ISVD case of the month August 2020

Three-year-old spayed female Berger Blanc Swiss dog with a 1-2 year history of slowly progressive skin lesions which began as alopecia and crusting of pinnal margins (Figure 1) that later developed into moist exudative dermatitis of the elbows and hock (Figure 2) and then into papules and nodules of the distal limbs (Figure 3).

Skin biopsy specimens were obtained and submitted for histopathology. The morphologic diagnosis was: Severe, diffuse interstitial, perifollicular and nodular dermatitis with sebaceous gland loss, orthokeratotic and parakeratotic hyperkeratosis and focal furunculosis with ulceration, suppurative epidermitis and serocellular crusts

Taking into consideration the information you have been provided, of the following choices, what is the most likely diagnosis:

A. Pemphigus foliaceous
B. Sebaceous adenitis
C. Sterile Pyogranuloma Syndrome
D. Leishmaniasis
E. Staphylococcal folliculitis and furunculosis

SIGNALMENT:

3-year-old, female spayed, Berger Blanc Swiss dog

CLINICAL HISTORY:

History of coming to the United States at one year of age from Barcelona, Spain. On arrival, the elbows were notably erythematous and scaly. In the next 12-18 months, limping was noted, and the owners saw very small open sores in the center of several paw pads. Dermatologic findings included marked thinning of the hair on the tips of the pinnae AU, with mild adherent scale. Five 4-6 mm dried firm papules were noted on the distal aspects of both forelimbs and there are punctate lesions in several paw pads, which were draining a serosanguineous exudate. The elbows and dorsal aspects of the hocks were mildly erythematous, with marked adherent and non-adherent crusts. Clinically, the dog is normal and the serum biochemistry was unremarkable.

HISTOPATHOLOGIC DESCRIPTION, haired skin: Examined are six sections of haired skin from three 6 mm punch biopsy specimens with similar changes (Figure 4). Throughout all sections, the superficial to mid dermis is diffusely infiltrated by a large number of macrophages and neutrophils, extending around the hair follicles (Figure 5). Frequently within the cytoplasm of macrophages are protozoal amastigotes, 2-3 um in diameter structures with a thin pale halo,

basophilic nucleus, and occasionally a smaller adjacent (perpendicular) kinetoplast (consistent with *Leishmania* spp. amastigotes) (Figure 6). Inflammatory infiltrates extend up to and into the subcutis in a perivascular to nodular pattern. All sebaceous glands are replaced by large aggregates of macrophages, neutrophils, lymphocytes and plasma cells (sebaceous adenitis) (Figure 7). In one section, there is a locally extensive ulceration over one ruptured hair follicle. The epidermis overlying this ruptured follicle is infiltrated with large numbers of neutrophils and serum. The surrounding dermis is moderately edematous and a few free hair shafts and shards of keratin are surrounded by small aggregates of macrophages and neutrophils. Overall, there is mild to moderate epidermal hyperplasia that is mildly irregular with multifocal lymphocytic exocytosis and intercellular edema (spongiosis), moderate orthokeratotic to parakeratotic hyperkeratosis and multifocal serocellular crusts. Small numbers of lymphocytes are also present in the outer root sheath of most hair follicles and within the walls of most epitrichial sweat glands. Mild superficial dermal fibrosis is present multifocally. The blood vessels are dilated and lined by plump endothelial cells (reactive).

MORPHOLOGIC DIAGNOSIS:

Haired skin: Severe, diffuse interstitial, perifollicular and nodular dermatitis with sebaceous gland loss, intrahistiocytic protozoal organisms, orthokeratotic and parakeratotic hyperkeratosis and focal furunculosis with ulceration, suppurative epidermitis and serocellular crusts

NAME THE CONDITION:

Leishmaniasis

COMMENTS:

Leishmania spp. was confirmed in this case via positive PCR. Leishmaniasis is a zoonotic worldwide disease caused by an obligate intracellular diphasic protozoa of the genus *Leishmania*, which infect a variety of species, including humans, wild and domestic mammals. Dogs are considered natural hosts and the primary domestic reservoir for human infection. Leishmaniasis is endemic in large areas of the tropics and subtropics, including Mediterranean countries, parts of Africa, Asia, the Middle East, Central and South America. Endemic foci have been reported in parts of North America, including Texas, Oklahoma, Ohio, Michigan and Alabama. These parasites are usually transmitted by a female sand fly vector (*Phlebotomous* sp and *Lutzomia* sp) and cause a wide range of clinical manifestations, such as visceral, mucocutaneous, and cutaneous leishmaniasis (CL). The outcome of infection is determined by the host immune response, genetic background and concurrent diseases.

Clinically and grossly, CL in dogs can cause nonpruritic exfoliative dermatitis, ulcerative dermatitis, focal or multifocal nodular dermatitis, proliferative dermatitis, or mucocutaneous ulcerative or proliferative dermatitis. Exfoliation with large silvery-white scales are most pronounced on the head, pinnae and extremities (where sandflies feed). Nasodigital hyperkeratosis and alopecia may occur. Periocular alopecia (“lunettes”) is common. Lymphadenopathy and oncychogryphosis (hypertrophy and increased curvature of the claws)

are also commonly found. Other findings include paronychia, sterile pustular dermatitis, and nasal depigmentation. Secondary bacterial pyoderma is the most common complicating co-morbidity, but leishmaniasis is often associated with other dermatoses, such as opportunistic fungal, parasitic, or other protozoal, autoimmune disease and neoplasia. The identification of species of *Leishmania* is possible by parasitological culture followed by multilocus enzyme electrophoresis (MLEE) and by PCR.

The immune response to *Leishmania* spp. is dependent upon a timely and appropriate Th1 response, including IL-12 production by dendritic cells and macrophages, efficient MHC II presentation, and subsequent IFNy production from T cells. Parasite killing is dependent primarily upon intracellular killing via superoxide and nitric oxide within phagolysosomes of infected macrophages. *Leishmania* organisms have several adaptations that allow their entry into and survival within macrophages. These include lipophosphoglycans that bind to C3b and iC3b and enhance phagocytosis, and protect organisms by scavenging oxygen free radicals and inhibiting lysosomal enzymes; Gp63, a zinc-dependent proteinase that cleaves complement and some lysosomal antimicrobial enzymes; and proton-transporting ATPase that allows the amastigotes to survive in the phagolysosomes extremely acidic environment.

REFERENCES:

1. Colombo S, Abramo F, Borio S, et al. Pustular dermatitis in dogs affected by leishmaniosis: 22 cases. Vet Dermatol. 2016;27(1):9-e4.
2. Gross TL, Ihrke PJ, Walder EJ. Infectious nodular and diffuse granulomatous and pyogranulomatous diseases of the dermis. In: Skin Diseases of the Dog and Cat, 2nd ed. Ames, IA: Blackwell Publishing; 2005: 312-316.
3. Kegler K, Haierski A, Hahn K, et al. Vaginal canine transmissible tumour associated with intra-tumoural Leishmania Amastigotes in an asymptomatic female dog. J Comp Pathol. 2013;149(2-3):156-61.
4. Koutinas AF, Koutinas CK. Pathologic mechanisms underlying the clinical findings in canine leishmaniasis due to Leishmania infantum/chagasi. J Vet Diagn Invest. 2014;26(2):286-90.
5. Kumar V, Abbas AK, Aster JC, eds. Robbins and Cotran Pathologic Basis of Disease. 9th ed. Philadelphia, PA: Elsevier; 2015: 393-394.
6. Mauldin EA, Peters-Kennedy J. Integumentary system. In: Maxie MG, ed. Jubb, Kennedy, and Palmer's Pathology of Domestic Animals. Vol 1. 6th ed. Philidelphia, PA: Elsevier Saunders; 2015: 663-664.
7. Miller WH, Griffin CE, Campbell KL. Viral, rickettsial, and protozoal skin diseases. In: Miller WH, Griffin CE, Campbell KL eds. Small Animal Dermatology. 7th ed. Philadelphia, PA: WB Saunders Company; 2013:354-357.
8. Nascimento MS, Albuquerque TD, Nascimento AF, et al. Impairment of interleukin-17A expression in canine visceral Leishmaniosis is correlated with reduced interferon-y and inducible nitric oxide synthase expression. J Comp Pathol. 2015;153(4):197-205.
9. Saridomichelakis MN, Koutinas AF. Cutaneous involvement in canine leishmaniosis due to Leishmania infantum (syn. chagasi). Vet Dermatol. 2015;26(1):69-70.
10. Saridomichelakis M. Advances in the pathogenesis of canine leishmaniasis: epidemiologic and diagnostic implications. Vet Dermatol. 2009;20(5-6):471-489.

CONTRIBUTORS:

Ileana Miranda, DVM, MS; Anatomic Pathology Senior Resident, Cornell University, College of Veterinary Medicine, Department of Biomedical Sciences Ithaca, NY USA

Jeanine Peters-Kennedy, DVM, Diplomate ACVP, ACVD; Associate Clinical Professor of Anatomic Pathology and Dermatology, Cornell University, College of Veterinary Medicine, Department of Biomedical Sciences Ithaca, NY USA

Alina Demeter, DVM, PhD; Anatomic Pathology Fellow, Cornell University, College of Veterinary Medicine, Department of Biomedical Sciences Ithaca, NY USA

Brian Scott DVM, Diplomate ACVD; Dermatologist, Tampa Bay Veterinary Specialist & Emergency Care Center Largo FL USA

FIGURES:

Figure 1. Pinna.

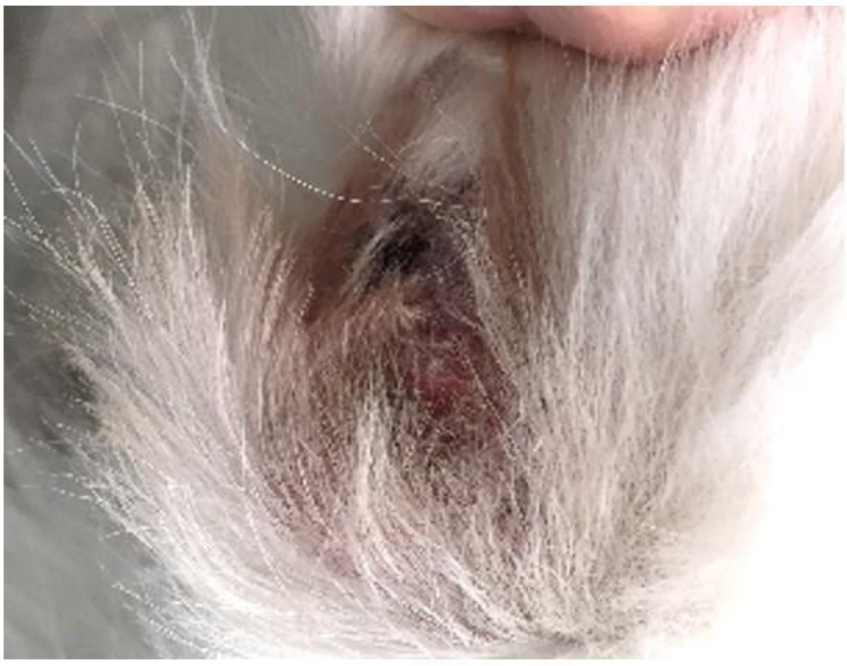

Figure 2. Elbow.

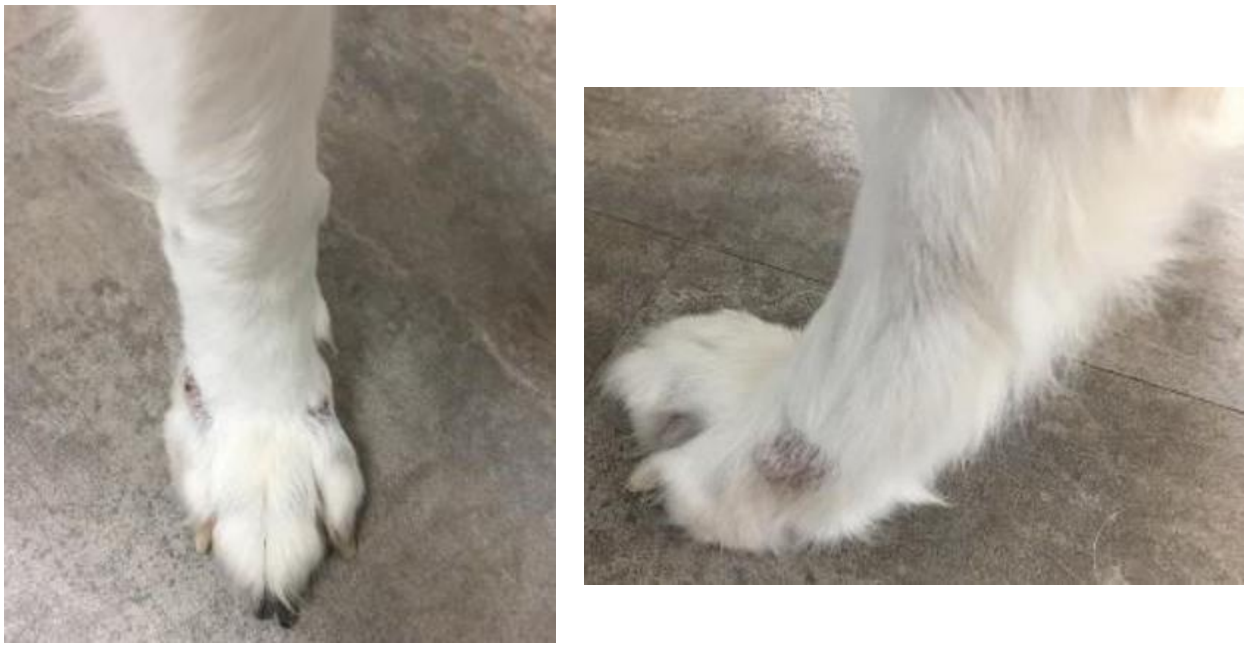

Figure 3. Distal limb.

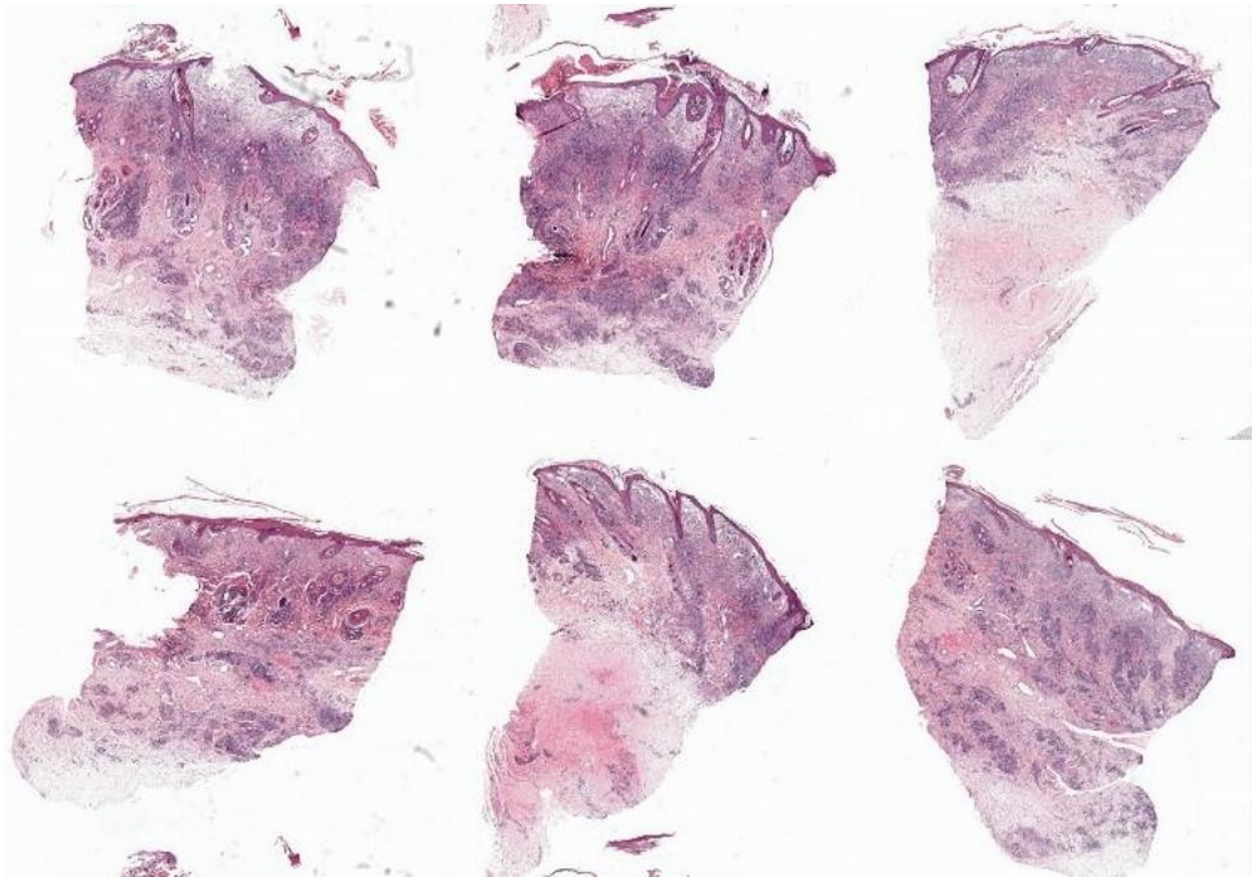

Figure 4.

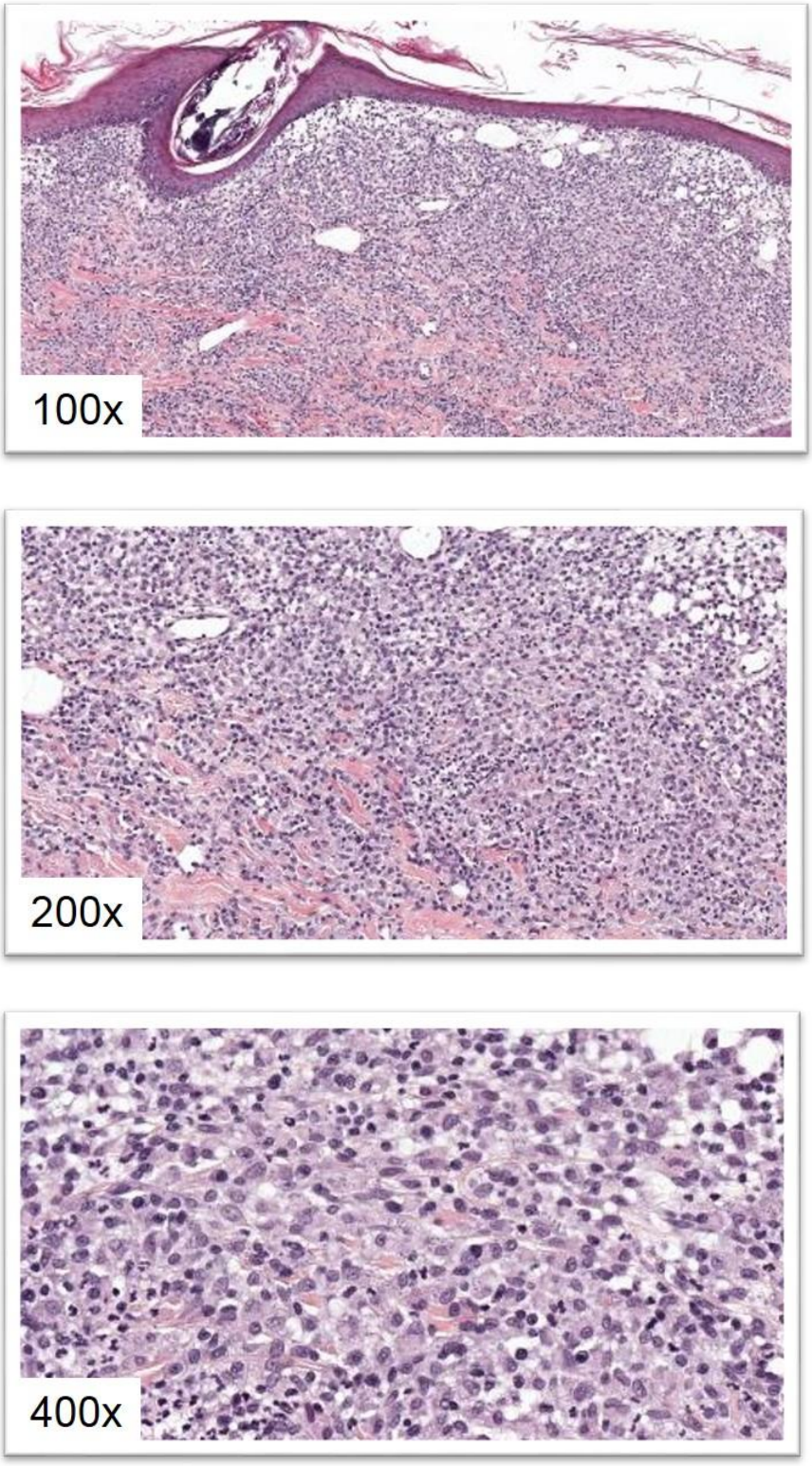

Figure 5. Large numbers of macrophages and fewer neutrophils in the superficial dermis.

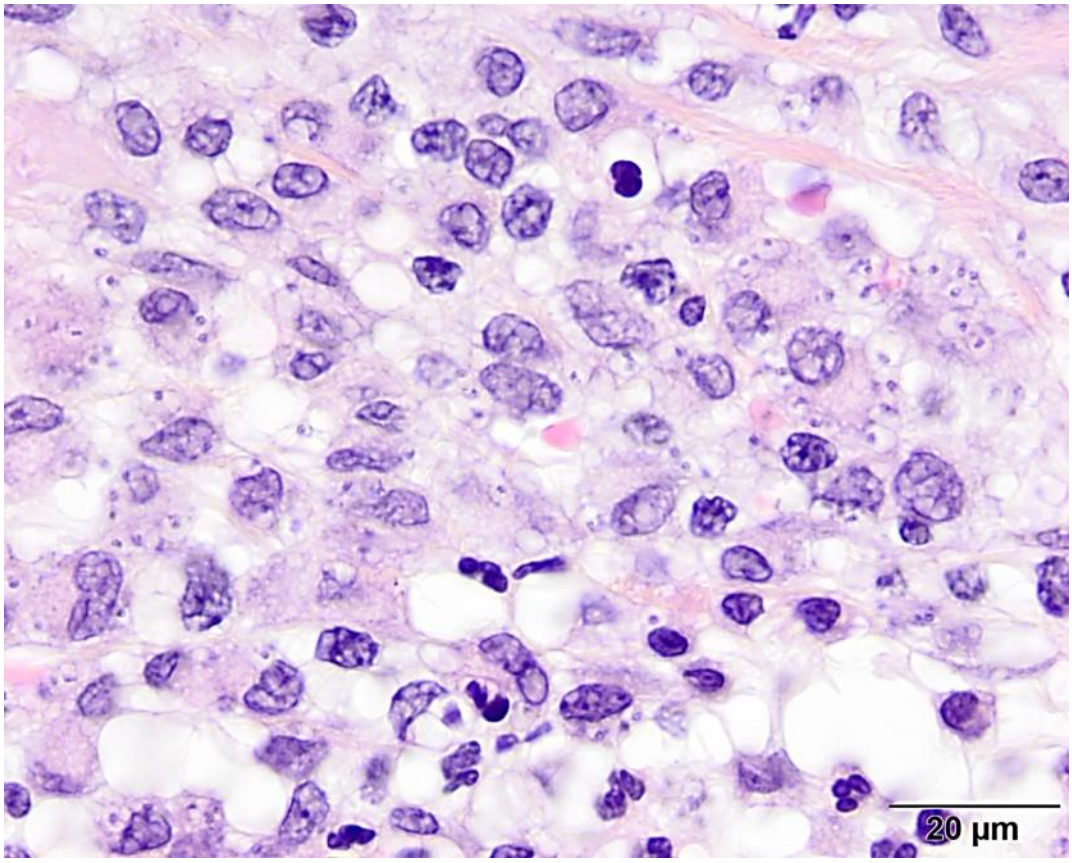

Figure 6. Amastigotes within macrophage cytoplasm.

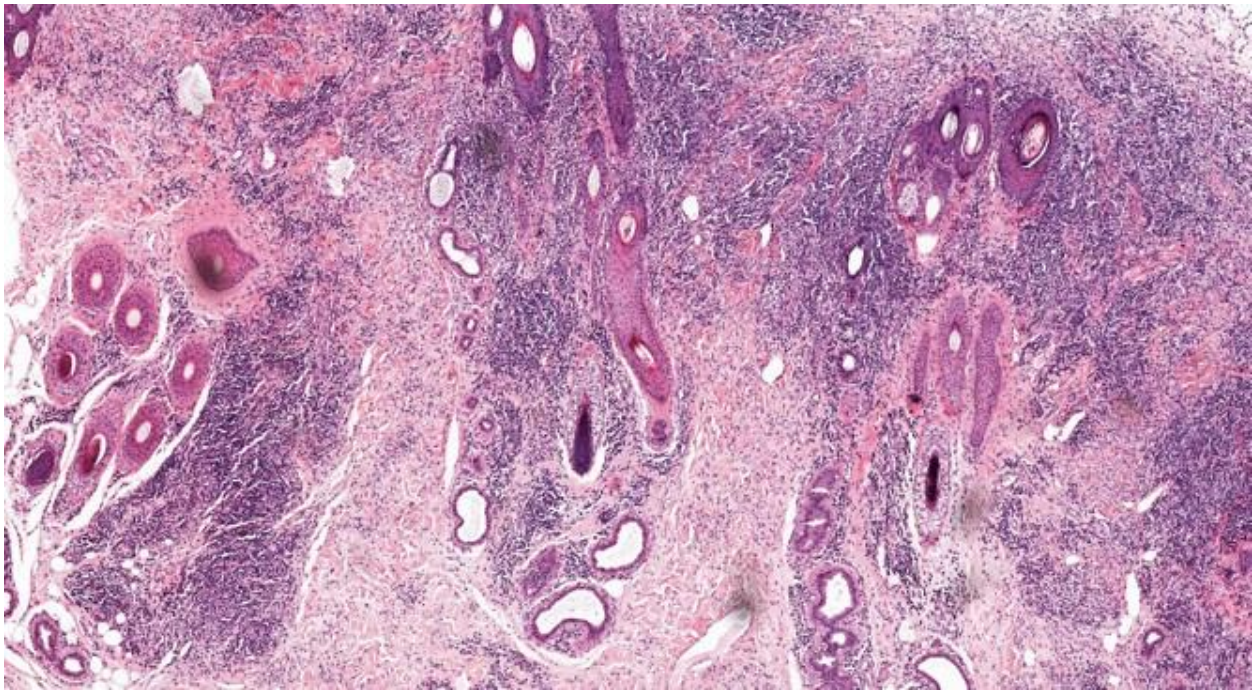

Figure 7. Perifollicular inflammation with loss of sebaceous glands.