Morphologic and Biologic Characteristics of the Canine Cutaneous Histiocytoma

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SUMMARY

Five hundred and twenty canine cutaneous histiocytomas (CCH) that developed in the dog population of Alameda and Contra Costa Counties, California, during 3 years were collected. Morphologic studies confirmed the noninvasive character of the tumors and the proliferative histiocytic nature of the cells. The average annual incidence rate during the 3-year period was 117 per 100,000 dogs. Although the CCH occurred over most of the body, a high proportion were found on the head. Boxers and dachshunds had a significantly higher risk than all other breeds, and purebred dogs in general had a higher risk than crossbred dogs. A followup study of 230 cases indicated that CCH rarely recur at the site of excision, at a new site, or at 2 sites simultaneously. Widespread metastases or death as a result of CCH were not observed. Efforts to transmit this tumor to dogs and hamsters were unsuccessful as were attempts to detect viruses, bacteria, or fungi as etiologic agents. The findings of this study help to establish the CCH as a distinct entity and make it possible to differentiate it from various mesodermal neoplasms on the basis of morphologic, biologic, and epizootiologic characteristics.

INTRODUCTION

Perhaps the earliest utilization of the term histiocytoma in reference to benign mesenchymal tumors in the skin of dogs was by Mulligan in 1948 (18). He later concluded that such tumors were identical to venereal lymphosarcoma (19).

Prior to this, similar tumors in the skin of dogs had been referred to as round cell sarcomas (14) or transmissible lymphosarcomas (10).

About the same time as Mulligan’s report appeared, Ottosen (21) reported on 201 skin neoplasms of dogs of which he considered 67 to be reticulosarcomata. With the exception of one large neoplasm which metastasized, the description of these tumors seems compatible with Mulligan’s description of histiocytoma. More recently, Orkin and Schwartzman (20) referred to such skin tumors as transmissible reticulum cell sarcomas and considered this term synonymous with transmissible venereal tumor.

Like Mulligan (19), Smith and Jones (26) associated the term histiocytoma with transmissible venereal tumor. However, they pointed out that, while cells of typical transmissible venereal tumors (those found on the external genitalia) contain only 59 chromosomes, cells of “extragenital venereal tumors” contain 76 chromosomes, the usual number for normal dog cells.

Moulton (15) categorizes such extragenital tumors as canine cutaneous histiocytomas (CCH) and considers them to comprise a distinct entity which is “clearly distinguishable from the usual forms of mastocytoma, fibroma, and reticulum cell sarcoma, and—despite claims to the contrary—is morphologically distinct from transmissible venereal tumor of the dog.”

The above views were based primarily on the morphologic characteristics of such tumors. Therefore, this project was undertaken to investigate the biologic and epizootiologic characteristics of a large series of skin tumors conforming to Moulton’s criteria for CCH and to gain additional information regarding their morphologic features.

MATERIALS AND METHODS

Neoplasms. Formalin-fixed specimens of the CCH were received through an animal neoplasm registry (ANR) in Alameda and Contra Costa Counties, California (3, 4). Fresh specimens of the CCH were acquired from veterinary practitioners who notified the ANR by telephone when an animal with a suspected CCH was presented at their hospitals. The specimens were collected aseptically, and portions were placed in tissue culture media, a dry vial, and/or 4.5% glutaraldehyde and transported to the laboratory at 4°C within 1 hour of the time of excision.

Light microscopy. Fifty specimens of CCH were selected for special light microscopic studies using tungsten, ultraviolet, and polarized light sources. Both phase and bright-field optics were used. Hematoxylin and eosin, Domini & White’s mast cell, Ziehl-Nielsen acid fast, Geimsa’s, Gridley’s fungus, Masson’s trichome, Gordon and Sweet’s reticulum, Mallory’s iron, the periodic acid-Schiff (PAS), oil red O, 3,4-benzpyrene (22), and acridine orange (1) staining procedures were applied to appropriate frozen or paraffin-embedded sections, impression smears, and cell cultures in order to define the histologic features.

2 All staining methods with exception of the 3,4-benzpyrene and acridine orange stains were according to the Manual of Histologic and Special Staining Technics, from the Armed Forces Institute of Pathology, Ed. 2, New York, Blakiston Division, McGraw-Hill Book Co., Inc., 1960.
Mitotic indexes were calculated as the number of mitotic figures per 1000 cells. This was accomplished by placing a grid, to facilitate counting, in the light path of a photomicrographic system so that the image of the grid was superimposed over randomly selected microscopic fields of stained sections. These microscopic fields were magnified 312 times by the microscope and photographically enlarged to 935 magnifications.

Epizootiologic Studies. Five hundred and twenty cases of CCH were reported to the ANR between July 1963 and June 1966. Two hundred and eighty cases were from Alameda county and 240 cases were from Contra Costa County. Population data, to serve as denominators and comparison groups (controls), were available only for Alameda County (5). Therefore, estimates of age-specific incidence rates and relative risk estimates (13) were obtained using the 280 cases from this county. A special followup study was conducted on 230 CCH collected from both counties during July 1963 through March 1965, to determine the number of recurrences or metastases that had occurred. Letters were sent to the veterinarians attending each case to request current information about the involved animals. Cards with appropriate followup questions and stamped, self-addressed envelopes were enclosed to facilitate the collection of information. Personal visits and telephone calls by a staff member were used to attain 100% return of the cards.

Cell Cultures. Secondary dog kidney cell cultures were obtained by trypsinization of day-old puppy kidneys. Primary cultures were initiated by inoculating 8-oz. prescription bottles with 10 ml of a 1:200 cell suspension in medium 199 in Earle's balanced salt solution (BSS) and 10% fetal bovine serum. Following the initial outgrowth, secondary cultures were made by inoculating 200,000 cells from trypsinized primary cultures into test tubes in 1.0 ml of the above medium. After monolayers had formed, the cultures were inoculated with the test material and maintained with 2.0 ml of medium 199 in Earle's BSS and 5% fetal bovine serum. Incubation was at 36°C in stationary racks: medium changes were made twice a week.

Fetal hamster lung and kidney cell cultures were prepared in the same manner, except that trypsinized cells were seeded directly into test tubes, and Eagle's medium in Earle's BSS with 10% fetal bovine serum was used for outgrowth and maintenance. These cultures were used in the primary passage. A continuous dog kidney (DK) cell line was acquired from Dr. A. H. Fields, Sanford Research Institute, Palo Alto, California. These cells were used from the 121st through the 145th passage, and test tube cultures were prepared in the same manner as the secondary dog kidney cells. In addition, 60-mm plastic Petri dishes were seeded with a 4.0 ml of a 1:200 dilution of cells and incubated in 5% humidified CO₂ at 36°C when the cells were to be used in virus interference tests.

Fresh CCH tissue was trypsinized and cell suspensions were placed in test tubes. Other specimens of fresh CCH were cut into explants and attached to the walls of the test tubes or round coverslips, 15 mm in diameter, with chicken plasma clots. The coverslips were placed in 60-mm plastic petri dishes. Rose chamber preparations (25) were also made. Puck's medium V-16, medium 199 in Earle's BSS, or Eagle's medium in Earle's BSS were added to these cultures with 10% fetal bovine serum.

Virus Isolation Attempts. Cell fragments of 10 CCH were inoculated into 6 test tube cultures of each of the DK cell line, secondary dog kidney cells, hamster fetal kidney cells, and hamster fetal lung cells. Each culture was examined twice weekly for cytopathic effects by comparing it to uninoculated controls. At 2-week intervals, all the cultures were frozen and thawed, and 0.2 ml of the resulting suspension of cellular debris was inoculated onto fresh cultures; 3 blind passages were made in this manner.

Ten CCH were tested for the presence of noncytopathic agents that would interfere with subsequent infection by the infectious canine hepatitis virus. Ground tissue from each specimen was frozen and thawed, then incubated with cells of the DK cell line in Petri dishes for 1 hour. The cultures were washed; then, along with untreated parallel cultures, they were inoculated with serial dilutions of the infectious canine hepatitis virus. Three cultures were used for each virus dilution. After 0.5 hour incubation, the cultures were overlayed with agar. Five days later the cultures were stained with 1:20,000 neutral red, and the numbers of plaques were counted to determine if there was interference of plaque formation in cultures treated with tumor extracts. Cultures treated with tumor extracts but not inoculated with the virus served as controls to detect cytopathology induced by the tumor extract.

Transmission Trials. Attempts to transmit 24 CCH were made in 30 young dogs and 11 fetuses. Viable trypsinized cells, explants, or cell fragments that had been ground, then frozen and thawed, were inoculated by subcutaneous or intradermal routes into young dogs. Trypsinized cells or explants were inoculated into young dogs by the intracranial route and into fetuses by intracranial and subcutaneous routes in order to place viable cells in immunologically privileged sites.

Forty-two weanling hamsters were inoculated in the cheek pouch with trypsinized cells or explants from 5 different histiocytomas. Each hamster was injected twice weekly with 2 mg of cortisone as an immunodepressant.

RESULTS

Gross Morphology. When seen by practicing veterinarians, dogs with CCH usually had a circular dome-shaped lesion in the skin, which had developed rapidly and ulcerated early, causing little or no discomfort. The surface was covered with thin shiny or ulcerated epidermis through which sparse hairs projected (Figs. 1–4). Erythema of this semiglabrous surface prompted the colloquially-used synonym "strawberry tumor." The lesions varied from 0.5 to 4.0 cm in diameter with the majority being 1.0 to 2.0 cm. The height that these tumors rose above the surface of the skin was usually less than 50% of the diameter (Figs. 3–5). Upon cutting, fresh CCH had a rather pliable but tough and resilient consistency. The cut surface of fresh tissue bulged slightly and was nearly white with varying light shades of yellow (Fig. 4). On cross section the deep margins of the tumors were well defined but not encapsulated. These margins described arcs varying from nearly flat to a crude half-circle extending for various depths into the subcutis (Figs. 4, 5).
Microscopic Studies. Sections of nonulcerated CCH appeared as uniform sheets of cells which infiltrated the dermis and subcutis causing the collagenous fibers and skin adnexia to appear rather widely dispersed (Fig. 5). Along the deep margins, fat vacuoles were trapped and the tumor cells compressed and infiltrated the subjacent connective tissue (Fig. 5). Superficially, the tumor cells were occasionally compressed against the overlying epidermis, but more often there were interstitial spaces causing cells in the subepithelial region to appear individually discrete (Fig. 6). Most commonly there was ulceration of the overlying epidermis, and the superficial tumor cells were mixed with inflammatory exudate (Fig. 7).

The cells comprising these tumors had many features compatible with Porter's (23) description of histiocytes (macrophages). This was apparent in smears and tissue culture preparations where flattened individual cells were available for study. In smears, the cells had round to oval or indented nuclei which were nearly twice the diameter of lymphocytes (Fig. 8). Usually one or more nucleoli were discernible, and the nuclear chromatin was finely particulate and evenly dispersed. The cytoplasm was faintly acidophilic, and vacuolated or granular, with indistinct limiting membranes (Fig. 8). In tissue culture preparations, the nuclei were more uniformly oval and multiple nucleoli were prominent. The cytoplasm was voluminous and vacuolated, with indistinct limiting membranes (Fig. 9).

In sections of paraffin-embedded tissue, the tumor cells were slightly larger than neutrophils (Fig. 7). Where cells were tightly packed, cytoplasmic membranes were indistinct (Fig. 10), but they became more apparent and rounded when separated by intercellular spaces (Figs. 6, 7). The cytoplasm was faintly acidophilic, rather abundant, and granular (Fig. 10). The nuclei were pleomorphic, being round or oval to indented, and the nuclear chromatin was rather scant and distributed as fine particles and filaments, with aggregates often distributed along the well-defined nuclear membrane (Fig. 10). About 73% of the cells had a single visible nucleolus and 9% had multiple nucleoli.

A distinctive feature of this tumor was its high mitotic index. Individual counts from 15 randomly selected CCH ranged from 2.4 to 8.7 mitotic figures per 1000 tumor cells with an average count of 5.5.

With ulcerated CCH the epidermis had sloughed, and necrotic tumor tissue, infiltrated by purulent inflammatory exudate, was present on the surface. The deep margins of ulcerated CCH were usually infiltrated by lymphocytes, plasma cells, and small numbers of neutrophils. Such tumors often contained small foci of coagulation necrosis which were also infiltrated by lymphocytes plus varying numbers of neutrophils. Small granules of PAS-positive material were present in and around areas of necrosis, but they were not seen in viable tumor cells. These granules were not digested by diastase.

Dominici's or Geimsa's stains did not demonstrate cytoplasmic metachromatic granules except in mast cells, which were usually present in small numbers in and around some tumors.

Detectable lipid was not present in tumor cells of frozen sections of formalin-fixed or fresh CCH tissue stained by the oil red 0 or 3,4-benzpyrene methods.

The collagen fibers in these tumors were variable in amount. Often they were sparse, providing the impression that they were derived from preexisting dermal connective tissue which had been spread apart by the tumor cells (Fig. 11).

Reticulum fibers were more numerous, and they segregated the cells into packets varying from 1 to more than 20 cells (Fig. 12).

Incidence. Of 4,842 canine neoplasm cases reported to the ANR during the period July 1963 to June 1966, 520 (10.7%) were diagnosed as CCH. The average annual incidence rate was 116.7 per 100,000 dogs in Alameda County (Table 1).

There were more CCH cases observed among male dogs than expected; however, the difference in relative risk as compared to female dogs was not statistically significant (Table 2). Likewise, there was no significant difference in risk between intact and neutered female dogs. The relative risk of developing CCH by neutered and intact male dogs was not computed due to the small number of neutered male dogs in case and control groups.

Purebred dogs had a higher risk of developing CCH than crossbred dogs (Table 2). Among dog breeds tested by comparing their risk with that of appropriate comparison groups of all other purebred dogs, boxer and dachshund dogs had excess risks which were statistically significant. The poodle breed had a significantly lower risk of CCH.

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<th>Age (years)</th>
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Numbers of cases and age-specific incidence rates for the canine cutaneous histiocytoma and other benign skin neoplasms of dogs, Alameda County, July 1963–June 1966. Rates are per 100,000 dogs.

The age-specific incidence rates for CCH were markedly different from the rates for other benign skin neoplasms (Table 1), being low at older ages and extremely high at younger ages; approximately 50% of the CCH occurred before the age of 2 years.

Acquisition of cases was nearly constant throughout the 3 study years, indicating no seasonal variations in incidence.

Sites. All of the CCH were located in the skin. They were most commonly found on the head (152 of 520, or 29%) (Chart 1). Seventy-two or nearly one-half of those on the head were located on the pinna of the ear. The remainder were distributed over the neck, limbs, trunk, and tail.

Course of the Disease. In the followup study of 230 cases of CCH that were submitted to the ANR from July 1963 through March 1965, adequate information was available on 204. Although responses were acquired on all the cases, in 26 instances information was inadequate because owners left the...
At the completion of the followup study in July 1956, 196 of the dogs had died, recurred, or failed to communicate with the attending veterinarian. The one dog that died of any cause was not made available for examination. Of the 197 dogs alive at the end of the followup study, 5 had acquired additional tumors. Four of these were in the skin and one involved the iris of the eye. Subsequent submissions of the skin tumors from 3 of these dogs were found to be benign neoplasms other than CCH plus 2 epidermal cysts. The fourth dog had a recurrence of CCH on the same ear from which a CCH was previously removed. The tumor from the eye was not made available for necropsy.

Of the 197 dogs alive at the end of the followup study, 5 had acquired additional tumors. Four of these were in the skin and one involved the iris of the eye. Subsequent submissions of the skin tumors from 3 of these dogs were found to be benign neoplasms other than CCH plus 2 epidermal cysts. The fourth dog had a recurrence of CCH on the same ear from which a CCH was previously removed. The tumor from the eye was not made available for examination.

Anamnetic data subsequently submitted to the ANR indicated that of the total 520 cases of CCH in this study, there was 1 additional instance when 2 CCH arose simultaneously on the same dog. Recurrences occurred at the site of excision in 3 cases, and CCH arose at new sites following surgery in 3 cases. In 1 instance, a CCH was reported to have regressed during a 2-week period following biopsy. There were no reports of generalized metastasis or death due to the direct effects of CCH.

Microbiologic Studies. No cytopathic agents were isolated from 10 specimens of ground CCH tissue in cell cultures of the DK cell line, secondary dog kidney, hamster fetal lung, or hamster fetal kidney. Noncytopathic agents were not detected where 10 specimens of ground CCH were inoculated onto DK cells in search of an agent that would interfere with subsequent infection of the same cells by the infectious canine hepatitis virus.

In sections from paraffin-embedded tissues of 50 CCH, staphylococcal organisms could be seen in the surface exudate of most of the ulcerated specimens. Occasionally Gram-positive bacilli could also be seen near the surface of ulcerated specimens. No bacteria were seen in specimens where the overlying epidermis was intact, and the Gridley stain for fungi failed to reveal mycotic elements.

Cell Cultures. Attempts to grow the cells of CCH in various cell culture systems had limited success. Trypsinization of CCH yielded very small numbers of cells, not only because of the small size of the tumors, but also due to the ineffectiveness of trypsin in dispersing the cells. Cultures of trypsinized cells required 2 to 3 weeks for significant growth to develop, and the resulting cells were of a fibroblastic type.

A few histiocytic cells began migrating from explants within 48 hours of explantation. These cells were evident for as many as 3 passages (Fig. 9). Foci of squamous epithelial cells (apparently derived from hair follicles, since the surface epithelium was trimmed away from the explants) persisted for as many as 8 passages, although all the cultures eventually became fibroblastic. Of a total of 25 CCH subjected to tissue culture methods, 12 were maintained for 5—9 passages, 4 for 10—14 passages, although all the cultures eventually became fibroblastic. Of a total of 25 CCH subjected to tissue culture methods, 12 were maintained for 5—9 passages, 4 for 10—14 passages, and 1 for 15 passages.

Transmission Studies. No evidence of cellular proliferation was seen during attempts to transmit the CCH to 30 young dogs and 11 fetuses. Explants could be found in the brains of dogs that died during the first week of life following intracranial inoculation as fetuses. The neoplastic cells were undergoing coagulation necrosis at that time with little inflammatory response or necrosis in the surrounding brain tissue (Fig. 13). The dogs that survived for extended periods of time did not develop neurologic abnormalities. Explants inoculated into dogs by the intracocular route persisted for several months, but there was a gradual reduction in size until the only residual effect was a small corneal opacity where the needle had been inserted. Suspended cells were dissipated more rapidly than explants. Dogs inoculated intradermally or subcutaneously did not exhibit any noticeable reaction.

No neoplastic growths were observed in the cheek pouches of the 42 hamsters inoculated with explants or trypsinized CCH cells. Some of the explants were visible for longer than 2 months, but there was a gradual reduction in size. Histologic
examination of the cheek pouches revealed small clumps of degenerating collagen fibers embedded in the subepithelial connective tissue. The inflammatory reactions at these sites were negligible.

**DISCUSSION**

It is apparent from previous work that lesions typical of CCH have been categorized with other neoplasms, principally the transmissible venereal tumor (19, 26), as well as lymphosarcoma (10) and reticulum cell sarcoma (20, 21).

The lack of identity of the CCH with the transmissible venereal tumor can be established on the grounds of morphology, biologic activity, and epizootiologic characteristics. The CCH is smaller than most transmissible venereal tumors and in our study was found only in the skin. In agreement with Lacroix and Riser (10), the head, and more specifically the ear, was a definite site of predilection for CCH (Chart 1).

Conversely, transmissible venereal tumors have been most often associated with the mucous membranes of the penis, prepuce, and vagina (26). They originate as nodular or papillary proliferations which may progress to large friable cauliflower-like masses (17). In this series only 3 CCH were associated with the external genitalia. These were in the skin of the prepuce. Only 5 typical transmissible venereal tumors were seen among the 4,842 neoplasms in this series. Four involved the mucous membranes of the penis and/or prepuce and 1 the mucous membrane of the vagina. It is of interest to note that 4 of these dogs had been brought to California from Texas, Louisiana, Costa Rica, or Guam a short time prior to the surgery. Only 1 dog had lived in California all of its life. This would indicate that the transmissible venereal tumor is rare in California and thus segregates it from the CCH on an epizootiologic basis.

In 520 cases of CCH, multiple sites of involvement, recurrences at the site of excision, and reports of spontaneous regressions were rare. Metastases or death due to direct effects of CCH were not observed. On the other hand, transmissible venereal tumors frequently regress spontaneously and metastases have been reported (17, 26).

As denoted by its name, the transmissible venereal tumor may be readily transmitted between dogs. Forty-one attempts to transmit the CCH between dogs failed. Therefore, the cytologic similarity between the cells of the CCH and transmissible venereal tumor seems to be the principal reason for difficulty in distinguishing the two. Even at this level, however, significant differences have been detected. Jackson (8) reported the presence of lipid droplets in the cytoplasm of cells of transmissible venereal tumors. Lipid was not evident in the cytoplasm of cells making up CCH in 50 cases that were examined specifically for this characteristic. Also, Smith and Jones (26) cited works which reported a difference in the numbers of chromosomes in cells making up the transmissible venereal tumor and lesions similar to CCH.

The mesodermal appearance of cells of the CCH may make it difficult to differentiate from malignant neoplasms such as lymphosarcoma. However, this and related terms are inapprop- riate since CCH cells are not of the lymphocytic series, as can be demonstrated by their morphologic and tinctorial qualities; particularly in cell cultures and smears (Figs. 8, 9).

In examining sections of paraffin-embedded tissue stained by routine methods, the reticulum cell appears to be a likely progenitor of the CCH, as indicated by application of terms such as reticulosarcoma (21), and transmissible reticulum cell sarcoma (20) to neoplasms that had the characteristics of CCH. Moulton contends (16) that reticulum fibers are intimately associated with individual cells in reticulum cell sarcoma. Other authors (11, 24) contend that reticulum cells vary in their ability to produce fibers. In this study it was doubtful that the cells of CCH played a role in the production of reticulum fibers (Fig. 12). This, plus the fact that the reticulum cell sarcoma generally is considered a part of the highly fatal malignant lymphoma group (11, 24), should discourage application of the term reticulum cell sarcoma to neoplasms with the characteristics of CCH.

There is also difficulty in distinguishing CCH from small mast cell tumors (2). Careful and routine application of Geimsa's stain or procedures employing toluidine blue, such as Dominici's stain, are very useful in differentiating between the two.

Considering the histiocytoma of the skin of man (12), there is evidence that these are related to injury since they are usually associated with considerable blood and/or blood pigments. Some contain numerous vascular channels, and fibrous connective tissue is a major component. The histiocytes may contain lipid (xanthomas) (12). Histopathologic differentiation between these and CCH is possible, based on the paucity of fibrous connective tissue, vascular channels, blood pigments, and lipid in CCH. Therefore, while the term histiocytoma seems as applicable to these benign canine tumors as other terms, it is important to qualify it as “canine cutaneous histiocytoma” in order to clearly separate it from other specific entities.

The CCH occurred with high incidence in the population studied, involving approximately 117 dogs per 100,000 per year and comprising 17.9% of the skin neoplasms. These results are similar to those of other reports (9, 10, 14, 20) which indicated that neoplasms of this and similar types occur among skin-associated neoplasms with frequencies ranging from 17% to 33%.

In this study approximately 50% of the CCH occurred in dogs before they became 2 years of age (Table 1).
agreement with Head (6), whose data indicated that the mean age for the occurrence of histiocytomas of dogs was 2.7 years. Therefore, age is a useful criterion in differentiating this tumor from neoplasms such as lymphosarcoma or reticulum cell sarcoma, where the most frequent age of occurrence is over 8 years (4).

The results of this study indicate that purebred dogs have a higher risk of developing CCH than crossbred dogs. Among breeds tested the boxer had the greatest risk of CCH (Table 2); this is also true with some other forms of neoplastic disease (7). Dachshunds also had an excess risk of CCH, and poodles apparently had a reduced risk, indicating that genetic factors regarding breed may also play a role in the development of CCH.

It has been suggested that the CCH might be a peculiar type of inflammation (15). In spite of ample opportunities for an etiologic agent to become manifest through virus isolation technics, histiologic examination for bacteria and fungi, and animal inoculation with tumor cells; no evidence of a specific infectious and/or oncogenic agent was detected.

The rapid proliferation of histiocytic cells in CCH, without the stimulus of a defined etiologic agent, supports the interpretations of others that they are benign neoplasms which arise de novo from histiocytes (15) or "primitive pluripotent mesenchyme" (9) in the dermis. Unfortunately, the morphogenesis of CCH cannot be unequivocally defined until methods to experimentally transmit the tumor are developed. This and further attempts to detect an etiologic agent are worthy of further study.

ACKNOWLEDGMENTS

Assistance in the epizootiologic studies by Dr. Peter Schantz and Mr. Harold Hibbard is gratefully acknowledged, and the technical assistance of Miss Anna Wiener and Mr. S. Edward Brock is appreciated. We are indebted to the veterinary practitioners of Alameda and Contra Costa Counties for their conscientious efforts in submitting neoplasms to the Animal Neoplasm Registry.

REFERENCES

Canine Cutaneous Histiocytoma

Fig. 1. Dorsal view of a canine cutaneous histiocytoma in the skin of the lateral posterior thoracic region. There is early necrosis of the overlying epidermis. × 0.9.

Fig. 2. Dorsal view of canine cutaneous histiocytoma at the commissure of the lips with ulceration of the overlying epidermis. × 1.5.

Fig. 3. Lateral view of canine cutaneous histiocytoma. The epidermis is still intact. × 4.

Fig. 4. Cut surface of a canine cutaneous histiocytoma which is a light shade of yellow. The neoplasm has lifted the epidermis off the dermis while separating but not elevating the hair shafts. × 4.

Fig. 5. The canine cutaneous histiocytoma has expanded in the dermis widely dispersing the skin adnexia. It extends into the subcutis and entraps fat globules. There is no capsule but the deep margin prescribes a well-defined arc. Masson’s trichome stain. × 6.

Fig. 6. Histiocytic cells that are separated by interstitial spaces and appear individually discrete near the intact epidermis on the surface of a canine cutaneous histiocytoma. Hematoxylin and eosin, × 660.

Fig. 7. Histiocytic cells separated by hemorrhage near the surface of an ulcerated canine cutaneous histiocytoma. Purulent exudate is present in the upper part of the photograph. Hematoxylin and eosin, × 425.

Fig. 8. Impression smear of a canine cutaneous histiocytoma. The cytoplasm is vacuolated and/or granular. Nuclei are pleomorphic and have finely particulate, evenly dispersed chromatin. Multiple nucleoli are evident. The small dark-staining cells are lymphocytes. Geimsa, × 1000.

Fig. 9. Histiocytic cells in the third tissue culture passage after 27 days incubation. The cytoplasm is vacuolated and the nuclei have finely particulate chromatin and multiple prominent nucleoli. Geimsa, × 660.

Fig. 10. Histiocytic cells of a canine cutaneous histiocytoma that have abundant granular cytoplasm and indistinct cytoplasmic membranes. The nuclei are pleomorphic with rather scant nuclear chromatin which is sometimes peripherally marginated. Nucleoli are prominent and frequently multiple. Three mitotic figures are present. Hematoxylin and eosin, × 660.

Fig. 11. Small numbers of dark-staining collagen fibers are widely separated by histiocytic cells in this section of a canine cutaneous histiocytoma. Masson’s trichome stain, × 290.

Fig. 12. Reticulum fibers in a section of a canine cutaneous histiocytoma. The fibers encompass large groups of histiocytic cells. Gordon and Sweet’s reticulum stain, × 250.

Fig. 13. Explant of a canine cutaneous histiocytoma in the lateral ventricle of a 7-day-old puppy inoculated during the last week of fetal life. Degenerating histiocytic cells are still evident among the collagen fibers of the explant, which may be recognized by the presence of 3 hair shafts. Hematoxylin and eosin, × 100.
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