Bovine Neonatal Pancytopenia: clinical signs and pathology

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Introduction

Bovine neonatal pancytopenia (BNP) is the consensus name for a bleeding and pancytopenic syndrome in neonatal calves which emerged in 2008 all over Europe. The objective was to describe clinical signs and pathologic findings of BNP.

Clinical signs and hematology

Between July 2008 and September 2009, 22 BNP calves, from 16 herds, were admitted for clinical examination. Breed distribution was 63% Belgian Blue, 31% Holstein-Friesian and 5% crossbreeds. There were no differences in gender (50% male, 50% female) and the affected animals were on average 16 days (7-27 days) old upon admission. In the histories, high fever (up to 41°C) was mentioned in 53% of the cases and the first sign of disease was most frequently prolonged bleeding after ear tag placement or injection. In the initial phase calves demonstrated variable degrees of cutaneous bleeding, pale mucosae with petechiae, melena and fever, but still had a normal mental state (Figure 1 and 2). As the disease progressed (Phase 2 and terminal phase), mental state became more depressed, bleeding increased and animals became recumbent. Only two calves (9%) survived. At the moment of sampling all cases had thrombocytopenia and marked leukopenia (granulocytes, lymphocytes and monocytes). In 8 calves anemia was present as well (Table 1).

Table 1. Haematology and coagulation tests of 12 bovine neonatal pancytopenia cases in relation to age and clinical symptoms

Calf ID	Age (days)	Tempe-rature (C)	Clinical phase (initial -phase 2- terminal - recovery)	WBC (x 10^9/L)	OTHR (x 10^9/L)	LYM (x 10^9/L)	PCV (%)	PLT (x 10^9/L)	PT (sec)	APTT (sec)	Fibrinogen (mg/dl)
3962	9	39.5	Initial phase	2.4	1.2	1.2	27.2	5	18.2	67.9	603
6182*	13	40.8	Initial phase	0.9	0	0.9	30.6	74	21.6	44.1	1154
5813	10	39.8	Initial phase	1.5	1.4	0.1	24.2	76	36.9	32.0	228
0639	13	39.8	Initial phase	1.0	0.0	1.0	32.7	26	40.2	35.4	284
941	7	36.0	Phase 2	2.0	1.2	0.5	8.5	1	15.8	47.3	609
4570	19	41.0	Phase 2	0.9	0.1	0.8	23.8	45	ND	ND	ND
6394	17	39.0	Phase 2	2.2	0.4	1.8	18.3	44	39.8	44	736
4567	16	41.1	Phase 2	0.6	0.0	0.6	18.5	0	ND	ND	ND
8711	17	40.5	Terminal phase	0	0	0	16.4	6	24.8	88	1726
3426	14	39.0	Terminal phase	0.7	ND	ND	12	14	20	58.	1340
2766	27	35.0	Terminal phase	3.0	2.7	0.3	6.4	15	ND	ND	ND
3597*	18	40.0	Recovery phase	1.8	0.5	1.3	6.6	8	43.4	27.5	298
reference				6-9	2-4	2.5-7.5	25-35	100-800	7-11	37-54	100-460

WBC= white blood cells; OTHR= granulocytes+monocytes; LYM= lymphocytes; PCV= packed cell volume; PLT= platelets; PT= prothrombine coagulation time; APTT= activated partial thromboplastin time; ND= not defined
*= survivor

Figure 1: Initial phase of BNP in a 10-day-old Belgian Blue calf: subtle skin bleeding and normal mental state.

Figure 2: Ecchymoses and petechia on the gingival mucosae of a 15 day old Belgian Blue calf.

Figure 3. Petechiae and ecchymoses on the serosa of the complete gastro-intestinal system of a 10-day-old Holstein Friesian calf with BNP.

Pathology and cytology

In total 25 BNP calves were autopsied. All cases showed generalized haemorrhages and had an anemic appearance (Figure 3). Histopathology of all mucosae showed haemorrhage with preservation of tissue architecture. Spleen and lymph nodes consistently showed severe diffuse lymphoid depletion in which T- and B-compartments were equally affected (Figure 4). In 18% of the calves the thymus was examined and lymphoid depletion was present. The bone marrow was characterized by depletion of hematopoietic tissue in which all cell lines were affected with reduction of stem cells and progenitor cells including megakaryocytes (total aplasia). Multifocally, single and groups of macrophages were present. In 10 live calves bone marrow aspiration and cytology was performed at different stages of the disease. In 5 animals groups of macrophages in close association with lymphocytes could be found in an otherwise aplastic bone marrow (Figure 5). In two cases macrophages were clearly activated and hemophagocytosis was present (Figure 6). Cytology of peripheral blood showed activated lymphocytes, thrombocytopenia and granulocytopenia in most cases. If present, the anemia was non regenerative, normocytic and normochromic. In one surviving calf normoblastosis and signs of regeneration were observed.

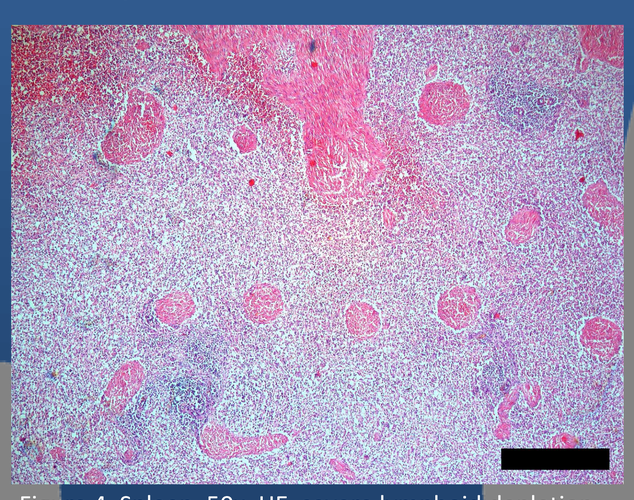

Figure 4. Spleen, 50x, HE, severe lymphoid depletion.

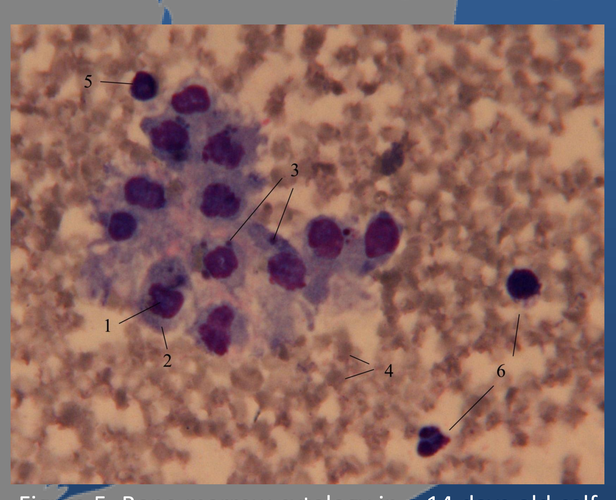

Figure 5. Bone marrow cytology in a 14 days old calf with BNP. Group of macrophages (1: nucleus; 2: cytoplasma) with phagocytised nuclear material (3). 4: red blood cells, 5: lymphocyte, 6: precursor cells (50 x 12,5, Giemsa stain).

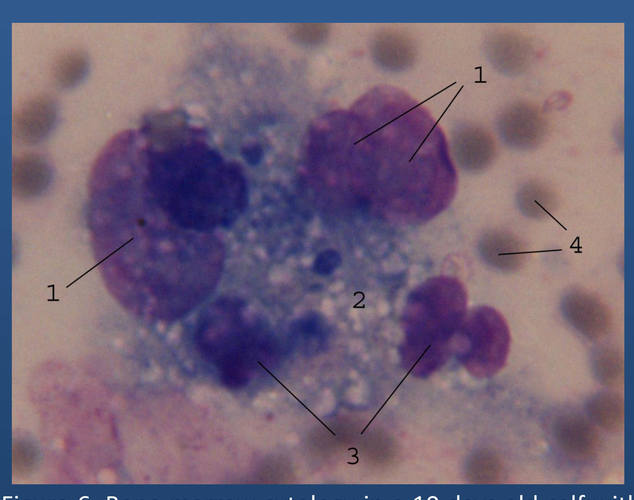

Figure 6. Bone marrow cytology in a 10 days old calf with BNP. Activated macrophages have a round to oval nucleus (1) and abundant cytoplasma with vacuoles (2). Hemophagocytosis is present. 3: nucleus of a phagocytised precursor cell; 4: red blood cell (50 x 12.5, Giemsa stain).