Recurrent aphthous stomatitis as an expression of pathergy in atopics

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ABSTRACT

Background: Recurrent Aphthous Stomatitis (RAS) may be part of the "atopic background." Recently it has been reported that aphtous stomatitis could be an expression of atopic diathesis. The aim of this study is to verify whether the prevalence of posttraumatic aphthae is higher in patients with RAS and atopic diathesis than in patients with RAS without atopy.

Material and Methods: In the past three years 39 new patients between 14 and 56 years of age and affected by idiopathic RAS have been observed. Atopic status and history of posttraumatic aphthosis were evaluated in all patients.

Results: The results appear to show that in our population the prevalence of posttraumatic aphthae is higher among atopic patients.

Conclusions: Not only RAS but also pathergy could be considered an expression of the rich clinical/symptomatic constellation of atopic diathesis.

Introduction

Recurrent aphthous stomatitis (RAS) has already been described by our team as possible heritage of an "atopic background" (1).

It has been reported that the pathogenesis of the aphthae is an immune-complex-mediated vasculitis and that innate immunity (2) as well as the free radicals, ROS (2), NO, and NO_2 may also play a role in particular (3, 4). This aphthoid reaction could be attributed to a tendency towards an aberrant immunologic response dominated by Th2 lymphocytes. (5–7).

Pathergy is a process that depends on innate or acquaired modified immunity, and reflects an exaggerated Th2/Th1 imbalance such as that usually prevalent in atopic diathesis (7, 8). Physical trauma is mentioned as a possible trigger of aphthous stomatitis (9).

Our intention in the present study was to verify the occurrence of posttraumatic aphthae in RAS patients, and particularly to observe if there is a difference in frequency of posttraumatic aphthae between atopic and non-atopic subjects.

KEY WORDS

stomatitis, aphthous, recurrent, atopy, pathergy

Table 1. Summary of the 27 patients with RAS and symptoms of atopy.

Name	Age	Sex	Related symptoms	PRIST	RAST	Patch test	Prick test	Family history	Causes of Traumatic Aphthosis
AL	18	M	AA	340	CH, Grs, HDM	–	CH, Grs, HDM	+	TCDI+
MS	32	F	AR	200	BT, HDM	–	HDM	+	M++
DD	48	M	AD, AA	2,000	Grs, HDM, Al, CF	HDM	Grs, HDM, Al, CF	+	TCDI++, M+++
FR	27	M	AD	280	CH	–	Grs	–	TCDI+
BR	18	M	AA	> 20,000	Pnt, HN, Grs, Al	HDM	Pnt, HN, Grs, Al Ca, HDM	+	M++
AC	43	F	AR	190	WP, WW	–	WP, Cmp	–	TCDI+
CV	22	M	AA, AR	680	CH	–	CH, PN	+	Oc++
BS	56	F	AR	280	CyT, HDM	–	HDM, Cmp	–	Oc+
JD	14	M	CU	640	CF, HDM	HDM	HDM, CF, WP, CM, Cl	+	M++
MM	37	M	AD	180	–	HDM	–	+	–
SC	14	F	AD, AA	320	Grs, HDM	–	Grs, HDM, Pnt, CM	+	M++, TCDI+
FF	22	M	AA, AR	1,200	Grs, WP, HDM	HDM	Grs, WP, HDM, CM	+	–
PA	21	F	AD, CU	1,200	HDM	–	HDM, CM, Pnt	–	M+++, TCDI+
GR	31	F	AA	720	CF, OlT, CyT	–	CF, OlT, CyT, Ca	+	Oc+
AT	42	F	AR, CU	360	HDM	–	HDM, Cc, Str	–	M+++, Oc++
BC	23	F	AR, AA	1,400	CH, DD, HD, HDM	HDM	CH, DD, HDM	+	M++
CB	40	F	AR	340	HDM	HDM	HDM	–	–
SA	11	F	AD	120	–	HDM	–	+	Oc+
ML	40	F	–	180	HDM	–	HDM	+	TCDI+
GG	16	M	AR	310	CH, PN	–	PN	+	–
MDF	18	M	AD	200	–	HDM	–	+	–
PV	14	F	AA, AR	400	WP, BT	–	WP	+	–
LL	16	M	AR	480	AF, LT, YD	–	AF, Cmp	–	–
PL	14	M	AR	280	HDM, Grs	–	HDM	+	–
FB	27	F	AA	310	HDM, Cmp	–	HDM, Cmp,	–	M++, Oc+
AT	41	F	AR, AD	430	HDM, Grs	Pb, HDM	HDM, Grs, Dl	+	M++, Oc+
SL	24	F	AD, AA, AR	> 9,000	HDM, Grs, CH, Dl	HDM	HDM, Grs, CH, Pnt, Cmp	+	–

Abbreviations:
AA: Allergic Asthma, AD: Atopic dermatitis, AF: Aspergillus fumigatus, Al: Albumen, AR: Allergic Rhinitis, BT: Birch Trees, Cc: Cocoa, CF: Corn Flour, CH: Cat Hair, Cl: Celery, CM: Cow's Milk, Cmp: Composite, CU: Chronic Urticaria, CyT: Cypress Tree, DD: Dog Dandruff, Dl: Dandelion, Grs: Grasses, HD: Horse Dandruff, HDM: House Dust Mites, HN: Hazelnut, LT: Linden Tree, M: Morsicatio, Oc: Other causes, OlT: Olive Tree, Pd: Potassium Dichromate, PN: Penicillum notatum, Pnt: Peanuts, Str: Strawberry, TCDI: Traumas Caused by Dentist's Interventions, WP: Wall Pellitory, WW: Wormwood, YD: Yellow Daisy

Materials and methods

In the past 3 years 39 new patients between the ages of 14 and 56 and affected by idiopathic RAS have been observed; none of them presented typical clinical of Behçet disease, iron deficiency, gastrointestinal diseases, endocrine alteration, or immunodeficiency.

All patients were investigated for family and personal history of atopy and had total IgE determination, specific IgE antibody test in serum, skin prick tests of common inhalant and food allergens (Lofarma, Italy). Skin patch tests of Dermatophagoides mix (Allergopharma, Germany). Our control group included 45 subjects, with an overall age and sex distribution similar to RAS patients group, who suffered from seborrhoeic dermatitis or tinea pedis/cruris or psoriasis o the scalp an/or the nails.

We considered 2+ and 3+ reactions to the skin prick tests of inhalant and food allergens and patch tests to be positive. We also considered concentrations of total IgE (PRIST) in the sera that were higher than 200 IU/ml to be elevated. In addition, antigen-specific IgE to common inhalant and food allergens were measured with the radioallergosorbent test (RAST).

All patients filled in a self-administered survey in which they were asked to state if they had ever noted the appearance of aphthae after an oral trauma such as bites, traumas caused by dentist's interventions, or other (use of a toothbrush, thermal injury, etc.), and if this

Table 2. Non-atopic patients.

Name	Age	Sex	Related symptoms	PRIST	RAST test	Patch test	Prick test	Family history	Causes of Traumatic Aphthosis
LB	48	M	–	60	–	–	–	–	–
CM	24	M	–	80	–	–	–	–	TCDI+
MT	25	F	–	40	–	–	–	–	–
AT	58	F	–	120	–	–	–	–	TCDI+
EC	17	F	–	140	–	–	–	–	–
OL	19	F	–	120	–	–	–	–	–
LF	41	M	–	40	–	–	–	–	TCDI+
MF	18	M	–	100	–	–	–	–	–
MT	14	F	–	100	–	–	–	–	–
AP	53	M	–	120	–	–	–	–	–
ST	23	F	–	130	–	Ni	–	–	–
RC	16	F	–	180	–	–	–	–	–

phenomenon, if present, had appeared a few times in life, more than once in a year (for a limited period of 1 to 3 years), or nearly constantly many times every year.

In processing the data, we assigned a value of 1+ (+) to subjects that remembered the occurrence of such episodes just a few times in life, 2+ (++) for more than one episode a year (for a limited period of 1 to 3 years), and 3+ (+++) for nearly constant episodes every year. Chi-square statistics were used to evaluate group differences.

Results

Twenty-seven out of 39 subjects presented clinical and/or laboratory evidence of atopy (Table 1) and 18 of them (66.7%) had a positive anamnesis, with variable degrees of severity, for posttraumatic aphthosis.

Of the 12 non-atopic patients, 3 (25.0%) reported posttraumatic aphthosis (Table 2).

Considering only subjects with 2+ and 3+ values for posttraumatic aphthosis, we registered 11 atopic patients and no non-atopic patients.

The prevalence of posttraumatic aphthosis is higher in females (59%) than males (47%), but due to the small size of the sample this result does not attain statistical significance.

There is no statistically significant correlation between the prevalence of posttraumatic aphthosis and other data analyzed (anamnesis, PRIST value, prick test, patch test, RAST).

Discussion

Data resulting from the present study seem to further confirm the relationship between RAS and atopy that has already been noted in our population, and seem to show that patients with this association more often have posttraumatic oral aphthosis ($\chi^2 = 5.8$; $p < 0.05$).

We believe that the low statistical significance ($p < 0.05$) achieved with our data should be ascribed to the small size of the sample, but the fact that 11 cases of aphthous stomatitis labeled as 2+ or 3+ have been discovered among the atopic subjects but none among the non-atopic ones could be an important clue.

Lastly, if posttraumatic aphthae are considered a pathergic reaction in RAS, their higher prevalence among patients with RAS and atopy would confirm the relationship between pathergy and atopy already assumed in the courses of other diseases (7, 8).

If the findings of our study are confirmed in a larger number of patients, this will constitute evidence for considering pathergy to be another expression of the rich clinical/symptomatic constellation of atopic diathesis.

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