SIGNIFICANCE OF THYROID MICROSOMAL ANTIBODY IN GRAVES' DISEASE

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ABSTRACT

Thyroid microsomal antibody (MsAb) was estimated in 48 patients with Graves disease (15 newly diagnosed, 15 on drugs for about 4 weeks and 18 euthyroid with drug treatment) and twenty age and sex matched controls. The diagnosis of Graves' disease (GD) was based on clinical history, physical examination and thyroid function tests, viz. 1311 uptake, thyroid scintigram and serum T3, T4 and TSH levels. MSAb was positive in 93.3% of newly diagnosed as well as hyperthyroid GD patients on drugs. Eighty-three percent euthyroid GD patients and 20% normal controls also showed MSAb positivity. The titres of newly diagnosed patients were significantly raised ($P < 0.05$) than those of euthyroid patients and controls indicating the diagnostic as well as prognostic significance of MSAb in Graves' disease (JPMA 43: 11, 1993).

INTRODUCTION

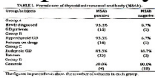
Graves' disease is a multisystem disorder of immunological origin. It is characterized by hypcr-thyroidism with diffuse toxic goitre, ophthalmopathy and dermopathy. The immunoglobulins directed against a receptor result in sustained stimulation of the target organ[1]. The disease is more prevalent in iodine rich areas (iodine content 2.0 pg/i) as compared to iodine deficient areas[2]. Several autoantibodies have been found in the scra of GD patients[3]. The detection of autoantibodies has diagnostic implications[4]. Thyroid microsomal antibody (MSAb) in serum correlates with lymphoid infiltration of the thyroid gland and is detected in most patients of autoimmune thyroid disease (AJTD) including, primarily, Graves' disease and Hashimoto's thyroiditis[5]. It may be beneficial to include this test in screening programme of pregnant women for postparturn painless thyroiditis. MSAb estimation is also useful to differentiate exophthalmos from other causes of orbital swelling[6]. The microsomal antigen (M-Ag) is a glycoprotcin and contains at least two antigenic determinants. Different patients have different antibodies against these epitopes[7]. The M-Ag normally located at the microvillar edge of thyroid follicles may be shifted to the vascular pool because of change in thyroid epithelial polarity thus permitting direct approach of circulating MSAb to the 'microsomal' follicular autoantigen[8]. The thyroid microsomal antibody participates in follicular cell damage by mediating complement dependent antibody mediated cytoxicity[9]. The structure presently referred to as M-Ag is identified thyroid pcroxidase (TPO) which is a complex glycoprotein with a prosthetic group[10]. The correlation of MSAh and TPO antibody titres was a general phenomenon independent of the nature of underlying AITD and what was presently called as MSAb arc antibodies directed towards TPO[11,12] This study was aimed to estimate the titres of MSAb in GD patients at different stages of treatment.

PATIENTS AND METHODS

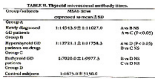
Forty-eight patients with Graves' disease (29 females and 19 males aged 14 to 60 years) and twenty age and sex matched control subjects were included in the study. They were divided into four groups: group A included newly diagnosed GD patients (15), group B were hyperthyroid GD patients undergoing methamizole therapy (15), group C were patients who had been rendered euthyroid after methamizole treatment (18) and group D included 20 controls who had neither systemic disease nor endocrine disorder. All patients were selected from thyroid clinic, Mayo Hospital, Lahore. The diagnosis of Graves' disease was made on Wayne's clinical diagnostic index[13], thyroid function tests, radioactive iodine (131J) uptake, thyroid scans, serum T4. T3 and TSH using T4 RIA, T3 RIA and TSH RIA kits (Amersham International Ltd., Amersham Buckinghamshire, England). All sera were stored at -4°C till required. Thyroid microsomal antibody (MSAb) was estimated using the Serodia-AMC kit (Fujcribio Inc., Tokyo, Japan). The test was based on indirect agglutination/microtitration technique14. Statistical analysis was done using students \'t\' test.

RESULTS

Thyroid microsomal antibody was positive in 93%, 93%, 83% and 20% cases in group A, B, C and D respectively (Table I).



Titrcs of MSAh in GD patients and controls are shown in Table II.



There was no difference in the mean titres between new GD patients and hyperthyroid patients on drugs; however, significant difference ($P < 0.05$) was noted in the mean titres in newly diagnosed patients, euthyroid patients and controls.

DISCUSSION

Graves' disease is an autoimmune thyroid disorder characterized by the presence of autoantibodies directed against the TSI-l receptors or nearby regions of thyroid cell membrances[15]. Circulating thyroid microsomal antibodies are frequently detected that react with the thyroid microsomal antigen[16]. Though not conclusive, there is evidence that these MSAb are of importance in the pathogenesis of GD[17]. We detected MSAb in 93.3% of newly diagnosed as well as hyperthyroid GD patients on drugs. Antibodies were present in 83.3% euthyroid GD patients also. Several other investigators have also reported MSAb positivity in GD patients varying from 76-90%[18-20]. The differences in antibody positivity may be due to racial and ethnic differences, methods of estimation and arbitrarily set limits between positive and negative results by various laboratories, Twenty percent controls were also antibody positive in our study which is similar to 10-20% reported by others[5,18,21]. It can he inferred that occasional finding of MSAb in the sera of otherwise healthy subjects is of no significance. It is, however, important to realise that accidental finding of MSAb in apparently healthy individuals may probably indicate unrecognised or incipient disease[22]. Significant reduction in antibody Litres were noted in group C patients when compared to group A has been reported at the end of a course of MMI therapy[23]. This change in the autoantibody levels was suggested to be due to the immunosuppressive action of MMI[24]. According to Romaldini et al[25] fall in the MSAh levels of euthyroid GD patients was due to a decreased availability of the microsomal autoantigen to the immune system. Thus it is suggested that reduction in the MSAb titres of euthyroid GD patients may be considered as an indicator

of immunological remission. Since the natural history of GD is one of the remissions and relapse, overall 30% spontaneous remission is generally accepted[26]. According to kandall-Taylor[27], GD patients after MMI therapy showed remission rates from 30-75% depending on the duration of treatment. Individual susceptibility to MMI has been demonstrated in GD patients by the unpredictability of the clinical course after cessation of the drug. This effect may be due to iodine intake, racial and ethnic changes and severity of hyperthyroidism[28]. Thus a laboratory test is required that will guide whether immunological remission besides biochemical remission (normal serum T3 and T) has occurred or not. The assay of thyroid stimulating antibody (TSAb) had been claimed to be the test of choice but the technical difficulties militate against its clinical usefulness[29]. Hence, in our opinion the detection of microsomal antibodies by microtitration technique which is cheaper and easier to perform should he instituted in the diagnosis and assessment of GD patients under treatment and at follow-up.

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