A Canine Pemphigus Foliaceus Case Showing Parallel Relationship of Disease Activity and Titer of Serum Anti-keratinocyte Cell Surface Antibodies

Koji NISHIFUJI1, Kumiko YOSHIDA-YAMAKITA2 and Toshiroh IWASAKI3

1) Department of Dermatology, Keio University School of Medicine, 35 Shinanomachi, Shinjuku-ku, Tokyo 160–8582, 2) Green Animal Hospital, 209 Irigaike, Nagakute-cho, Aichi-gun, Aichi 480–1116, and 3) Department of Veterinary Internal Medicine, Faculty of Agriculture, Tokyo University of Agriculture and Technology, 3–5–8 Saiwai-cho, Fuchu, Tokyo 183–8509, Japan

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ABSTRACT. A seven-year-old, spayed female mongrel dog was diagnosed as pemphigus foliaceus (PF) by clinical, histopathological and immunopathological observations. Serum antibodies against the cell surface of keratinocytes in the dog were detected by indirect immunofluorescence (IIF) using cryosectioned bovine esophagus as well as living cultured-canine keratinocytes as the substrates. When we compared the titers of IIF on bovine esophagus with its disease activity, the IIF titers reflected the disease activity throughout the time course. Our findings will suggest that sequential titration of serum antibodies by IIF will be useful for monitoring the serological disease activity in canine PF.

KEY WORDS: canine, indirect immunofluorescence, pemphigus.

Pemphigus foliaceus (PF) is an antibody-mediated autoimmune skin disease recognized in humans and domestic animals, including dogs [2, 9]. In PF, autoreactive IgG against the cell adhesion molecule disrupts the cellular attachment of keratinocytes and results in intra-epidermal blister or pustule formation. The target molecule for serum autoantibodies in human PF is desmoglein (Dsg) 1, a desmosomal cell-cell adhesion molecule [1, 11]. Detection of serum IgG autoantibodies in human PF can be accomplished by indirect immunofluorescence (IIF) using cryosectioned normal epithelia or an enzyme-linked immunosorbent assay (ELISA) against recombinant human Dsg1 produced by baculovirus [3, 4, 6, 8]. It has also been reported that sequential IIF titers as well as ELISA values of human patients with PF showed parallel fluctuation with the disease activity [6].

Characterization of serum autoantibodies in canine PF has been of lagging progress for many years because of the lower detection of the antibodies by conventional IIF technique [10]. However, the sensitivity of IIF for diagnosis of canine PF could be improved when cryosectioned bovine esophagus was used as substrate, although a few dogs with non-pemphigus dermatoses showed false-positive immunoreactivity [5, 7]. In addition, despite of its low sensitivity, living keratinocyte staining using a canine keratinocyte cell line, MCA-B1, has provided a highly reliable serological diagnostic tool to detect serum autoantibodies in canine PF with its high specificity [5]. These techniques have the potential to be used for monitoring the disease activity of canine PF, as similarly reported in human patients [6]. In this report, we introduce a canine case with PF, in which the titers of serum anti-keratinocyte cell surface antibody reflected the disease activity.

A seven-year-old, spayed female mongrel dog was presented with highly pruritic, crusted and erosive eruptions on the face, muzzle, pinna, groin, extremities and mucocutaneous junctions (Fig. 1). The dog had not received any therapy such as antibiotics or immunosuppressive drugs prior to the development of skin lesions. Cytology of exudates from the skin lesion showed multiple acantholytic keratinocytes and neutrophils. Since the clinical and cytological observations of the canine patient were suggestive for PF, skin biopsy was performed on an intact pustule under generalized anesthesia. Histopathologically, the lesion showed subcorneal pustule with neutrophils and acantholytic keratinocytes (data not shown). Confirmation of canine PF was further accomplished by identification of IgG deposition between keratinocytes in the perilesional skin by immunoperoxidase staining using peroxidase-conjugated goat anti-dog IgG (Kirkegaard&Perry laboratories, Gaithersburg, MD) (Fig. 1) [12].

To demonstrate the presence of serum anti-keratinocyte cell surface antibodies in the canine patient, we tested two IIF techniques that had recently been developed; IIF on cryosectioned bovine esophagus and living MCA-B1 cell staining (Fig. 2) [5, 7]. Fluorescent deposition on the cell surface of keratinocytes could be observed when both substrates were used, but maximum IIF titer on bovine esophagus (1:10240) was considerably higher than that on living MCA-B1 cells (1:80). Because of its higher detection of serum antibodies, the former technique was used for the following studies to monitor the fluctuation of IIF titers with time.

From November 1996 to October 1997, multiple serum samples were obtained at several stages during the time course and subjected for IIF on bovine esophagus. Disease activity of the dog at several stages was assessed on a scale of 0 to 3 according to the following criteria described previously in a human report [6]: 0, no lesions; 1, 10% or less of the skin surface involved; 2, up to 30% of the skin surface involved; 3, >30% of the skin surface involved. The disease activity was compared with the movement of IIF titer along
the time course, except for the period during the end of March and the beginning of May, while the serum samples were not collected (Fig. 3). Interestingly, IIF titers fluctuated in a similar fashion with disease activity throughout the time course with two flares, and the titers ranged between 1:640 and 1:10240. It was noteworthy that in early May, when the disease was in remission, the IIF titer was also subdued to the lowest level in the study period.

In this study, we observed parallel relationship between IIF titers and disease activity. These observations suggest that PF in the present case is indeed an antibody-mediated autoimmune disorder, as is in human PF cases. It is our hope if sequential titration of serum autoantibodies by the IIF technique will provide objective serological information useful in monitoring disease activity, and thus helpful in guiding the decision of immunosuppressive therapy for the canine cases. Further accumulation of similar observation would help us to determine the usefulness of the IIF technique as a guide for understanding the serological disease activity in canine PF.

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REFERENCES

Fig. 3. Comparison of the fluctuation of the disease activity and IIF titers on bovine esophagus over a time course. Movement of IIF titers with time was compared with the disease activity. Serum samples were not collected from the end of March to the beginning of May, when the disease activity was temporary worsened (dashed line).