Intramedullary Plasma Cell Myeloma Occurring Spontaneously in a Dog

Frank Bloom, D.V.M.

(From the Department of Pathology of the Long Island College of Medicine, The Hoagland Laboratory, Brooklyn, New York)

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Some human neoplasms are unknown in animals and there are animal tumors that have not been described in man. Included among the former are neoplasms of the myeloid type. Engelbreth-Holm (2) states that plasma cell leukemia and the related multiple myelomatosis has not yet been observed in lower animals. A survey of the veterinary literature discloses no references to intramedullary plasma cell myelomas in any domestic animal. A tumor of this type was recently encountered in a routine necropsy of a dog and this report, therefore, represents the first example of a spontaneous plasma cell myeloma in a lower animal.

MATERIAL AND METHODS

The dog was brought to the animal hospital for euthanasia, which was accomplished with a lethal dose of pentobarbital given intravenously. Immediate necropsy was performed and the tissues were fixed in Bouin's solution and 10 per cent solution of neutral formaldehyde. Paraffin sections were stained with hematoxylin and eosin, Mallory's phosphotungstic acid hematoxylin, Unna's polychrome methylene blue, methyl green pyronin, Hitchcock and Ehrlings mixture, Dominici's and Masson's stains. Frozen sections of formaldehyde-preserved tissue were stained with Sudan IV and Nile blue sulphate.

CLINICAL DATA

The animal was a 12 year old, male English setter that had shown pain and lameness of increasing severity of the left front leg for a period of 18 months. Palpation revealed a painful enlargement of the upper two-thirds of the left humerus. The affected limb was held in the characteristic position of radial paralysis with inability to extend the lower portion of the leg. Physical examination was otherwise negative and the owner stated that the dog appeared normal with the exception of the lameness.

RADIOGRAPHIC OBSERVATIONS

Films were made in the antero-posterior and lateral positions after removal of the left humerus from the dog's body and fixation in 10 per cent formalin. As shown in Fig. 1 the bone had been transected just below the head and the two parts separated about 1 cm. The bone structure of the upper two-thirds of the shaft and the upper extremity was definitely abnormal. The cortex particularly of the shaft was considerably thinner than usual. The medullary and subcortical trabecular markings were definitely coarsened and particularly in the mid-third of the shaft of the bone there were inter-trabecular depressions on the inner aspect of the cortex which extended deep into the cortex appearing, in some instances, almost through the cortex. In the upper third of the shaft the breadth of the bone was increased, particularly on the medial aspect of the cortex, and the compact bone of the cortex had entirely disappeared in this region. No complete perforation of the cortex was demonstrated in these films.

In the head and tuberosities the coarsened trabecular structures and thinning of the cortex was as in the upper portion of the shaft of the humerus. There was some periosteal proliferation on the anterior aspect of the upper third of the shaft of the bone. These x-ray findings indicated the presence of an

DESCRIPTION OF FIGURES 1 TO 4

Fig. 1.—Radiographic appearance of plasma cell myeloma involving the upper two-thirds of left humerus.

Fig. 2.—Longitudinal section of left humerus illustrating the gross appearance of the neoplasm.

Fig. 3.—Photomicrograph depicting the general tumor structure. A thickened fibrous trabecula is present in the upper portion and the deep-staining granular material is hemosiderin. Dominici's stain. Mag. X 200.

Fig. 4.—Photomicrograph showing the fibrous stroma. Masson's stain. Mag. X 200.
expanding tumor originating in the medullary cavity. A diagnosis of malignant growth could not be made on the basis of the x-ray findings alone.

MACROSCOPIC OBSERVATIONS

The entire upper third of the humerus was expanded in thickness and measured 5 cm. in diameter at its widest point (Fig. 2). The periosteum was irregularly thickened and the adjacent muscles were edematous with occasional small hemorrhagic areas. The cortex was thinned and the affected bone cut easily despite the presence of numerous small bony trabeculae. On section, the upper two-thirds of the marrow cavity was replaced with a soft, reddish-grey tissue interspersed with hemorrhagic areas of a deeper red color. Small foci of necrosis and fibrous trabeculae were present. The medullary cavity of the lower third of the bone contained a pale grey, fatty marrow.

MICROSCOPIC OBSERVATIONS

Humerus.—The general cellular structure of the neoplastic cells was similar to that of the plasma cells described in human myelomas (Figs. 5 to 10). The tumor cells were round, oval or polyhedral and the spherical or oval nucleus was centrally or eccentrically located. The nuclear structure consisted of coarse chromatin blocks that were usually marginated on a distinct nuclear membrane and nucleoli were absent. Occasional nuclei were larger and hyperchromatic. Some cells contained two or more nuclei and mitotic figures were not uncommon. The cellular dimensions averaged 9.36 μ and the nuclei averaged 5.39 μ.

The cytoplasm was amphophilic with hematoxylin and eosin, pale brownish-red with Mallory’s phosphotungstic acid hematoxylin, pale blue with Dominici, reddish-purple with Masson’s stain, pale greenish-blue with Unna’s polychrome methylene blue, pale red with methyl green pyronin and pale blue with Hitchcock and Ehring’s stain.

In the majority of cells, the cytoplasm was homogeneous, agranular and sometimes contained a paranuclear clear zone. Cytoplasmic vacuoles occurred in occasional cells and fat stains indicated the absence of lipids in the vacuoles (Figs. 9, 10). Scattered among the tumor cells were larger cells that averaged 12.16 μ and whose cytoplasm contained fine or coarse, acidophilic granular structures (Figs. 5, 7, 8). Their nuclei, however, were identical morphologically with those of the myeloma cells. The granular material differed from the granules of eosinophils and existed as irregular clumps and granules. The cytoplasm was frequently vacuolated and the oxyphilic material occurred between the vacuoles and occasionally within the vacuoles. Quantitative variations indicated few granules in some cells and many in others. The granular material stained blue with Mallory’s phosphotungstic acid hematoxylin and red with eosin, Dominici and Masson’s stain. This granular material did not show special characteristics with Hitchcock and Ehring’s stain, polychrome methylene blue and methyl green pyronin.

The tumor structure consisted of large compact masses of cells in loose and solid arrangements, smaller collections and as separated solitary cells (Figs. 3, 4). In certain regions there was considerable fibrosis with hyalinized strands of fibrous connective tissue separating groups of cells so that a somewhat alveolar appearance was produced. Silver stains showed no intercellular reticulum but fine argyrophilic fibers encircled small and large cellular masses. Bony trabeculae in various stages of atrophy and resorption occurred in some regions and foreign body giant cells and fibrosis were not uncommon in their vicinity. The persisting Haversian canals often contained tumor cells. Hemorrhages were extensive in many areas and foci of necrosis were not infrequent. The vascular supply was not conspicuous and golden yellow pigment (hemosiderin) occurred in many localities. The periosteum was thickened and edematous and the neighboring muscles showed edema and atrophic changes. Tumor cells only occasionally invaded the periosteum and muscles. In the tumor tissue, marrow fat persisted in some areas while other regions were completely replaced with neoplastic cells. No marrow cells were seen except rare polymorphonuclear leukocytes, normoblasts and lymphocytes.

Sections of the marrow from the radiographically normal distal portion of the humerus indicated that the cellular components consisted principally of tumor cells. In addition, the sinusoids were often congested and hemorrhagic.

DESCRIPTION OF FIGURES 5 to 10

Fig. 5.—A less compactly grouped collection of tumor cells indicating the resemblance to plasma cells. Several cells have a distinct paranuclear clear zone. The arrows point to larger cells with eosinophilic granular material in the cytoplasm. Dominici’s stain. Mag. × 850.

Fig. 6.—Another area showing the cellular structure. Dominici’s stain. Mag. × 850.

Fig. 7, 8.—The arrows indicate larger tumor cells with eosinophilic cytoplasmic granulations. Dominici’s stain. Mag. × 850.

Fig. 9, 10.—Neoplastic cells with cytoplasmic vacuoles (arrows). Dominici’s stain. Mag. × 850.
Kidneys.—The epithelium of the proximal portion of the proximal convoluted tubules showed various degrees of degeneration progressing from cloudy swelling to necrosis. Many tubular lumina contained a granular, eosinophilic material. The epithelium of the broad ascending limbs and the distal convoluted tubules manifested these regressive changes to a lesser degree. A conspicuous finding was the presence of giant-sized, hyperchromatic, solitary nuclei with large nucleoli that indicated regenerative activity. These nuclei were often embedded in a deeply eosinophilic cytoplasmic syncytium and showed loss of cellular polarity. A moderate number of collecting tubules contained eosinophilic, hyaline casts in their lumina but no foreign body giant cells encircled them. The glomeruli and arteries were normal and inflammatory cells were absent in the interstitial tissue.

Other organs.—With the exception of nodular fibrous intimal aortic plaques, moderate fatty metamorphosis and focal congestion in the liver, pulmonary anthracosis and physiologic splenomegaly, the remaining organs were normal. Metastatic myeloma lesions were absent in all organs examined.

DISCUSSION

The absence of reports on plasma cell myelomas in animals suggests that these neoplasms are either extremely rare or that they are not recognized. Inasmuch as the described case is the first in a series of over 300 neoplasms observed in a group of 12,000 dogs, the former conclusion seems more plausible.

The microscopic appearance of the dog tumor resembled in all respects the usual myelomas in man. The material at hand offered no solution to the controversy concerning the histogenesis of the myeloma cells. A prominent feature of the canine myeloma was the relatively large number of cells with vacuoles and eosinophilic granular material in the cytoplasm. Similar degenerative forms occur in human myelomas and Michels (4) mentions the presence of vacuoles and granules in inflammatory plasma cells. Miller (5) observed comparable cytoplasmic changes in plasma cells experimentally produced in rabbit omentum by intraperitoneal injections of tuberculoprotein.

The x-ray films resembled those described by Paul and Pohle (6) for human solitary myelomas of bone. The lesions in the dog are similar to solitary myeloma lesions characterized by an osteolytic, multicytic area of rarefaction centrally located and expansive with irregular trabeculae. In the differential roentgen diagnosis, single myelomas can easily be confused with giant cell tumor, localized fibrocystic disease of the bone, osteogenic sarcoma, Ewing's tumor and some of the rarer bone tumors.

The question whether the canine tumor was solitary or multiple cannot be answered with any degree of certainty. Unfortunately, the character of the bone lesion was not suspected until the microscopic slides were studied so that roentgen and histologic examinations of the other bones were not made. That the process was disseminated might be suggested by the microscopic finding of myeloma cells in the radiographically normal distal third of the humerus. The roentgenographic appearance of the upper humerus, however, resembled that of human solitary myelomas.

The renal changes consisting of degenerative and reparative epithelial alterations with occasional casts in the collecting tubules are not the typical findings observed in human myelomas associated with Bence-Jones proteinuria. In the latter, Bell (1), Forbus and his group (3) and others consider that the tubular casts mechanically obstruct the tubules causing tubular dilatation and atrophy. The kidney damage is therefore indirect and is not the result of any specific toxic effect on the tubular epithelium. In the dog case, as no urine tests for Bence-Jones protein were performed, the renal findings preclude any opinions relative to the character of the microscopic kidney changes.

The age and sex incidence of the myeloma in the dog coincided with that observed most commonly in man. In the latter, the disease occurs in later life and males are more frequently affected.

SUMMARY

A review of the literature indicates that myelomas of the plasma cell type are unknown in animals. This report is the first record of such a neoplasm that involved the left humerus of a 12 year old, male dog. The lesion was intramedullary and consisted of cells of the plasma cell type. The histologic structure of the canine myeloma was similar to that seen in human myelomas. The radiographic appearance resembled that of solitary myelomas in man.

REFERENCES

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