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MONOCLONAL GAMMOPATHY
A THREE YEAR STUDY ON PARAPROEINEMIAS

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ABSTRACT

Sera from 22 patients (16 males + 6 females) with electrophoretically and immunologically secured diagnosis of monoclonal gammopathy were tested for various biochemical parameters. The final clinical diagnosis showing gamma-globulinemias in them was in the order of multiple myeloma (MM) 20 nos, Waldenstrom macroglobulinemia (MW) 1 no. and light chain disease (LCD) 1 no. The incidence of plasma cell neoplasm among Saudies is not very rare. The predominant type is IgG myeloma (74%) with a kappa to lambda ratio of 2 : 1. Bence Jones Proteinuria is comparativly less common. Elevated levels of gamma glutamy1 transpeptidase (GGT) in a good number of patients indicate the high occurrence of hepatic involvement in such patients.

INTRODUCTION

Laboratory investigations of paraproeinemias can provide useful evidence about beta-cell proliferations. The identification, typing and measurement of paraproteins are consequent in the diagnosis and management of beta-cell tumours[1,2,3,4] Clinicopatholocial importance of paraproteins lies in their use as tumour markers for the diagnosis and monitoring of malignancies of bet-cell origin. Myeloma is by far the common of the disorders giving rise to paraprtoeins of neoplastic origin.

The incidence of paraproteins in peripheral blood in general population has been estimated as 0.2 - 0.9 per cent and the annual occurrence of MM varies from 2.0 - 3.1 per 100,000 of general population or 6.3 per 100,000 in persons older than 30 years[5]. It is slightly more in males than females and the incidence varies in different ethnic groups and in different parts of the world[5,6,7,8]. In Saudia Arabia, some work has already been done at various centres to evaluate the incidence and pathophysiology of the disease[9,10].

A review of current literature on monoclonal gammopathies and paraproteins reveals that the appearance of paraproteins precedes other malignancies by many years[4,5,11]. Of the several types of uncontrolled neoplastic proliferations of paraproteins producing clone, MM is the most frequently observed neoplasm. The course and prognosis of MM appears to relate to some extent to the class of heavy chain or light chain of the paraprotein relates to tumour cell mass in myeloma[12,13]. Thus, WM, MM and alpha HCD may be

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used in monitoring these conditions[14]. Majority of paraproteins belongs to IgG class and approximately 2/3 has kappa light chain but the ratio of kappa or lambda chain varies among different classes of heavy chains.[5] Identification of Bence Jones proteins (BJP) or free light chains in urine is essential for the assessment of renal function impairment in myelomatosis[15,16].

PATIENTS AND METHODS

Riyadh Central Laboratory is a referral Centre for a large number of hospitals and clinics all over the region, as well as out patient clinics for the patients. During the period commencing from June 1984 to May 1987, five hundred forty five samples of sera were mad available by there centres for elecrophresis aiming at the separation and identification of serum proteins.

In this study cellulose acetate membrane was used as a supporting medium (supplied by M/S Helena Laboratories Beaumont, Texas, U.S.A.). Each electropherogram was then classified as per reference chart supplied by M/S Helena Laboratories. Samples exhibiting monoclonal gammopathy were further subjected to immunoglobulin typing and other tests. Concentrated urine samples (Minicon B-15 concentrator was used for this purposes) of these patients were also subjected to heavy and light chains typing.

Heavy chains were identified by immunochemical method using a ca III autoanalyser (M/S. DuPont Company Clinical Systems Div., Wilmington, DE, U.S.A.). Light chains were typed by the technique of immunofixation[19] (M/S Helena Laboratories). Estimation of total protein in urine was done by sulphosalicylic acid method[20,21]. Urea, Creatinine, Calcium, Gamma glutamyltrans-peptidase (GGT) and total protein in sera were measured by using a c a III autoanalyser.

RESULTS AND DISCUSSION

The elecropherogram of 545 sera, on comparison with reference chart, revealed a total of 159(29%) abnormal patterns. Out of these 159 cases, 22 were typical monoclonal gammopathies. At the time of presentation or later, all these patients were diagnosed clinically, with strong biochemical, cytological and radiological evidence, as neoplasm of plasma cells. Break up of the diagnosis showed 20 cases of MM, 1 of WM and 1 of plasma cell cytoma. Age range of these patients was 42-72 years. Although the study group was small but its male : female ratio is greater as compared to the Western world[26]. We are not sure of its statistical significance in large groups which needs to be investigated. Inclusion of three patients of other nationalities in table 1 is purposive. They displayed a dissimilar biochemical profile in their analyses. We consider that this would help to have a more comprehensive comparison.

TABLE I : Identification of Twenty Two Patients

Patient No	Age in Years	Sex	Nationality
1.	49	Male	Saudi
2.	58	Male	Saudi
3.	68	Male	Saudi
4.	56	Male	Saudi
5.	62	Female	Saudi
6.	48	Male	Saudi
7.	62	Male	Saudi
8.	54	Female	Saudi
9.	72	Male	Saudi
10.	52	Male	Saudi
11.	62	Female	Saudi
12.	50	Female	Saudi
13.	42	Male	Saudi
14.	60	Male	Saudi
15.	48	Female	Saudi
16.	58	Male	Saudi
17.	64	Male	Saudi
18.	46	Female	Saudi
19.	61	Male	Saudi
20.	54	Male	Syrian
21.	52	Male	Yemeni
22.	60	Male	Egyptian

It is clear from table 2 that the predominant class of myeloma is IgG type (72.7%) with a kappa to lambda ratio of 1 : 1 WM and LCD are rare.

TABLE 2 **Serum Parameters of Twenty Two Patients**

Patient No.	GGT U/L	Urea mg/dl	Calcium mg/dl	Creatinine mg/dl	Light chain	Heavy chain	Concentration of paraproteins gm/dl
1	85	28	11.6	1.4	Kappa	Gamma	6.0
2	112	46	10.8	2.1	Kappa	Gamma	6.4
3	310	48	13.2	2.4	Lambda	Gamma	8.2
4.	180	29	9.6	1.2	Kappa	Gamma	5.4
5.	42	38	8.8	1.6	Lambda	Alpha	4.6
6.	85	32	9.0	1.0	Kappa	Gamma	4.2
7.	116	36	10.6	1.9	Kappa	Gamma	7.2
8.	45	44	9.8	1.4	Kappa	Gamma	5.0
9.	98	58	9.0	3.0	Kappa	Mieu	0.9
10.	85	40	11.2	1.6	Lambda	Gamma	6.1
11.	55	28	9.4	0.9	Kappa	Gamma	2.8
12.	240	48	10.4	3.0	Lambda	Alpha	4.2
13.	32	28	10.8	1.2	Kappa	Gamma	3.2
14.	128	54	12.0	1.8	Kappa	Gamma	8.2
15.	106	42	10.8	2.0	Lambda	Gamma	6.2
16.	38	40	9.0	1.2	Kappa	Alpha	3.2
17.	42	68	9.8	2.4	Lambda	Gamma	5.8
18.	96	28	10.8	0.8	Lambda	Gamma	5.4
19.	52	32	8.8	1.6	Kappa	Gamma	3.4
20.	48	42	10.0	2.0	Kappa	—	—
21.	212	22	11.0	1.2	Kappa	Alpha	3.8
22.	68	45	12.4	2.8	Lambda	Gamma	9.8

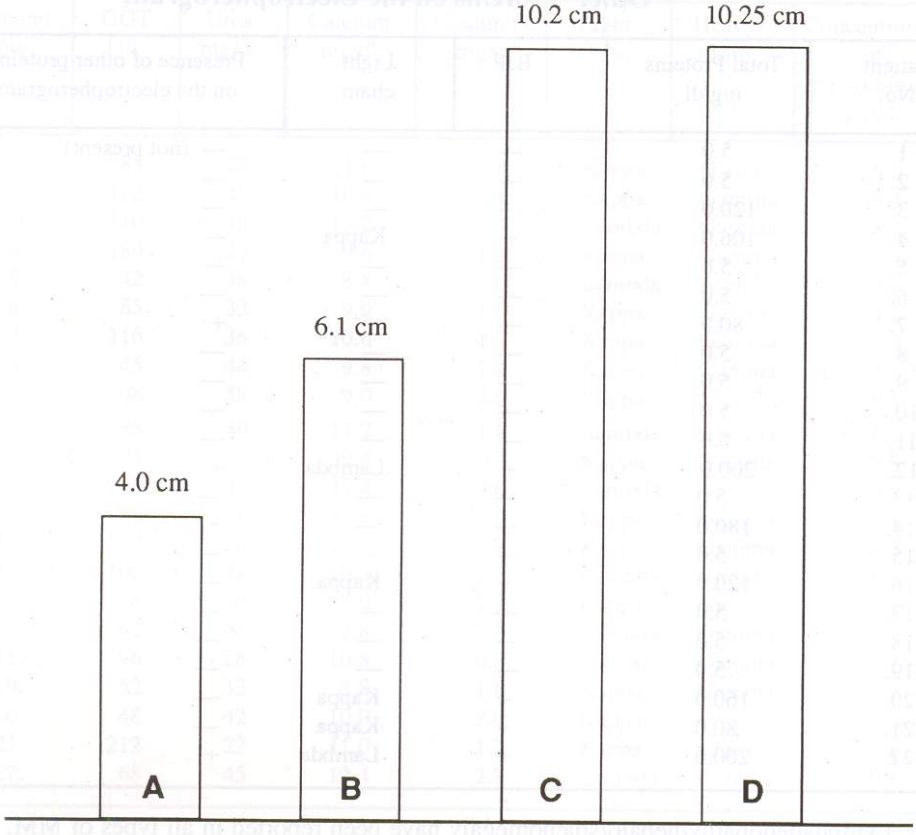
Table 3 reveals a picture of B.J. proteinuria and/or other forms of proteinuria. Impairment of renal function is a serious condition in MM[6,22]. Precipitation of B.J.P. and other plasma proteins in tubules may lead to myeloma kidney[23]. Up to 70% of patients with MM develop B.J. proteinuria. But our experience is strikingly different. In the present study only 27.3 % B.J proteinuria was observed. Half of the B.J. proteinuria patients were repatriates. This shows that MM patients in Saudia Arabia develop B.J. proteinuria to a lesser extent.Although the assessment of mortality rate was beyond the scope of this study, our findings agree with those of Under[10]. The amount of B.J.P. in urine depends on the rate of synthesis and degradation, size of molecules, glomerular permeability, tubular catabolism, and urinary volume. Which of these factor/factors influence the law percentage of B.J.P. patients among the Saudia MM patients is presently unclear. Some of he patients developed tubular proteinuria as was evidenced by urinary proteins of alpha$_1$, alpha$_2$ and beta , mobility withtout B.J.P. So, according to the renal status of individual patients, some of them are predisposed to proteinuria at a certain age of the progression of the disease which may accompany B.J. proteinuria.

TABLE 3 Urine Parameters Showing Total Proteins, BJP, Light Chain and Other Proteins on the Electropherogram

Patient No.	Total Proteins mg/dl	BJP	Light chain	Presence of other proteins on the electropherogram
1.	5.0	—	—	— (not present)
2.	5.0	—	—	—
3.	120.0	—	—	—
4.	106.0	+	Kappa	—
5.	5.0	—	—	—
6.	5.0	—	—	—
7.	80.0	—	—	+
8.	5.0	—	—	—
9.	5.0	—	—	—
10.	5.0	—	—	—
11.	5.0	—	—	—
12.	200.0	+	Lambda	+
13.	5.0	—	—	—
14.	180.0	—	—	+
15.	5.0	—	—	—
16.	120.0	+	Kappa	—
17.	5.0	—	—	—
18.	5.0	—	—	—
19.	5.0	—	—	—
20.	160.0	+	Kappa	—
21.	80.0	+	Kappa	—
22.	200.0	+	Lambda	+

Lymphadenopathy/hepato/splenomegaly have been reported in all types of MM, but highest in IgD group (50%)[5]. In our study, we found that hepatomegaly; as evidenced by raised GGT serum levels (with normal GPT and normal to moderately increased ALP) gives a good comparative study of this phenomenon (figure 1).

Figure 1 : Electro Pherogram : Mean GGT values for various groups



A. Mean of the normal reference range assigned for the methodology
B. Mean of the values obtained for 19 number of patients with normal electropherogram.
C. Mean of the values obtained for 19 Nos. monoclonal gammopathy patients.
D. Mean of the values obtained for 19 Nos of polyclonal gammopathy.

Immunoparesis has been observed in 90% patients with paraproteinemia[24]. The present study showed suppression of polyclonal immunoglobulin in 70% of IgG class and 50% in IgA class. The patients with WM, IgG and IgG were suppressed significantly. Serum of this patient showed hyperviscosity and positively responded to Sias test.

In general the paraproteinemia in Saudis exhibits certain typical and special features in their pathophysiology.

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