HUMORAL IMMUNE RESPONSE IN LIBYAN PATIENTS WITH CHRONIC AND ACUTE BACTERIAL INFECTIONS

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SUMMARY: Serum immunoglobulin levels in 34 Libyan patients (age: 45 ± 14 years; sex: 25 males, 9 females) with chronic active pulmonary tuberculosis (CAP-TB) and 25 Libyan patients (age; 41 ± 12 years; sex: 17 males, 8 females) with acute urinary tract infection with Klebsiella species (AUTI-KS) together with 26 health Libyans (CS) (age: 40 ± 20 years; sex: 23 males, 11 females) were studied to evaluate and compare humoral immune response in chronic (CAP-TB) and acute (AUTI-KS) infections. It was observed that mean serum concentration of all the immunoglobulin classes (IgG, IgA, IgM, IgD, IgE) in CAP-TB were significantly higher than CS as well as AUTI-KS (P<0.05). Also, significantly high proportion of patients with CAP-TB had all the classes of immunoglobulin above the normal range. In case of patients with AUTI-KS significantly high proportion had only IgG and IgM levels above the normal range (P<0.05), whereas the distribution for IgA, IgD, and IgE were similar to those of CS (P>0.05). These findings are discussed in comparison with reports from other parts of the world and are taken as evidence to reflect the different nature and extent of humoral immune response in chronic (CAP-TB) and acute (AUTI-KS) infections. It is suggested that quantitative estimation of total serum immunoglobulin in all classes may help to make differential diagnosis of whether a bacterial infection is chronic or acute.

Key Words: Immunoglobulin, Tuberculosis, Urinary tract infection.

INTRODUCTION

Humoral immunity has an important role to play in host defense against infections, particularly, of bacterial origin. The race, age, environmental and genetic factors we well as the type of infection seem to influence the course of host immunoglobulin response (2). The reports regarding serum immunoglobulin levels in patients with chronic active infection, e.g. pulmonary tuberculosis (CAP-TB) are conflicting (1,7,9). There is also not sufficient data a vailable about serum immunoglobulin concentrations in patients with acute upper urinary tract infection with Klebsiella species (AUTI-KS). CAP-TB is a chronic infection while AUTI-KS is an acute infection. As we were not aware of any study of humoral immune response in Libyan patients with CAP-TB and AUTI-KS, the present study was undertaken for comparison.

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MATERIALS AND METHODS

Subjects

Blood samples from 34 patients (mean age ±SD: 45±14 years; sex: 25 males, 9 females) suffering from CAP-TB were obtained from El-Kwafia Hospital, Benghazi and Chest Centre, Benghazi. The serum specimens were separated and stored at -40°C until analyzed. These patients were in the hospital for various lengths of time varying from 9 months to 14 months and were since under treatment for tuberculosis. The diagnosis of CAP-TB was based on clinical picture (cough, malaise, easy fatigability, weight loss, low grade afternoon fever, night sweat and some times blood in the sputum), chest X-ray findings (hilar lymph node enlargement associated with a small parenchymal lesion with calcification, cavitation, and apical and subapical infiltration) and positive skin test (Mantoux test) and was confirmed by the demonstration of acid-fast bacilli in sputum by Zeihl-Neelsen method (12). The 25 patients with AUTI-KS (mean age ±SD:41±12 years; sex: 17 males, 8 females) were obtained from

7th October Hospital, Benghazi and 7th April Hospital, Benghazi. The diagnosis of AUTI-KS was based on clinical presentation (burning and pain on urination, chills and fever, urinary urgency and frequency, suprapubic and low back pain, noctruia and some patients with gross haematuria) and was confirmed by positive urine culture for KS (4). These patients were bled before any antibiotic therapy was started, serum specimens were collected and stored at -40°C until analyzed. Twenty-six, healthy Libyans (mean age ±SD: 40±20 years; sex: 23 males, 11 females) were also included in the study as control subjects (CS) for comparison.

Estimation of serum immunoglobulins

Quantitative determination of serum levels of immunoglobulin G (IgG), immunoglobulin A (IgA), immunoglobulin M (IgM) and immunoglobulin D (IgD) were made by the single radial immunodiffussion technique of Mancini *et al.* (8) using immonukits of bioMereieux, France and the results were expressed as milliograms per deciliter (mg/dl). The serum levels of immunoglobulin E (IgE) was measured by enzyme-linked immunosorbent assay (ELISA) method using IgE-ELISA Kits of BioMerieux, France (5) and the results were expressed as international units per ml (iu/ml).

Statistical Analysis

The results were compared statistically by Student's t-test for differences between means and by Chi-square (χ^2)-test for differences between proportions.

RESULTS

The results of the estimation of serum immunoglobulins are shown in Table 1. The statistical analysis by Student's t-test revealed that mean serum concentration of all the immunoglobulin classes (IgG, IgA, IgM, IgD, IgE) in CAP-TB were significantly higher than CS as well AUTI-KS, whereas only IgG and IgM levels in AUTI-KS were significantly higher than CS (Table 2). This was reflected well when serum levels of immunoglobulins were distributed according to whether they were above the normal range (> mean of CS plus 2 SD) or within normal range (≤ mean plus 2 SD) (Table 3). A significantly high proportion of patients with CAP-TB had all the classes of immunoglobulin above the normal range (Table 3, Table 4). In case of patients with AUTI-KS significantly high proportions had serum IgG and IgM levels above the normal range, whereas the distribution for IgA, IgD and IgE were similar to those for CS (Table 3, Table 4).

Table 1: Serum immunoglobulin profiles in patients and control subjects.

SERUM IMMUNOGLOBULIN		SUBJECTS		
		CAB-TB	AUTI-KS	CS
IgG (mg/dl)	n	34	25	26
	Mean ± SD	2021± 344	1510± 253	1031± 148
	Range	1304-2912	1259-2016	702-1378
IgA (mg/dl)	n	34	25	26
	Mean ± SD	408± 95	259± 46	239± 38
	Range	285-610	201-355	175-366
IgM (mg/dl)	n	34	25	26
	Mean ± SD	330± 52	232± 44	120± 25
	Range	155-495	140-360	75-195
IgD (mg/dl)	n	34	25	26
	Mean ± SD	3.8± 0.6	2.2± 0.5	1.9± 0.4
	Range	2.4-6.6	1.6-3.6	1.4-3.0
IgE (iu/ml)	n	34	25	26
	Mean ± SD	365± 100	81± 27	72± 31
	Range	130-652	51-190	29-170

Table 2: The statistical analysis by Student's t-test of the results stated in Table 1.

	'P' values*		
	CS vs CAP-TB	CS vs AUTI-KS	CAP-TB vs AUTI-KS
IgG	S	S	S
IgA	S	NS	S
IgM	S	S	S
IgD	S	NS	S
IgE	S	NS	S

* S: Significant (P< 0.05); NS: Not significant (P>0.05).

Table 3: The distribution of subjects in relation to their serum immunoglobulin levels grouped as within normal or above normal range*.

	CAP-TB		AUTI-KS		CS	
	Within normal	Above normal	Within normal	Above normal	Within normal	Above normal
Immunoglobulin G	2/34 (6%)	32/34 (94%)	5/25 (20%)	20/25 (80%)	24/26 (92%)	2/26 (8%)
Immunoglobulin A	4/34 (12%)	30/34 (88%)	20/25 (80%)	5/25 (20%)	24/26 (92%)	2/26 (8%)
Immunoglobulin M	7/34 (20%)	27/34 (80%)	2/25 (14%)	23/25 (86%)	25/26 (96%)	1/26 (4%)
Immunoglobulin D	8/34 (24%)	26/34 (76%)	23/25 (92%)	2/25 (8%)	25/26 (96%)	1/26 (4%)
Immunoglobulin E	3/34 (9%)	31/34 (91%)	22/25 (90%)	3/25 (10%)	25/26 (96%)	1/26 (4%)

* Within normal range ($\leq$ Mean $\pm$2SD) $\rightarrow$Immunoglobulin G: $\leq$1328 mg/dl, Immunoglobulin A: $\leq$315 mg/dl, Immunoglobulin M: $\leq$159 mg/dl, Immunoglobulin D: $\leq$ 2.7 mg/dl, Immunoglobulin E: $\leq$134 iu/ml;
Above normal range (> Mean $\pm$2 SD) $\rightarrow$ Immunoglobulin G: > 1328 mg/dl, Immunoglobulin A: >315 mg/dl, Immunoglobulin M: > 159 mg/dl, Immunoglobulin D: >2.7 mg/dl, Immunoglobulin E: > 134 iu/ml.

DISCUSSION

In an attempt to evaluate and compare the humoral immune response in patients with chronic (CAP-TB) and acute (AUTI-KS) infections, serum immunoglobulin levels were determined. Our findings that all classes of immunoglobulin were elevated in patients with CAP-TB are in accordance with previous reports from Nigeria (9), Washington (7) and Iraq (1). In contrast, other studies done in India (6) and Israel (11) reported significant increases only in mean IgG and IgA levels in patients with CAP-TB. In our patients with AUTI-KS we observed elevation of both IgG and IgM levels in contrast to the report of only IgM elevation (11). Serum IgA, IgD and IgE levels were not affected in our patients with AUTI-KS in contrast to our patients with CAP-TB. These differences in nature and extent of humoral immune response in our patients reflect the different nature of these two infections. CAP-TB is a chronic infection and presents a chronic antigenic stimulation while AUTI-KS results in acute antigenic stimulation of the immune system. Chronic antigenic stimulation is known to induce increased immunoglobulin production in all classes, but acute antigenic stimulation results in primary immune response leading to elevation of IgM-class of immunoglobulin mainly (10). The hypergammaglobulinaemia found in patients with CAP-TB may reflect specific as well as non-specific polyclonal activation of B-lymphocytes (3). Although the IgG and IgM response in patients with AUTI-KS can be explained on the bases of primary immune response the mechanism of polyclonal B-cell activation can still be implicated. Many bacterial species are known to be capable of non-specific stimulation of B-lymphocytes and cause polyclonal B-cell activation, DNA-synthesis and proliferation and immunoglobulin synthesis (3). The quantitative estimation of total serum immunoglobulin in all clesses (IgG, IgA, IgM, IgD, IgE) may therefore help to make differential diagnosis of whether a bacterial infection is chronic or acute in nature.

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Table 4: The statistical analysis by Chi-square (χ^2) test of the distribution of subjects in relation to normal and abnormal serum immunological levels as stated in Table 3.

	CS vs CAP-TB		CS vs AUTI-KS		CAP-TB vs AUTI-KS	
	χ^2	P	χ^2	P	χ^2	P
IgG	28.536	< 0.001	25.125	< 0.001	0.874	> 0.1
IgA	8.687	< 0.01	1.432	> 0.1	7.213	< 0.01
IgM	7.835	< 0.01	7.934	< 0.01	0.645	> 0.5
IgD	6.826	< 0.01	0.312	> 0.5	8.214	< 0.01
IgE	22.645	< 0.001	0.968	> 0.1	24.352	< 0.001

P< 0.05: Significant; P> 0.05: Not significant.

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