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LETTER TO THE EDITOR

Linear IgA disease and desquamative gingivitis: time for inclusion in mucous membrane pemphigoid

Dear Sir,

In the article by Leao *et al* (2008), that appeared recently in *Oral Diseases*, we read that linear immunoglobulin A (IgA) disease (LAD) was diagnosed in three of 187 patients affected by desquamative gingivitis. According to the data reported, such patients were affected only by oral lesions and were diagnosed 'upon recognized relevant clinical, histological, immunostaining and serological criteria' (Leao *et al*, 2008).

An exclusive mucosal involvement has been reported very rarely in LAD (Table 1) (Kumar *et al*, 1980; Porter *et al*, 1990, 1992; Kirtschig *et al*, 1998; Cohen *et al*, 1999; Egan *et al*, 1999; Lazzaro and Lazzaro, 1999; Letko *et al*, 2000; Eguia del Valle *et al*, 2003; Talhari *et al*, 2006; Angiero *et al*, 2007; Lewis *et al*, 2007). All 14 patients were adult (mean age 61 years, range 29–79); males/females ratio was 7/6. Oral mucosa was involved in 12 cases, conjunctiva in 4 (sole localization in 2) and glans penis in one. The main features of histologic examination were a subepithelial split and a dermal inflammatory infiltrate, both found in eight of 10 cases. Direct immunofluorescence assay (DIF) findings included linear IgA deposits at the basement membrane zone (BMZ) in all cases. Indirect immunofluorescence assay (IIF) was performed in five cases, only two resulting positive. Immunoblotting (IB) detected IgA to 97-kD antigen (LAD-1) in two cases and was negative in another.

The BMZ linear deposition of IgA, although defines LAD itself, may be also found in other subepithelial autoimmune bullous diseases, that is, cicatricial pemphigoid (CP) and epidermolysis bullosa acquisita (EBA). Moreover, a mucosal involvement is far more common in CP and EBA than in LAD. Definite differentiation between these three diseases results therefore from additional laboratory assays. First, salt-split-skin immunofluorescence assays show that both circulating and tissue-fixed IgA autoantibodies deposit most often on the roof of the split in LAD and on the floor in CP, and always on the floor in EBA. Second, the identification of autoantigens by IB or enzyme-linked immunosorbent assay is able almost always to achieve a diagnosis, since LAD sera mainly recognize 97 (LABD97) or 120 kDa antigens (LAD-1), CP sera 180 (BPAg2) or 168 kDa antigens (laminin 5), and EBA sera 145 or 290 kDa antigens (type VII collagen).

Moreover, in 2002 an international Consensus Conference proposed that CP, bullous pemphigoid, LAD and EBA with predominant mucosal involvement had to be comprised under the same term, i.e. mucous membrane pemphigoid (MMP) (Chan *et al*, 2002). MMP was defined as a group of putative autoimmune, chronic inflammatory, subepithelial blistering diseases predominantly affecting mucous membranes that is characterized by linear deposition of IgG, IgA, or C3 along the BMZ (Chan *et al*, 2002).

On the basis of the above mentioned arguments, we believe that the diagnosis of LAD can not be confirmed in any of the cases with exclusive mucosal involvement reported to date (including those by (Leao *et al*, 2008), but in those mentioning a positive and specific IB (Egan *et al*, 1999; Letko *et al*, 2000).

Besides, we propose that all cases of 'desquamative gingivitis' featuring linear BMZ deposit(s) of Ig(s) (and/or C3) at DIF (and/or IIF) should be rather diagnosed as MMP.

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Table 1 Reported cases of linear IgA disease with exclusive mucosal involvement

Reference	*Age (years)*	*Gender*	*Mucous membranes involved*	*Histologic examination*	*DIF (linear BMZ deposits)*	*IIF*	*IB*
Kumar *et al* (1980)	69	F	Oral, ocular	Liquefaction degeneration of basal layer Lymphoplasmacytic dermal infiltrate	IgA	Negative	N.p.
Porter *et al* (1990)	69	M	Oral	Subepithelial split	IgA, C3	N.p.	N.p.
Porter *et al* (1992)	29	M	Oral	Subepithelial split	IgA	N.p.	N.p.
Kirtschig *et al* (1998)	38	M	Oral, genital	N.p.	IgA	Negative	Negative
Lazzaro and Lazzaro (1999)	59	M	Oral, ocular	N.p.	IgA	N.p.	N.p.
Cohen *et al* (1999)	78	F	Oral	Subepithelial split, Lichenoid infiltrate	IgA	N.p.	N.p.
Cohen *et al* (1999)	58	F	Oral	Lichen planus, Ulceration with chronic inflammation	IgA	N.p.	N.p.
Egan *et al* (1999)	N.p.	N.p.	Oral	N.p.	IgA	IgA to BMZ	IgA to 97 kDa
Letko *et al* (2000)	67	M	Ocular	N.p.	IgA	IgA to BMZ SSS: IgA on roof side	IgA to 97 kDa
Eguia del Valle *et al* (2003)	72	F	Oral	Subepithelial split, br/> Lymphoplasmacytic infiltrate	IgA, fibrinogen	N.p.	N.p.
Eguia del Valle *et al* (2003)	43	M	Oral	Subepithelial split, Lymphoplasmacytic infiltrate	IgA, fibrinogen	N.p.	N.p.
Talhari *et al* (2006)	75	M	Ocular	Subepithelial split, Mixed infiltrate	IgA	Negative	N.p.
Lewis *et al* (2007)	79	F	Oral	Subepithelial split, Mixed infiltrate with prevalence of eosinophils	IgA	Negative	N.p.
Angiero *et al* (2007)	57	F	Oral	Subepithelial split, Chronic infiltrate	IgA	N.p.	N.p.

DIF, direct immunofluorescence assay; BMZ, basement membrane zone; IIF, indirect immunofluorescence assay; IB, immunoblotting; F, female; M, male; N.p., not performed/reported; SSS, salt-splitted skin.

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