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Case Report

Cutaneous B-Cell Lymphoma in a Perdido Key Beach Mouse (*Peromyscus poliontus trissyllepsis*)

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The Perdido Key beach mouse (*Peromyscus poliontus trissyllepsis*) is an endangered mammal indigenous to the panhandle beaches of Northwest Florida. A captive 3.5-y-old female mouse was evaluated because of severe pruritus, diffuse alopecia, skin reddening, and ulcerations over the dorsum of her body. Initial skin biopsy of the affected area suggested bacterial dermatitis but was inconclusive. Despite empiric antibiotic, anthelmintic, and antihistamine treatments, she continued to decline and developed severe ulcerations over the majority of her body. Postmortem histopathologic evaluation led to a tentative diagnosis of epitheliotropic lymphoma, suggestive of a mycosis fungoides T-cell–type cutaneous lymphoma. However, immunohistochemistry results challenged this diagnosis, indicating that the lesion was actually an epidermotropic B-cell lymphoma. Spontaneous cutaneous B-cell lymphomas are rare in rodents and had not previously been reported to occur in Perdido Key beach mice. This case report provides initial evidence that the Perdido Key beach mouse is susceptible to cutaneous B-cell lymphoma.

The Perdido Key beach mouse (*Peromyscus poliontus trissyllepsis*) is one of the most endangered mammals in North America. Since its listing as an endangered species in 1985, the population of this pale tan to gray-colored mouse has remained below 500 individuals, which are divided among the costal sand dunes of Gulf Islands National Seashore and Perdido Key State Park in Florida.[10] Habitat loss due to hurricanes and real estate development continue to threaten the future of this species. As a result, active captive breeding and reintroduction programs are used to safeguard and augment the wild population.[10] These captive breeding populations have provided unprecedented access to this highly endangered native mouse. Despite this accessibility, there is scant information on disease susceptibility of this species, posing challenges to veterinarians responsible for diagnosing and treating captive Perdido Key beach mice. This case report describes the first disease reported in Perdido Key Beach mice and details the clinical presentation, gross pathology, histologic evaluation, and immunohistochemistry of spontaneously occurring cutaneous epidermotropic B-cell lymphoma.

Case Report

A captive 3.5-y-old, 18-g, intact female Perdido Key Beach mouse was examined because of asymmetrical alopecia and pruritus of approximately 2 wk duration. Prior to presentation, this mouse was housed with a male conspecific and had bred successfully producing 3 offspring as part of a Florida Fish and Wildlife Conservation Commission supported captive breeding program (FFWCC permit WX06404A, USFWS permit TE145047). Both this mouse and her mate were housed in a glass enclosure (60 × 30 × 38 cm) with a hard screen lid and sand substrate 12 to 18 cm deep with enclosure furnishings consisting of a partial coconut shell, short PVC pipe, cypress bark strips, plastic exercise wheel, and fresh-cut bamboo. The mice were fed rodent pellets (Mazuri, PMI Nutrition International, St Louis, MO) and water ad libitum.

Physical examination under isoflurane anesthesia (by face mask) revealed asymmetrical alopecia from the base of the tail extending over the dorsum and head, with generalized reddening of the skin and multifocal areas of ulceration without lymphadenopathy. The history and physical findings suggested overgrooming by a conspecific; trauma; allergic, bacterial, or fungal dermatitis; or ectoparasites. Both skin scraping and skin tape preparation were performed, but cytologic examination showed no ectoparasites or fungal hyphae. The beach mouse was isolated in a new enclosure to prevent conspecific overgrooming and treated empirically with enrofloxacin (5 mg/kg PO twice daily; Baytril, 68-mg tablets compounded by University of Florida Veterinary Medical Center Pharmacy into 20 mg/mL liquid oral suspension, Bayer Healthcare, Pittsburgh, PA), ivermectin (0.2 mg/kg topically once weekly; Ivomec, Merial, Duluth, GA), and diphenhydramine (2 mg/kg PO twice daily; Children's Benadryl, Johnson and Johnson, New Brunswick, NJ).

Two weeks after the initial presentation, the area of alopecia had progressed to multifocal ulcerations and scab formations over most of her body (Figure 1 A). The mouse was anesthetized so that a full-thickness skin biopsy could be obtained. Histopathologic evaluation of the biopsy indicated chronic, marked lymphoplasmacytic dermatitis with epidermal pustules, and basilar

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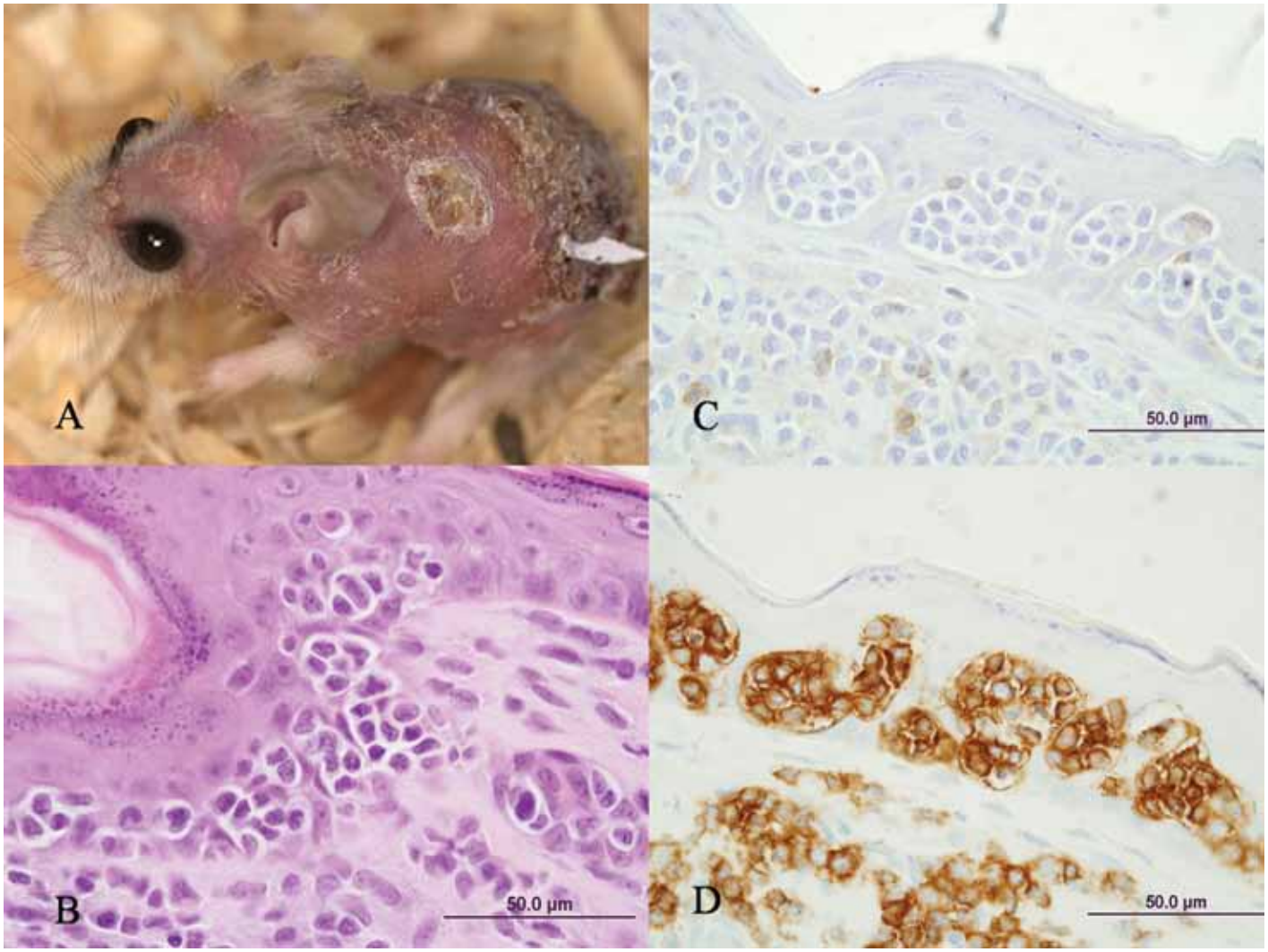

Figure 1. (A) Adult (3.5 y) female Perdido Key beach mouse (*Peromyscus poliontus trissyllepsis*) with severe dermatitis caused by epidermotropic cutaneous B-cell lymphoma 4 wk after initial signs of erythema and alopecia. Ear notching was for identification. (B) High-magnification (×100) cross-section of skin over head of mouse stained with hematoxylin and eosin. Note the sheets of round cells and the halo around the clusters of lymphocytes. (C) Immunohistochemical labeling for CD3 T-cells by using diaminobenzidine as the stain and hematoxylin as the counterstain. Results of testing were negative. (D) Immunohistochemical labeling identified the neoplastic lymphoid cells as positive for CD45R (a B-cell marker), indicating that this lesion was a B-cell neoplasm. The stain was diaminobenzidine and hematoxylin was the counterstain. The histopathologic changes were suggestive of epidermotropism, and immunohistochemistry was consistent with a B-cell lymphoma, leading to a diagnosis of epidermotropic cutaneous B-cell lymphoma.

cell apoptosis, suggesting bacterial dermatitis but without ruling out cutaneous neoplasia. Because there was no clinical improvement after 3 wk of therapy, immune-mediated disease or neoplasia was suspected, and prednisolone (0.5 mg/kg PO twice daily) was initiated, and enrofloxacin (Bayer Healthcare) therapy was continued. By 1 wk later, the condition of the beach mouse had declined further, and she was anesthetized with isoflurane before euthanasia by intracardiac injection of euthanasia solution (0.1 mL Beuthanasia-D, Schering-Plough Animal Health, Kenilworth, NJ). The carcass was submitted for postmortem evaluation.

Necropsy examination revealed severe generalized alopecia with occasional hair tufts covering the body with several thick, dark-red, firmly adherent crusts distributed on the dorsum of the head, thorax, and pelvis. Histopathologically, the most significant lesion was associated with the skin over the head and deep ear canal. The changes noted on histopathologic evaluation were ulcerative dermatitis with multifocal infiltration of lymphocyte sheets. These neoplastic cells were characterized by scant amounts of amphophilic to basophilic cytoplasm, round to oval to reniform nuclei, stippled to clumped chromatin, and small to medium basophilic nucleoli. The lymphocyte infiltration extended into the overlying epidermis, where it formed discrete aggregates surrounded by a clear halo (Pautrier microabscesses), and into the dermis, it was admixed with variable numbers of plasma cells, neutrophils, and mast cells (Figure 1 B). The lesions of the dermis were accompanied by moderate orthokeratotic hyperkeratosis and expansion of the stratum corneum by large numbers of degenerate neutrophils surrounded by granulation tissue and edema, suggesting chronicity. The submandibular lymph nodes, the lymph nodes closest to the changes noted in the skin of the

head, contained dense plasmacytic infiltrates. The resulting anatomic and histopathologic postmortem diagnosis was multifocal epitheliotropic lymphoma without involvement of other organs. Tissues were submitted for immunohistochemistry to further characterize the neoplastic round cells visualized within the dermis and epidermis.

Immunohistochemical labeling for CD45R (also known as B220) for B cells and CD3 for T cells was performed at the Diagnostic Center for Population and Animal Health at Michigan State University according to routine protocols.[3] Briefly, deparaffinization, antigen retrieval using ER1 for 20 min (Vision BioSystems, Leica, Bannockburn, IL), immunohistochemical labeling, and counterstaining were performed on an automated staining system (Bond maX, Vision BioSystems, Leica) using the Bond Polymer Detection System (Vision BioSystems, Leica). Primary antibodies were rabbit polyclonal antihuman CD3 (dilution, 1:500; Dako Cytomation, Carpinteria, CA) and rat monoclonal antimouse CD45R (dilution, 1:100; B220, Invitrogen, Carlsbad, CA). Diaminobenzidine was used as the chromogen and hematoxylin as the counterstain. Sections of normal mouse lymph nodes were included as positive controls. For negative controls, the primary antibodies were replaced with homologous nonimmune sera. Immunohistochemical labeling identified the neoplastic lymphoid cells as negative for CD3 (Figure 1 C) but positive for CD45R (Figure 1 D), indicating that the lesion was a B-cell neoplasm. The histopathologic changes were suggestive of epidermotropism, leading to an initial diagnosis of epitheliotropic lymphoma (T cell); however, immunohistochemistry was consistent with a B-cell lymphoma, leading to a final diagnosis of epidermotropic cutaneous B-cell lymphoma that mimicked epitheliotropism.

Discussion

Cutaneous lymphoma typically is described as either epitheliotropic or nonepitheliotropic.[1,2] Epitheliotropic lymphoma is characterized as being T cell in origin and distinguished by neoplastic lymphocytes in the dermis and epidermis that occur singly or in clusters surrounded by a clear halo. Nonepitheliotropic lymphoma can be of B- or T-cell origin.[1,2,6] This simplified classification is challenged in domestic mice. In laboratory mice, B-cell lymphomas occur either spontaneously or are induced by using irradiation, chemicals, or murine leukemia and are classified as small B-cell lymphoma, splenic marginal zone B-cell lymphoma, follicular B-cell lymphoma, diffuse large B-cell lymphoma, Burkitt-like lymphoma, and plasma cell neoplasm.[5] Classification of murine B-cell neoplasms is accomplished by using morphologic description and immunohistochemistry.[5,6] Cutaneous B-cell lymphoma does not occur spontaneously in laboratory mice but instead is induced to facilitate the biomedical study of human B and T-cell lymphoma.[7] When induced in laboratory mice, the resulting cutaneous B-cell lymphoma showed epidermotropic behavior histopathologically.[7] Epidermotropic cellular changes in cutaneous B-cell lymphoma is an uncommon presentation and makes nonepitheliotropic cutaneous B-cell lymphoma appear to have histopathologic characteristics similar to epitheliotropic T-cell lymphoma, resulting in misclassification in the absence of immunohistochemistry.[1,7] This scenario, as reported in laboratory mice, describes what occurred in the Perdido Key beach mouse we present here. However, immunohistochemistry was necessary to augment the initial histopathologic description to enable accurate diagnosis of epidermotropic cutaneous B-cell lymphoma in the mouse we present.

Although primary cutaneous B-cell lymphoma is rare in animals and generally not well characterized,[6,8] the lesion in people is described as primary cutaneous marginal zone B-cell lymphoma (prognosis good), primary cutaneous follicle-center lymphoma (prognosis good after surgery, radiation, and chemotherapy), primary cutaneous diffuse large B-cell lymphoma leg-type (fair to poor prognosis), and primary cutaneous diffuse intravascular large B-cell lymphoma (excellent prognosis).[9] Classification of cutaneous B-cell lymphoma in people is based on lymphocyte phenotypic ratios, clinical presentation, lesion location, and immunologic differentiation and is crucial for appropriate treatment protocols.[9]

Applying the human cutaneous B-cell lymphoma classification scheme to further described the epidermotropic cutaneous B-cell lymphoma in this Perdido Key beach mouse is difficult because of the unique histopathologic presentation, the paucity of information on beach mouse physiology, and the limited amount of tissue (18-g beach mouse) available for further testing and evaluation. At the time of necropsy, samples were evaluated grossly and preserved in formalin to accommodate later histopathologic evaluation and immunohistochemistry, but because of the lack of frozen sections for additional evaluation, further classification and description of this cutaneous B-cell lymphoma are not possible. In humans, classifying the type of cutaneous B-cell lymphoma is crucial when attempting treatment and determining prognosis. However, for the Perdido Key Beach mouse we present here, even if it had been possible, antemortem classification of the cutaneous B-cell lymphoma may not have changed the outcome. Surgical excision, radiotherapy, and systemic intravenous chemotherapy were impractical treatment options because of the patient's exceptionally small size.

The cause of the epidermotropic cutaneous B-cell lymphoma in this Perdido Key beach mouse is unknown. In other species, although no single etiology has been identified, contributing genetic and environmental influences are suspected.[5,8] In laboratory mice, murine leukemia virus can cause B-cell neoplasia[5,6] but the prevalence of this virus within the wild or captive populations of Perdido Key Beach mice is unknown at this time. Cutaneous T-cell lymphoma often occurs in older animals,[4,6] and cutaneous B-cell lymphomas are reported frequently in older people.[1] It is difficult to speculate on the influence of age in the development of cutaneous B-cell lymphoma in Perdido Key beach mice, particularly in light of the uncertainty regarding the typical lifespan in this species. However, cutaneous B-cell lymphoma must be considered for any aging beach mouse with skin abnormalities.

In summary, this report represents the first case of any clinical disease in Perdido Key beach mice. Specifically, this is the only report of neoplasia for this species. The paucity of information on this species poses challenges for veterinary care professionals associated with captive breeding programs and recovery plans. Despite the lack of health information about the Perdido Key beach mice, this rare species should be compared with other species of mice when evaluating disease. In the current report, cutaneous B-cell lymphoma mimicked the unusual histopathologic presentation of B-cell lymphoma induced in the skin of laboratory mice. Cutaneous B-cell lymphoma is rare in other species and likely is rare in Perdido Key beach mice but should be considered along with other more benign skin conditions when evaluating skin disorders in aged beach mice.

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