Canine Cutaneous Histiocytoma: 
Ultrastructural and Cytochemical Observations

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Abstract. Five canine cutaneous histiocytomas were studied by electron microscopy 
and esterase cytochemistry. The tumor cells contained irregular nuclei, characteristic 
lysosomal granules, and perinuclear microfilaments. The cells showed activity with α-
naphthyl acetate esterase stains. These characteristics are evidence that this tumor origi-
nates from the mononuclear phagocyte system.

Canine cutaneous histiocytoma is considered to be a distinct morphologic 
entity, distinguishable from other neoplasms of the skin [10, 11]. The biologic 
and light-microscopic characteristics of this clinically benign tumor have 
been described [15]. Although it is considered to be of histiocytic origin, 
one ultrastructural study [5] found that the cells were compatible with 
histiocytes but did not definitely establish their origin from the mononuclear 
phagocyte system.

Materials and Methods

Cutaneous tumors from five dogs were surgically removed. Fresh tissue was used to 
make impression smears. Sections stained with hematoxylin and eosin (HE) were prepared 
in the routine manner.

For electron microscopy, tissue fragments were fixed in 2% glutaraldehyde in Tyrode’s 
buffer at pH 7.3 [7, 14], then in Millonig’s phosphate buffered osmium tetroxide [6]. The 
tissues were stained en bloc with 0.5% uranyl acetate, dehydrated in a graded ethanol 
series and propylene oxide, and embedded in araldite. Ultra-thin sections were cut on an 
LKB ultratome, stained with uranyl acetate and lead citrate [13], and examined with a 
Philips EM 200 electron microscope.

Impression smears were stained for esterase by the method described [18].
Results

On light microscopic study sections appeared typical of canine cutaneous histiocytoma and had diffuse accumulations of mononuclear cells in the dermis. Superficial ulceration of the epidermis was common. The cells had variably folded or indented nuclei with abundant pale cytoplasm (fig. 1). Mitoses were frequent.

Esterase stains of tumor impression smears demonstrated clumps of large tumor cells that had diffuse cytoplasmic staining for α-naphthyl acetate esterase (fig. 2). Occasionally there were negatively stained lymphocytes; there were also scattered polymorphonuclear leukocytes and mast cells stained positively for chloroacetate esterase.

With electron microscopy the predominant cell in the dermal infiltrate was a large irregular cell with abundant cytoplasm (fig. 3). Nuclei had predominantly dispersed chromatin and occasionally there were large nucleoli. Some cells had more margined chromatin (fig. 4). Most nuclei were irregularly folded or indented. The cytoplasm was composed of numerous ribosomes, some of which were aggregated, varying numbers of medium-sized mitochondria, several rough endoplasmic reticulum profiles, and prominent Golgi regions. There were also varying numbers of cytoplasmic vesicles. Microfilament accumulations were common and most often in perinuclear configurations (fig. 5). Cytoplasmic granules were in many, but not all, cells. These were small, dense, irregularly shaped, membrane-bound structures (fig. 3, 4). Irregular pseudopodal extensions were often seen.

Many of the cells in two tumors contained cytoplasmic inclusions (fig. 6). These were large reticular aggregates of tubular arrays with an almost crystalline regularity.

In addition to the tumor cells, occasional polymorphonuclear leukocytes, mast cells, and large fibroblasts were scattered throughout a loose collagenous background.

Discussion

The mononuclear phagocyte system, including promonocytes, monocytes and macrophages (histiocytes), is composed of cells with common morphologic and functional characteristics and a common origin from bone marrow cells [17]. The ultrastructural characteristics of mononuclear phagocytes have been well documented [3, 4]. Major distinguishing characteristics include
Fig. 1. Cellular infiltrate in dermis. Note mitotic figure. HE.

Fig. 2. Reaction for α-naphthyl acetate esterase. a Blood smear; positive reaction by monocytes and negative reaction by adjacent polymorphonuclear leukocyte. b Impression smear of canine cutaneous histiocytoma; cells have positive reaction.
Fig. 3. Canine cutaneous histiocytoma with folded nucleus, nucleolus, and granules (G). Uranyl acetate and lead citrate.

Fig. 4. Canine cutaneous histiocytoma with numerous granules (arrows).
Fig. 5. Canine cutaneous histiocytoma cell with perinuclear microfilaments.

Fig. 6. Reticular aggregate in canine cutaneous histiocytoma cell.
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a population of a single type of dense cytoplasmic granule, nuclear folding and indentation, frequent bundles of perinuclear microfilaments, and surface irregularity. All of these characteristics were found in our study of canine cutaneous histiocytoma tumor cells. Although the previous ultrastructural study [5] reported microfilaments in canine cutaneous histiocytoma cells, few lysosomal granules were identified. We frequently noted granules that appeared to be of the type seen in cells of the mononuclear phagocyte system.

Recent improvements in esterase cytochemistry [18] have made possible the positive identification of cells of the mononuclear phagocyte system on smears. Staining for activity of α-naphthyl acetate esterase marks mononuclear phagocytes as granulocytes, and mast cells are stained for activity of chloroacetate esterase. Canine cutaneous histiocytoma tumor cells on impression smears in our study had diffuse staining for α-naphthyl acetate esterase.

The combined evidence of ultrastructural characteristics and cytochemical staining indicates that the cells of canine cutaneous histiocytoma are histiocytes and that they are proliferating cells of the mononuclear phagocyte system. The type of histiocyte involved in canine cutaneous histiocytoma apparently is different from that involved in human skin neoplasms since no Langerhans’ granules were seen in these cells [8].

The stimulus for the proliferation of histiocytic cells in canine cutaneous histiocytoma remains obscure. Causative agents have not been isolated nor is the tumor transmissible [15]. The reticular aggregates in two of our tumors are of unknown significance. Such structures commonly have been found in endothelial cells, lymphoid cells, and mononuclear cells in the skin, kidney, and other organs in systemic lupus erythematosus in man [12,16]. A number of studies suggest a relationship between these structures and such viral diseases as equine viral arteritis [2], infectious mononucleosis [9], and viral-induced tumors [1]. Reticular aggregates, therefore, may indicate that canine cutaneous histiocytoma is viral induced.

References

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