

Table 1 Lymphocyte subpopulations in patients and controls

	Patients	Controls	Significance
Subpopulations*			
CD4	36.26 ± 2.22	43.44 ± 2.25	NS
CD8 <i>total</i>	50.24 ± 3.73	23.40 ± 1.85	<i>P</i> < 0.01
CD8 ^{dim}	4.56 ± 0.76	6.54 ± 1.29	NS
CD8 ^{bright}	45.66 ± 3.64	16.27 ± 1.36	<i>P</i> < 0.01
Ratios			
CD4/CD8	0.74 ± 0.09	1.80 ± 0.15	<i>P</i> < 0.01
CD4/CD8 ^{dim}	8.91 ± 0.46	7.45 ± 1.16	NS
CD4/CD8 ^{bright}	0.83 ± 0.11	2.83 ± 0.30	<i>P</i> < 0.01

* Percentages within lymphocyte population

Values are means ± SEM

NS: not significant

■ Defects in T-cell function are known to be present in patients with CVI, but the nature of these defects has still to be revealed. Loss of T-cell help and an excess of T-cell suppression (2) have both been documented. Pandolfi et al. (3), showed profound alteration in the lymphocyte subpopulations in CVI patients, including increased CD8⁺ cells, severe defect of CD4⁺ cells, and reduction of CD19⁺ cells. The increased proportion of CD8⁺ cells in CVI patients has been putatively associated with a possible veto effect of these cells on Ig production (2).

The use of flow cytometry allows the differentiation of two CD8⁺ subpopulations: one of high affinity (with a larger number of receptors: CD8⁺ ^{bright}), and another of low affinity (with a lower number of receptors: CD8⁺ ^{dim}) (4). Such subpopulations can be distinguished by staining intensity with anti-CD8 monoclonal antibodies. CD8⁺ ^{dim} and CD8⁺ ^{bright} subsets further appear to represent two distinct populations on the basis of functional analyses. The CD8⁺ ^{dim} subset would be more representative of cytotoxic cells, having cell markers of the natural-killer type (5); CD8⁺ ^{bright} cells contain a CD3⁺ subset with suppressive effect on antibody production and MHC-restricted cytolytic activity. Subsequently, it has been suggested that the true helper suppressor ratio is the CD4⁺ CD8⁺ ^{bright} ratio (4).

Our data show that CVI patients have an increased percentage of CD8⁺ cells compared to healthy volunteers, and that is mainly due to the increase in the CD8⁺ ^{bright}-cell percentage. Such alterations lead to the decrease in the CD4⁺ CD8⁺ ^{bright} ratio, and that change could suggest a decrease in the helper suppressor ratio. Nevertheless, caution should be used in extrapolating functional activities of T-cell subpopulations from the characterization of surface markers. Functional tests are required to identify such altera-

tions of CD8⁺ T-cell subsets as a possible pathogenetic mechanism. Therefore, the results should be considered preliminary.

Key words: common variable immunodeficiency; CD8; flow cytometry.

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Anaphylactoid reaction in relation to sialolithiasis

SOME anaphylactoid reactions are presumably associated with immunocomplex formation and subsequent complement activation.

We report the case of a 46-year-old man who presented eight episodes of severe anaphylaxis during a 3-year period, exclusively in relation to acute episodes of sialolithiasis. He had pruritus and swelling of the lips and tongue, dysphagia, dysphonia, and progressive upper respiratory difficulty, as well as intense facial and palpebral edema. He also had hypotension and vomiting. The symptoms remitted after administration of epinephrine, corticosteroids, and fluid therapy in the emergency unit. The gland was removed in September 1994, and the patient was asymptomatic at last follow-up.

We performed skin prick tests with common inhalants of our environment and several foods (eggs, milk, nuts, and shellfish; C.B.F. Leti,

Barcelona, Spain). Stool examination and chest radiography were done, and laboratory analyses included blood count and chemistry, sedimentation rate, urinalysis, proteinogram, and determination of immunoglobulin and cryoglobulin levels in serum. In addition, serum was screened for auto-antibodies (rheumatoid factor, antinuclear, anti-DNA, antimitochondrial, and anti-smooth-muscle antibodies).

Assays for total IgE levels (EIA-PRIST, Pharmacia, Uppsala, Sweden), and specific IgE levels to *Ascaris* and *Equinococcus* antigens (CAP System, Pharmacia) were performed in serum samples.

Before and after the gland was removed, we measured serum levels of complement factors C3 and C4 (NOR-Partigen®-C4 and C3, Behring), C1inh (NOR-Partigen C1 inactivator, Behring), and circulating immune complexes (CIC) (Enzyme immunoassay, Quidel), according to the manufacturers' instructions. All measurements were based on the radial immunodiffusion technique, and were repeated several times.

In two blood samples obtained after anaphylactic episodes, we measured fibrinogen (ACL 3000 Coagulation System, Instrumentation Laboratory, Milan, Italy) and D-dimers (D-Dimer test, Boehringer, Mannheim, Germany) to test activation of the fibrinolytic system, as reported by other authors (1, 2).

The salivary glands were examined with computed tomography (CT) and echography. Tissue samples obtained from the removed gland were used for histologic examination and direct and indirect immunofluorescence assays.

All the results of our laboratory analyses and of the rest of our studies and tests were normal.

The only exception was the CIC, C3, and C4 factor levels, found before and after the gland was removed (Table 1). Complement factor C1inh was within the normal range both before and after the surgery. These findings suggested activation of the classic complement pathway by an immune complex reaction. This mechanism can lead to the

generation of the anaphylatoxins C3a and C5a (3-5), which can contract smooth muscle directly and induce the release of mediators from mast cells and basophils (products of C3a and C5a could not be measured in our laboratory).

Echographic and CT studies showed the presence of calculi and dilation of the intragland duct in the left submaxillary gland. Histologically, the left gland showed dilated ducts with localized areas of inflammatory infiltrate, and atrophy of the acini.

Indirect immunofluorescence showed a deposit of IgG on the apical surface of the epithelial cells of the interlobular excretory ducts and on the vessels, suggesting the presence of an antigen in these areas.

We believe that the patient developed an autoimmune response to an antigen located in the ductal epithelium, and that the injury produced by the stone caused the release of the antigen into the bloodstream. This led

*Is this a new form of
autoimmune disease?*

to the formation of CIC and subsequent complement activation, which caused the anaphylactoid episodes. Our hypothesis is supported by the fact that there is no other apparent cause, by the immunologic alterations observed, and by the fact that the patient was free of symptoms at the time of writing. We were not able to determine the nature of the antigen, and we do not know whether it is a normal antigen of the salivary glands or a neoantigen expressed only in this patient's gland.

A review of the literature revealed no similar cases in which an autoimmune response showed exclusively anaphylactoid symptoms.

Key words: autoimmune disease; anaphylactoid reaction; circulating immune complexes; sialolithiasis.

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Table 1 Serum levels of complement factors and circulating immune complexes before and after removal of left submaxillary gland in September 1994

Time	C3 mg/dl (NR = 52-120)	C4 mg/dl (NR = 20-49)	C1inh mg/ml (NR = 15-33)	CIC µgEq/ml (NR < 4 µgEq/ml)
January 1994	40	8	28	10
April 1994	45	8	30	10
July 1994	42	7	30	10
October 1994	65	25	29	0
November 1995	70	30	31	0
May 1995	68	27	30	0

NR = normal range

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