similar case was reported in a Holstein heifer from Canada in 1996 (Ammann). Although the Canadian heifer was diagnosed with bone marrow aplasia, a cause was not determined. Clinical presentation and lab findings of the two Holstein case reports were similar to those for calves observed recently in Europe with the bleeding syndrome.

The lack of a case definition for the syndrome impedes progress in determining the cause of the syndrome. The pathogenesis appears to be complex with multi-factorial components potentially including infection, genetics, and immune-mediated bone marrow destruction.

Risk to the U.S. Cattle Industry

Bleeding calf syndrome does not pose a risk to the U.S. cattle industry through European imports because the United States does not import cattle from the European Union. Bleeding calf syndrome has been recognized only since 2007, and the cause has yet to be identified; therefore, it is difficult to determine if cases may appear beyond Europe.

If the cause of the bleeding calf syndrome is a feed contaminant, it is possible that the contaminant is widely distributed. The example of melamine from China, found in multiple brands of pet food and in

baby formula, demonstrates the potential for widespread impact if the cause is identified as a toxin in feed.

Another possible cause that could have widespread impact is a genetic abnormality. If a genetic cause is identified, it is possible that cattle outside of Europe would also experience the syndrome because cattle semen is shipped throughout the world.

Research in Progress

Efforts to determine the cause of the bleeding calf syndrome are continuing throughout Europe. The Scottish Agricultural College (SAC) and the Veterinary Laboratories Agency (VLA) are offering free post-mortems for suspected cases. Since April 2009, the Bavarian State Office of Health and Food Safety has systematically tested milk and blood (the report did not specify for which agent(s) the tests are targeted). Research also is continuing at multiple German institutions.

References

Ammann, V. J. 1996. Pancytopenia associated with bone marrow aplasia in a Holstein heifer. Canadian Veterinary Journal 37(8): 493–495.

Friedrich, A.; Rademacher, G.; Weber, B.K.; Kappe, E.; Carlin, A.; Assad, A.; Sauter-Louis, C.; Hafner-Marx, A.; Buttner, M.; Bottcher, J.; Klee, W. 2009. Increase in the incidence of a bleeding disorder in young calves due to bone marrow damage. Tierärztliche Umschau 64: 423–431. <http://www.pei.de/SharedDocs/Downloads/tieraerzte/tieraerztliche-umschau-blutschwitzen,templateId=raw,property=publicationFile.pdf/tieraerztliche-umschau-blutschwitzen.pdf> English translation: ProMED 20091018.3578

Kappe, E.C.; Halami, M.; Schade, B.; Bauer, J.; Dekant, W.; Buitkamp, J.; Boettcher, J.; Mueller, H. 2009. 27th Meeting of the European Society of Veterinary Pathology and European College of Veterinary Pathologists. Krakow , Poland. September 9–12, 2009. p. 118.

Penny, C.D.; Bell, C.; Morrison, L.; Howie, F; Willoughby, K. 2009. Pancytopenia and haemorrhage in young beef calves. The Veterinary Record 164(24):762.

ProMED Articles:
Undiagnosed disease, fatal, bovine - Europe (03): France 20091006.3465
Undiagnosed disease, fatal, bovine - Europe (02): RFI 20091005.3459
Undiagnosed disease, fatal, bovine - Europe: RFI 20091003.3441
Undiagnosed disease & deaths, bovine - UK: (Scotland) RFI 20090923.3345
Undiagnosed disease & deaths, bovine - Germany (03): ongoing 20090329.1214
Undiagnosed disease & deaths, bovine - Germany (02): sugg. etiology 20090208.0566
Undiagnosed disease & deaths, bovine - Germany: RFI 20090202.0470
Undiagnosed disease, fatal, bovine - Europe (04): Germany 20091018.3578

SAC (Scottish Agricultural College). 2009. Monthly Report: April 2009. <http://www.sac.ac.uk/consulting/services/s-z/veterinary/publications/monthlyreports/2009/apr/cat>.Accessed October 27, 2009

Shimada, A.; Onozato, T.; Hoshi, E.; Togashi, Y.; Matsui, M.; Miyake, Y.; Kobayashi, Y.; Furuoka, H.; Matsui, T.; Sasaki, N.; Ishii, M.; Inokuma, H. 2007. Pancytopenia with bleeding tendency associated with bone marrow aplasia in a Holstein calf. The Journal of Veterinary Medical Science 69(12): 1317–9.

Surman, W. 2009. Help solve the mystery of ‘blood sweating’ in young calves. Farmers Guardian: October 23, 2009.