

Pancytopenia with Bleeding Tendency Associated with Bone Marrow Aplasia in a Holstein Calf

Asuka SHIMADA¹⁾, Tomoya ONOZATO¹⁾, Eriko HOSHI²⁾, Yoshihiko TOGASHI²⁾, Motozumi MATSUI¹⁾, Yoh-Ichi MIYAKE¹⁾, Yoshiyasu KOBAYASHI¹⁾, Hidefumi FURUOKA¹⁾, Takane MATSUI¹⁾, Naoki SASAKI¹⁾, Mitsuo ISHII³⁾ and Hisashi INOKUMA^{1)*}

¹⁾Department of Clinical Veterinary Medicine, Obihiro University of Agriculture and Veterinary Medicine, Inada-cho, Obihiro, Hokkaido 080-8555, ²⁾Tokachi Agricultural Mutual Aid Association, Obihiro 089-1182, and ³⁾Research Center for Diseases, Obihiro University of Agriculture and Veterinary Medicine, Inada-cho, Obihiro, Hokkaido 080-8555, Japan

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ABSTRACT. An 11-day-old Holstein calf presented with a high rectal temperature and tachypnea. Treatment with antibiotics and non-steroidal anti-inflammatory drugs did not improve the clinical signs. Bleeding tendency, with several hemorrhage spots on the body surface, appeared five days after admission. Severe pancytopenia was observed in the blood examination. The calf died on the 11th day after admission with severe bleeding from an injection site. Necropsy findings revealed that the pancytopenia had resulted from severe bone marrow aplasia. A congenital disorder was suspected to be the cause of pancytopenia associated with bone marrow aplasia.

KEY WORDS: bone marrow aplasia, calf, pancytopenia.

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Pancytopenia, a deficiency of all cellular elements of the blood, including red blood cells, white blood cells and platelets, is a rare disease in animals. Especially in large animal practice, there have been few case reports of pancytopenia. In cattle, pancytopenia has been attributed to bone marrow necrosis [13] and bone marrow depression by infiltrated neoplastic lymphocytes [8]. Fatal pancytopenia related to toxic protein derivatives from trichloroethylene-extracted soybean oil meal has been documented in cattle [9, 10]. A case of pancytopenia associated with bone marrow aplasia that was either inherited or induced by drugs was reported in a Holstein heifer [1]. In the present report, a clinical case of pancytopenia with fatal bleeding tendency associated with aplastic anemia in a Holstein calf is described.

An 11-day-old Holstein calf was presented to a local veterinarian with a high rectal temperature (39.8°C) and tachypnea (Day 1). The calf was diagnosed with pneumonia and treated with non-steroidal anti-inflammatory drugs (a compound of sulpyrine (300 mg/head), chlorpheniramine (1.5 mg/head) and methylephedrine (30 mg/head)) and kanamycin (100 mg/head) on Day 1, and penicillin (150,000 U/head) on Day 2. The general condition of the calf did not improve. On Day 6, the calf had a high rectal temperature (40.2°C), and several hemorrhage spots were found on its body. A combination of the antibiotics penicillin and streptomycin was administered on that day. The general condition of the calf worsened, with the appearance of astasia and melena on Day 9. The calf was then transferred to the Animal Teaching Hospital at the Obihiro University of Agriculture and Veterinary Science.

On initial physical examination at the hospital, lethargy,

high rectal temperature (39°C), dehydration (more than 5%), tachycardia (160 beats/min), pallor of the mucosal membranes, and melena were recorded. A large amount of clotted blood adhered to the hair on the calf's body. Hematologic examination of the peripheral blood revealed severe non-regenerative anemia (red blood cell count, $1.94 \times 10^6/\mu\text{l}$; hemoglobin concentration, 2.4 g/dl; and packed cell volume, 8%), leucopenia (400/ μl (neutrophils 200/ μl and lymphocytes 200/ μl)), and thrombocytopenia (platelet count 13,000/ μl). No abnormality was found in the blood chemistry (BUN, 23 mg/dl; AST, 14 U/l; Na, 136 mEq/l; K, 3.9 mEq/l; Cl, 100 mEq/l; and total protein, 6.0 g/dl). When blood samples were taken from the jugular vein the blood did not coagulate easily at the collection site, suggesting a prolonged bleeding time. Coagulation status was therefore evaluated. Activated partial thromboplastin time (45 sec), prothrombin time (18.5 sec), and fibrinogen concentration (490 mg/dl) were all within the normal range. Severe thrombocytopenia was suspected to be the cause of the hemorrhagic tendency.

Based on the above findings, bone marrow failure was considered as a possible cause of the pancytopenia. Differential diagnoses for bone marrow failure included bone marrow necrosis, myelofibrosis, myelodysplasia, myelophthisic anemia, and bone marrow aplasia. Although further diagnostic evaluation would have required bone marrow findings, a biopsy was not performed because of the poor condition of the calf. After the first evaluation of the calf, lactated Ringer solution was administered to treat the dehydration, and penicillin was injected for protection against infection. However, the calf died on Day 11 after admission, with severe bleeding from the injection site.

Macroscopic examination of the calf revealed widespread subcutaneous hemorrhages at the cervical and rostral thoracic areas, and multifocal hemorrhages in the muscles of

* CORRESPONDENCE TO: INOKUMA, H., Department of Clinical Veterinary Medicine, Obihiro University of Agriculture and Veterinary Medicine, Inada-cho, Obihiro, Hokkaido 080-8555, Japan. e-mail: inokuma@obihiro-u.ac.jp

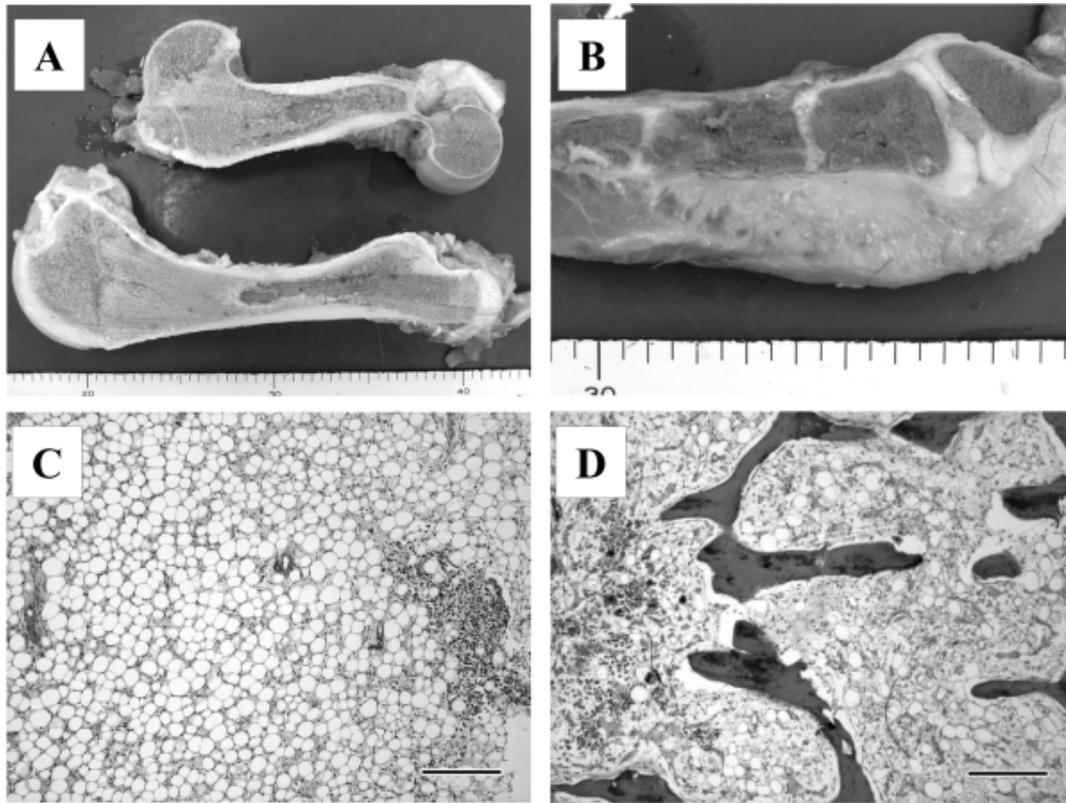


Fig. 1. Femoral and humeral bone marrow was pale pink in color (A), and sternum bone marrow also showed pinkish discoloration (B). Sections of the bone marrow showed almost complete serous atrophy. Histopathologically, there was severe bone marrow hypoplasia characterized by a marked decrease in the numbers of all cell lineages. Normal hematopoietic tissue is replaced by fatty marrow in both humeral (C) and sternum bone marrow (D). Bar = 500 μ m.

the four limbs and in the endocardium. In the rumen, reticulum, and abomasum, there were mucosal and submucosal hemorrhages with ulceration and/or proliferation of granulation tissue. Petechial hemorrhages were also noted in the thymus, mesenterium, pericardium, and intestinal mucosa. Reddish hard nodules one cm in diameter were scattered in the lungs. The liver showed orange-yellowish discoloration, and the femoral and humeral bone marrow was pale pink in color (Fig. 1A). The sternum bone marrow also showed pinkish discoloration (Fig. 1B). Histopathologically, there was severe bone marrow hypoplasia characterized by a marked decrease in the numbers of all cell lineages (Fig. 1C and 1D). Mild extramedullary hematopoiesis was noted in the liver, thymus, and spleen. In addition to the hemorrhagic changes, multifocal hepatocellular necrosis and multiple lung abscess-like necrotic lesions were observed, as well as some fibrin thrombi in and around the inflammatory foci of the rumen, reticulum, abomasum, and lung. Thus, the calf was pathologically diagnosed with bone marrow aplasia.

Bone marrow aplasia can be caused by both congenital and acquired factors. Congenital causes including inheritance, viral infection, toxin, radiation, drugs, and chemicals, might be associated with pancytopenia of newborn calves.

Bovine viral diarrhea virus (BVDV) infection is a well known cause of bone marrow abnormality of newborn calves, resulting in neutropenia and thrombocytopenia [2, 6]. Although the infectious status of BVDV in the mother cow was unknown, both polymerase chain reaction and the culture examination for BVDV were negative in this case. Because there were no other abnormal calves or cows in the same farm around this time period, epidemiological factors including viral infection, toxins, radiation and chemicals, were considered to be unlikely causes of the disease. Because there had been no other similar cases reported in calves of the same father bull, there is no evidence for an inherited disorder being the cause of the bone marrow aplasia in this case. The patient presented with a rectal temperature and tachypnea on the first day of admission. These signs were initially attributed to infection caused by pancytopenia, although no complete blood count data were obtained on that day.

Drugs may also be a possible cause of bone marrow aplasia in human medicine. Antibiotics can cause pancytopenia [4] and non-steroid anti-inflammatory drugs have been reported to be associated with neutropenia [3, 5]. Drug-associated aplastic anemia has also been reported in dogs and in a horse [7, 11, 12]. On the first and the second days

of admission, the calf was injected with kanamycin, penicillin, and a compound of sulpyrine, chlorpheniramine and methylephedrine. There is no report of pancytopenia associated with bone marrow aplasia caused by these drugs in cattle. No evidence for drug-induced pancytopenia was found in this case.

In conclusion, a congenital disorder was suspected to be the cause of a rare case of bone marrow aplasia with associated pancytopenia in a Holstein calf. Additional similar cases should be analyzed to clarify the cause of pancytopenia associated with bone marrow aplasia in calves.

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