



HUMAN AND CANINE PEMPHIGUS FOLIACEUS: A REVIEW ON THE DIAGNOSTIC PROTOCOL

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1 INTRODUCTION

- Pemphigus foliaceus (PF) is an autoimmune disease characterized by the formation of superficial cutaneous blisters. It's caused by the union of autoantibodies to desmosomal epithelial cadherins.
- It's rare in humans, but is the most frequent autoimmune cutaneous disease in dogs.
- The diagnostic protocol includes physical and histologic exams in both species, and in humans it also includes serological tests.



3 RESULTS

Table 1 IIF sensibility in the diagnosis of human PF. Substrate influence in the results.

Articles	Sensibility	Substrate
[1]	-	ME and GPE; Reactivity: GPE > ME
[2]	86%	ME and GPE; Reactivity: GPE > ME
[3]	71%	ME and RL; Reactivity: RL > ME
[4]	67%	ME
	100%	HS
[5]	84%	HS
[6]	89%	HS

Table 2 ELISA sensibility and specificity in the diagnosis of human PF.

Articles	Sensibility	Specificity	rDsg-1*
[6]	96%	96%	Expressed in cultured insect cells, using a baculovirus as vector
[7]	97,9%	98,9%	
[5]	92%	98,5%	MESACUP Desmoglein TEST "Dsg-1" (MBL)
[4]	92%	99%	
[8]	100%	95,7%	
[8]	96%	99,1%	Human cell line (HEK293) expression

Table 3 Correlation of disease activity with serum autoantibody levels in human patients.

Articles	Patients	Correlation disease activity - ELISA	Substrate IIF	Correlation disease activity - IIF
[6]	5	+	HS	+
[7]	1	+		
[8]	5	+(p<0,001)		
[9]	2	+		
[10]	7	+(p=0,091)	ME	-
[11]	9	-	ME, RE, HS	+
[12]	9	+	ME	+

Abbreviations: ME (monkey oesophagus), GPE (guinea pig oesophagus), RL (rabbit lip), HS (human skin), RE (rat oesophagus), BT (bovine tongue), BE (bovine oesophagus), BN (bovine nose), CN (canine nose skin), CO (canine oral mucosa), MS (Neonatal mouse skin), CF (canine footpad), rDsg-1 (recombinant Dsg-1), MCA-B1 (culture of canine oral acanthomatous epulis cell line)

References: [1] Sabolinski et al. 1987. Substrate specificity of anti-epithelial antibodies of pemphigus vulgaris and pemphigus foliaceus sera in immunofluorescence tests on monkey and guinea pig oesophagus sections. [2] Jiao et al. 1997. Sensitivity of indirect immunofluorescence, substrate specificity, and immunoblotting in the diagnosis of pemphigus. [3] Cozzani et al. 1994. Comparative study of indirect immunofluorescence and immunoblotting for the diagnosis of autoimmune pemphigus. [4] Harman et al. 2000. The use of two substrates to improve the sensitivity of indirect immunofluorescence in the diagnosis of pemphigus. [5] Harman et al. 2000. Diagnosis of pemphigus by ELISA: A critical evaluation of two ELISAs for the detection of antibodies to the major pemphigus antigens, desmoglein 1 and 3. [6] Ishii et al. 1997. Characterization of autoantibodies in pemphigus using antigen-specific enzyme-linked immunosorbent assays with baculovirus-expressed recombinant desmogleins. [7] Amagai et al. 1999. Usefulness of enzyme-linked immunosorbent assay using recombinant desmogleins 1 and 3 for serodiagnosis of pemphigus. [8] Schmidt et al. 2010. Modern diagnosis of autoimmune blistering skin diseases. [9] Cheng et al. 2002. Monitoring disease activity in pemphigus with enzyme-linked immunosorbent assay using recombinant desmogleins 1 and 3. [10] Herrero-González et al. 2010. Correlation of immunological profile with phenotype and disease outcome in pemphigus. [11] Bellon et al. 2014. The Value of Anti-Desmoglein Enzyme-Linked Immunosorbent Assay in the Immunological Follow-Up of Pemphigus. [12] Barnadas et al. 2015. Usefulness of specific anti-desmoglein 1 and 3 enzyme-linked immunoassay and indirect immunofluorescence in the evaluation of pemphigus activity. [13] Iwasaki et al. 1996. Detection of canine pemphigus foliaceus autoantigen by immunoblotting. [14] Honda et al. 2004. Detection of circulating autoantibodies using living keratinocyte staining on MCA-B1 method in dogs with pemphigus foliaceus. [15] Hogan et al. 2002. Immunofluorescent determination of the isotype of serum antikeratinocyte autoantibodies in dogs with Pemphigus foliaceus. [16] Olivry et al. 2009. Investigations on the nature and pathogenicity of circulating antikeratinocyte antibodies in dogs with pemphigus foliaceus. [17] Bizikova et al. 2011. Cloning and establishment of canine desmocollin-1 as a major autoantigen in canine pemphigus foliaceus.

2 HIPOTESIS AND OBJECTIVES

AIM: Improve the diagnostic protocol of canine PF using the human protocol as a model.

How?

- 1) To revise the sensibility and specificity of the serological tests used in the diagnosis of human PF.
- 2) To study the correlation of the disease activity and the serum autoantibody levels in human patients.
- 3) To analyse the existent studies about the use of serological tests used in the diagnosis of canine PF.

Table 4 IIF sensibility in the diagnosis of canine PF. Substrate influence in the results.

Articles	Substrate	Sensibility	Specificity
[13]	BT	64,3%	100%*
	BE	12,5%	100%*
	BN	0%	100%
	ME	44,4%	69%
[14]	CN	-	0%
	BE	29,6%	83,9%
	CO	18,5%	93,5%
	MCA-B1	14,8%	100%
[15]	MS	82%	20%
[16]	MS	84%	20%
[17]	CF	100%	-
	CO	18%	-

4 CONCLUSIONS

SEROLOGICAL TESTS IN HUMAN PF:

- ELISA is the best serological test for the diagnosis of human PF. It provides higher sensibility and specificity than IIF, among other advantages. When performing IIF, the most indicated substrate is human skin.
- Serological tests can become a useful tool to monitor the activity of the disease, but further investigation is required.

SEROLOGICAL TESTS IN CANINE PF:

- The studies conducted on the use of IIF for the diagnosis of canine PF hasn't been very successful up to now.
- Research on the usefulness of ELISA in the diagnostic protocol of this disease should be accomplished.