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Salivary Immunoglobulin Related Proteins in 24 Patients with Multiple Myeloma

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Mixed saliva and blood of 24 cases of multiple myeloma (MM) were collected and the immunoglobulin and light chain concentrations compared with that found in the saliva and blood of 16 age matched control patients. The concentrations of salivary IgA, IgG and lambda light chains were significantly increased in IgA-, IgG- and lambda light chain producing MM respectively. Salivary IgA concentration in non-IgA MM and salivary IgG concentration in non-IgG MM were within normal ranges. Despite a significant decrease in circulating normal immunoglobulins, this study fails to support suppression of normal salivary immunoglobulin concentrations in patients suffering MM.
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INTRODUCTION

IN THE majority of patients with multiple myeloma (MM) serum protein electrophoresis will disclose the presence of a monoclonal paraprotein which may present as an increase in one of the immunoglobulin classes and/or immunoglobulin-related light chains (Bence-Jones proteins). MM are immunochemically typed according to the circulating monoclonal immunoglobulin and/or light chain type produced by the disseminated neoplastic plasma cells. This typing is helpful in predicting complications and prognosis of patients suffering MM [1]. The decrease in the concentrations of circulating normal immunoglobulins predispose to opportunistic infections, a serious and often terminal complication in MM [2].

Reports on the presence of abnormal immunoglobulin-related proteins in secretions of MM patients are infrequent in the literature. Analysis of saliva of 10 patients with MM [3], identified monoclonal IgA in 5 out of 7 patients with IgA MM and monoclonal IgG in both patients with IgG MM. No free light chains were detected in the saliva of the 1 patient with light chain producing MM. An increased concentration of IgG was present in the saliva of 1 case of IgG MM studied by Brandtzaeg [4].

The purpose of this study was to determine the concentrations of immunoglobulins and light chains in saliva and serum of 24 patients with MM and to compare the values obtained with that found in age matched, systemically healthy patients.

PATIENTS AND METHODS

Whole saliva and blood of 24 patients with MM and 16 age matched systemically healthy control patients were collected after a thorough clinical oral examination. The saliva was expressed with the aid of a sterile syringe from a cottonwool swab after it had been chewed for 3 min. Patients with overt signs of gingivitis or periodontitis were excluded from the control group of the study. Quantitation of IgA, IgG and IgM levels in serum were done with rate nephelometry (Auto ICS, Beckman Instruments Inc. Fullerton, U.S.A.). Immunochemical typing of the light chains in serum was carried out with immunofixation electrophoresis (Paragon™ IFE gels, Beckman Instruments Inc.).

Salivary immunoglobulins and light chains were quantitated with low concentration radial immunodiffusion plates (LC-Partigen® and M-Partigen®, Behringwerke AG, Marburg, West Germany). The concentrations were expressed in grams per litre (g/l), compared with the respective circulating concentrations and the findings were subjected to statistical analysis using Student's *t*-test for uncorrelated data.

RESULTS

Clinical examination of the MM patients revealed no signs of oral mucosal infections. 17 patients had IgG MM, 4 IgA MM and 3 light chain producing MM (two kappa- and one lambda MM). The mean concentrations and standard deviations of the major immunoglobulin classes in MM patients and the control group are expressed in Table 1 and the immunoglobulin light chain concentrations in Table 2. The circulating residual immunoglobulin concentrations in MM patients were generally below the normal ranges (Table 3) and that of the control group (Table 1). No significant differences were found between salivary IgA concentrations in non-IgA MM and the control group ($P > 0.05$) and salivary IgG levels in non-IgG MM and the control group ($P > 0.8$). In IgA MM, salivary IgA concentrations were found to be significantly higher than in the control group ($P < 0.01$). A significant increase in salivary IgG in IgG MM ($P < 0.01$ was also present. The concentration of lambda light chains in the saliva of lambda-producing MM was significantly higher than the control group ($P < 0.01$). Although salivary kappa light chain concentrations in kappa-producing MM showed great variations, with single values far above those of control patients, statistical analysis failed to prove a significantly higher concentration of kappa light chains in kappa-producing MM when compared to the control group ($P > 0.05$).

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Table 1. Concentrations of major immunoglobulin types in MM- and control patients

	Saliva g/l		Serum g/l		
	IgG	IgA	IgG	IgA	IgM
IgA MM (2 × IgA κ's 2 × IgA λ's)	0.04 ± 0.03	1.1 ± 0.9	5.85 ± 4.4	41.5 ± 25.3	2.0 ± 3.5
IgG MM (12 × IgG κ, 5 × IgG λ)	0.22 ± 0.16	0.05 ± 0.05	75.9 ± 32.4	0.63 ± 0.6	0.57 ± 0.42
Lambda MM ($n=1$)	0	0.14	5.5	0.3	0.2
Kappa MM ($n=2$)	0.7 ± 0.01	0.04	13.1 ± 1.5	0.65 ± 0.07	0.25 ± 0.07
Control ($n=16$	0.047 ± 0.03	0.081 ± 0.03	20.0 ± 6.6	3.28 ± 1.3	2.16 ± 1.7

Table 2. Light chain concentrations in MM- and control patients

	Saliva g/l		Serum g/l	
	κ	λ	κ	λ
κ-producing MM ($n=16$)	0.44 ± 1.0	0.006 ± 0.01	43.5 ± 24.5	2.2 ± 1.8
λ-producing MM ($n=8$)	0.03 ± 0.06	0.16 ± 0.12	4.4 ± 2.9	55.1 ± 37.0
Control ($n=16$)	0.03 ± 0.03	0.02 ± 0.01	13.4 ± 5.3	7.04 ± 1.5

Table 3. Normal ranges

Serum	
IgG	14.4—22.7 g/l
IgA	1.9—4.7 g/l
IgM	0.7—2.6 g/l
κ	5.66—13.0 g/l
λ	3.04—7.35 g/l
Saliva	
IgA	0.05—0.48 (mean 0.137) g/l*
IgG	0.007—0.037 (mean 0.016) g/l
κ	N/A
λ	N/A

*Grönblad 1981 [5].

DISCUSSION

This study represents the largest series in which the concentrations of immunoglobulin related proteins in saliva of patients with multiple myeloma were determined. Although changes in the circulating immunoglobulin concentrations are well documented [2], little is known of alterations in salivary immunoglobulins and immunoglobulin related proteins in this disease.

A study using immunoelectrophoresis to determine the presence of salivary immunoglobulins in 10 patients suffering MM [3] failed to express the concentrations and the findings can therefore not be compared directly to ours. These authors conclude that although the concentration of monoclonal immunoglobulin is low in saliva, its presence is adequate proof that circulating immunoglobulins can find their way into external secretions. The technique employed in our study is more sensitive and made accurate quantitation of the different immunoglobulin-related proteins possible. All our cases of IgA MM had significantly increased concentrations of IgA in saliva when compared to the salivary IgA concentrations found in the control group. The same applies to salivary IgG in IgG MM and lambda light chain concentrations in the saliva of lambda producing MM. Despite a few kappa producing MM that had high salivary kappa concentrations, statistical analysis failed to support a significant increase in salivary kappa concentrations in kappa producing MM when compared to control values. Although transmission of circulating immunoglobulin related proteins to saliva appears to be enhanced by elevated serum concentrations, no direct correlation could be found between these values.

The occurrence of systemic immune suppression in MM is well documented. This study supports the findings of Coelho *et al.* [3] which failed to identify salivary immunoglobulin impairment in MM. No statistical evidence of a decrease in the concentration of normal salivary IgA in non-IgA MM patients could be found in our study. This was confirmed in that no clinical evidence of an opportunistic infection was seen in the oral cavities of our MM patients. The mechanism by which normal immunoglobulin production is suppressed in MM, is not clearly understood [6]. It has been postulated that neoplastic plasma cells secrete a factor capable of activating suppressor macrophages which in turn inhibit normal B cell function [7]. The observation that salivary gland associated immunoglobulin production is not altered in MM, adds an interesting parameter to the debate on MM-induced immunoparesis.

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