Bone and Bone Marrow Necrosis Associated with the Calf Form of Sporadic Bovine Leukosis

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The presence of neoplastic cells in the medullary cavity of bone may have various consequences including erosion of cortical bone, fat and marrow embolism, peripheral blood cytopenias, pathologic fracture, and necrosis of medullary bone and bone marrow elements. In man, infarction of bone is recognized to have many causes including intramedullary lymphoid tumors. In this report, we describe multiple bone infarcts in six calves that had sporadic bovine leukosis.

Each of these animals was presented individually with one of the following complaints: unthriftiness and inactivity, posterior ataxia, superficial lymph node enlargement, lameness, and/or respiratory distress. Both sexes (three male, three female) and various breeds (Simmental (3), Hereford (1), Holstein (1), not recorded (1)) were represented. The age range was 3 weeks to 8 months.

At necropsy all animals had generalized lymph node enlargement, and all had a final diagnosis of sporadic bovine leukemia. Other organs which were involved in the neoplastic process included bone marrow (6), liver (4), kidney (3), spleen (3), and urinary bladder (1). Posterior ataxia in one animal was associated with a tumor causing spinal cord compression in the lumbar area. Three of the six animals had widespread petechial hemorrhages. All animals had variable sized areas of infarction involving the medullary cavity of vertebrae and long bones (Figs. 1–3). Typically these were pale areas that were often surrounded by a hemorrhagic zone. Ribs and cranial base were involved in two animals. Infarcts often

Fig. 1. Humerus from calf with sporadic bovine leukosis. Large area of necrosis (N) of bone marrow and trabecular bone in medullary cavity. Multiple smaller infarcts (arrows) in the epiphysis.

Fig. 2. Longitudinal section through lumbar vertebrae and spinal cord of calf with sporadic bovine leukosis. Note paled areas of ischemic necrosis in vertebral bodies.

Fig. 3. Rib from calf with sporadic bovine leukosis. Multiple infarcts are surrounded by a zone of hemorrhage.
Fig. 4. Section of bone from calf with sporadic bovine leukosis. Most marrow spaces are filled with tumor cells (arrows). Pale area represents an area of infarction where marrow elements have been replaced by poorly cellular fibrous tissue and necrotic bone is overlain by woven bone.

abutted on the articular or metaphyseal growth plate cartilage although some were large and involved most of the medullary cavity of the metaphyseal and diaphyseal part of the bone.

Microscopically, all six animals had evidence of marrow spaces filled with tumor cells in the area of infarction. In two cases, tumor cells had penetrated and extended beyond the vertebral cortex, and there was evidence of new periosteal bone formation in the area. In most cases, pale areas of infarction were represented as areas of tumor cell pyknosis and/or karyorrhexis. Two animals had evidence of repair characterized by marrow replacement by poorly cellular fibrous tissue and deposits of basophilic, newly formed, woven bone on the surface of necrotic trabeculae which had empty lacunae or which contained pyknotic or fragmented osteocytes (Figs. 4, 5).

In four of the six cases, infarction of bone and marrow elements appeared to be a terminal event. As such, the lesion may be largely of academic interest since cattle are not expected to survive the disease. However, extensive marrow necrosis and ensuing pancytopenia could contribute to the death of the animal. Severe bone pain caused by tumor-associated bone infarction occurs in man,5,6 and could have been responsible for the lameness seen in two of the animals in this study. Thrombocytopenia and/or disseminated intravascular coagulation could have been responsible for the pethelial hemorrhages seen in three animals although clinical pathology studies were not done to evaluate this possibility.

While bone infarcts have been associated with lymphoid and granulocytic leukemia and various other intramedullary tumors in man1,2,6,8 and in animals,5,6,7,8 a recent report5 describes marrow necrosis in dogs with various non-neoplastic processes including chronic ehrlichiosis, estrogen toxicity, endometrial cystic hyperplasia, and glomerulonephritis. Although the pathogenesis of tumor-associated marrow necrosis is poorly understood, failure or obstruction of bone marrow circulation due to masses of tumor cells causing extra-sinusoidal compression or by intravenous obstruction is likely important.5,7 In any case, the antemortem diagnosis of marrow necrosis should be followed by a search for neoplastic process involving the bone marrow.

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References


Fig. 5. High power view of Fig. 4. Centrally-located necrotic bone (N) has empty lacunae and is surrounded by woven bone.
Ganglioglioma of the Spinal Cord in a Calf

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A ganglioglioma is a tumor consisting of neuronal cells in various degrees of differentiation mixed with glial elements which may participate in the neoplastic process.2,4 Gangliogliomas are rare in man2,4,5 and domestic animals.1,5 In man, they usually present in the cerebrum of a child or young adult and are rarely found in the spinal cord.2,4 In domestic animals gangliogliomas have been documented in unusual sites, e.g., an intraocular tumor in the dog,6 but not in the spinal cord.

A Holstein steer, normal at birth, was weak and ataxic in both rear limbs at 3 months of age. By 4 months of age, the calf was paraplegic. Temperature, pulse, and respiratory rates were normal. Withdrawal reflexes in the front and rear limbs were considered normal during neurologic examination. Patellar reflexes were hyperactive (3+/4). Anal reflex and tail tone were normal. The steer required assistance to stand, and at a walk, the front limbs appeared normal, but the hindlimbs were markedly weak and ataxic. Lateral radiographs of the thoracolumbar vertebral column appeared normal. Analyses of cerebrospinal fluid aspirated from the atlanto-occipital and lumbosacral spaces were normal. The calf was euthanized.

Moderate muscle atrophy of both hindlimbs was present at necropsy. A 1 × 3 cm red-tan mass was within the spinal cord between T12 and L1. It was moderately firm, caused distortion of the surrounding spinal cord, and could not be easily separated from the adjacent parenchyma. Sections of the mass, spinal cord, and major organs were fixed in 10% neutral buffered formalin, embedded in paraffin, and sectioned at 4 to 6 μm. Sections were stained with hematoxylin and eosin (HE) for light microscopic examination. Other sections of the mass and spinal cord were examined using the Bielschowsky silver method and by immunoperoxidase techniques using monoclonal antibody against the 200 KD neurofilament protein subunit and a polyclonal antiserum against glial fibrillary acid (GFA) protein.

The neoplasm consisted of several cell types characteristic of ganglioglioma (Fig. 1). Some cells had typical neuronal nuclei which were large, vesiculated, and eccentrically located with distinct nucleoli. In some cells Nissl substance was present. The ganglionic nature of these cells was confirmed by Bielschowsky silver impregnation for neurites (Fig. 2), and neuronal processes were also immuno-positive with the neurofilament protein monoclonal antibody. Variation in size and shape of these cells, some of which were binucleate, random orientation, and abundant tortuous neurites indicated that they were neoplastic and not pre-existing neurons entrapped by tumor cells. A second group of cells were neoplastic astrocytes which were immunopositive for GFA protein (Fig. 3). In addition to these two types of cells, there were also smaller cells with small darkly staining nuclei and scanty cytoplasm, resembling lymphocytes (Fig. 1) that are commonly seen in gangliogliomas. The identity of these cells is not clear, but they are believed to be either neuroblasts (presumably the source of the larger more mature ganglion cells), or small adult granular neurons. Likewise, the small cells with delicate nuclear chromatin and small nucleoli are also thought to be ganglion cell precursors.4

It is not clear whether ganglioneuromas arise from primitive neuroepithelial cells committed to divergent neuronal and glial differentiation, or from pre-existing mature cells which have resumed replication.1,4 Normal mature neurons do not divide. Tumors consisting of neuronal or neuron-committed cells are usually divided into those of a more primitive type, including medulloblastoma and neuroblastoma, and those of an adult type, including ganglioneuroma and ganglioglioma. It is important to distinguish between these two categories as the primitive type pursues a more malignant course while the adult type has a favorable prognosis.4 In gangliogliomas the outcome depends on the de-