Rheumatoid arthritis and thyroid disease

Sirs,

The usefulness of screening for the early detection of thyroid disease (TD) is a very important issue, because even subclinical forms of thyroid dysfunction may contribute to morbidity in a number of pathophysiological states. However, because of the significant costs associated with TD screening, identifying patients at risk for TD is mandatory. In particular, it is still unsettled whether or not patients with rheumatic autoimmune diseases are at increased risk for TD and therefore need thyroid screening. On the other hand, the existence of associations between different diseases may provide clues to their as yet not clearly understood pathogenesis.

The co-occurrence of rheumatoid arthritis (RA) and TD has been investigated with conflicting results (1-4). The recent report of a high prevalence of anti-thyroid antibodies (AT Ab) in a cohort of Italian patients (5) prompted us to communicate our data on a large cohort of patients from northern Italy.

We determined the prevalence of AT Ab (anti-peroxidase, anti-TPO and anti-thyroglobulin, anti-TG) and measured circulating fT3, fT4 and TSH in 91 consecutive out-patients (78 females), aged 55 ± 16 yrs, fulfilling the American College of Rheumatology criteria for RA (6). One hundred consecutive osteoarthritis (OA) patients (81 females) aged 59 ± 11 yrs, coming from the same geographic area, served as controls.

In agreement with the results of Del Puente *et al.* (5), circulating fT3 and fT4 were within the normal range in both groups (fT3: 3.2±0.8 and 3.5±0.8 pg/ml; fT4: 11.7 ±3.0 and 9.7±2.3 pg/ml, RAand OA). Thyroid dysfunction, albeit only subclinical, was found in 12 RA and 11 OA patients (13.2% and 11.0%). Subclinical hypothyroidism was the primary dysfunction (19 subjects, 9.9%), with no significant differences between RA(11 patients, TSH: 4.5 – 11.5 mU/l) and OA (8 patients, TSH: 4.7 – 20.2 mU/l). Subclinical hyperthyroidism was found in 1 patient with RA and in 3 with OA. The prevalence of AT Ab in our RA patients (23.1%) was lower than that reported by Del Puente *et al.* (5), but similar to what was observed in our OA patients (18.0%) and in previous studies (7, 8). No differences were found for anti-TG (10.2% and 10.4%, RAand OA), but a slight significant difference was seen for anti-TPO (23.2% versus 11.1%, RA versus OA, $p < 0.05$). We obtained similar results when considering only women, as Del Puente (7) (Table I).

Table I. Prevalence of subclinical hypothyroidism and anti-thyroid antibodies in women with reaumatoid arthritis (RA) or osteoarthritis (OA). (TPO: anti-peroxidase).

	No. of pts.	Subclinical hypo-thyroidism	Anti-thyroid antibody	Anti-TPO anti-body
AR	78	10.3	25.6	25.7
OA	81	9.9	19.8	11.3*

* $p < 0.05$

We did not find any relationship between the prevalence of AT Ab or hypothyroidism and the presence of rheumatoid factor (RF). In fact, 57.1% of AT Ab-positive patients had RF, and subclinical hypothyroidism was found in 12.3% of RF-positive and in 12.1% of RF-negative RApatients. Furthermore, the frequency of anti-TPO positive women with TSH >6 mU/L, a condition associated with an increased risk of developing overt hypothyroidism (9), was similar in RA (4 out of 78 RA women, 5.1%) and OA(4 out of 81 OAwomen, 4.9%).

In conclusion, although the different areas (southern versus northern Italy) from which Del Puente's and our patients came from, as well as the RAdrugs that our patients were receiving, might be relevant (5, 10), we do not recommend thyroid screening for RA patients.

B. MARASINI M. MASSAROTTI

Dipartimento di Medicina, Chirurgia e Odontostomatologia, Ospedale San Paolo, Università degli Studi di Milano, Milano, Italy.

Address correspondence to:
Prof. Bianca Marasini, Ospedale San Paolo, Via Di Rudini 8, 20142 Milan, Italy.
E-mail: bianca.inarasini@uniini.it

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Reply

Sirs,

We acknowledge the interesting contribution of Marasini and colleagues. The authors did not find any significant relationship between evidence of thyroid disease (TD) and rheumatoid arthritis (RA) as compared to a control group of patients with osteoarthritis. Their data, obtained in a Northern Italy population, further stimulate our interest in evaluating this relationship and its potential determinants (1). In fact, populations with varying disease frequencies are of interest because they offer the possibility of identifying characteristics or factors that predispose to unusual frequencies of the disease or condition.

Our geographical area, for example, is characterized by mild to severe iodine deficiency (2). It will be of interest to evaluate if this could be one of the factors which may predispose to a higher prevalence of autoimmune TD in subjects who already suffer from a systemic autoimmune disease (3). From this point of view it is also relevant to outline that subjects of our study were all with a first diagnosis of RA (1). This element may additionally affect interpretation of data. Finally, comparison of data from different populations, surely prompt to collaborative studies.

A. DEL PUENTE A. ESPOSITO
S. SAVASTANO G. LUPOLI
V. NUZZO

Correspondence to: Dr. Antonio Del Puente, Divisione di Reumatologia, II Università di Napoli, via Sergio Pansini n. 5, 80131 Napoli.

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Gabapentin in the treatment of bipolar depression in patients with systemic lupus erythematosus

Sir,

Bipolar disorder is frequently associated with systemic lupus erythematosus (SLE) (1) and the nature of this connection is still unclear. A recent review showed that patients with SLE or rheumatoid arthritis (RA) exposed to psychological stressors have a poorer cytokine reaction than healthy controls (2). Some rheumatologic manifestations (such as hypothyroidism secondary to autoimmune thyroiditis) increase the risk of developing a mood disorder. Oomen *et al*. (3) found thyroid dysfunction to be associated with resistance to anti-depressant treatment and rapid cycling in patients with bipolar disorder.

It is also important to consider the possible involvement of the central nervous system due to vasculitis or other causes in patients with SLE. Pain symptomathology has also been demonstrated to cause depression. On the other hand, it has been shown that depression influences the intensity of pain symptoms (4). Moreover the drugs used to treat autoimmune diseases have been demonstrated to influence mood. Corticosteroids may induce manic or dysforic symptoms in predisposed patients, whereas their interruption is associated with depressive syndromes. Therefore depressed patients with concomitant SLE have a high risk of manic switches due to concomitant corticosteroid therapy.

Carbolithium or lamotrigine, which was demonstrated to be effective in bipolar depression, frequently cannot be used in patients with SLE because of their general medical condition. Moreover these mood stabilizing drugs can interact dangerously with those used to treat SLE. Therefore a mood disorder associated with SLE is quite a difficult condition to treat.

Recently, Carta *et al*. (5) reviewed the efficacy of gabapentin (GBP) in the treatment of bipolar spectrum disorders, showing that it was well tolerated and useful, especially during depressive phases. The aim of the present study was to evaluate gabapentin efficacy in the treatment of bipolar depression in patients with SLE.

Four female patients suffering from Bipolar Disorder II (according to the DSM-IVcriteria, 6) and SLE (according to ACR criteria, 7) were recruited. The average age was 38.5 ± 9.1. Patients were treated with gabapentin at a dose of 900 mg/day over a 9-month period. The severity of the psychopathology was assessed using the Clinical Global Impression Severity scale (CGI) (8) at baseline and after 1, 3 and 9 months. Depressive symptoms were evaluated using the Hamilton Depression Rating Scale (HDRS) (9) at baseline and after 9 months.

Two patients were treated with GBPmonotherapy. In the other 2 patients, GBP was added to the anti-depressant and mood stabiliser treatment after 2 months of no response. Specifically, one patient was treated with GBP, fluoxetine (20mg/day) and carbamazepine (600 mg/day), whereas the other was treated with GBP, clomipramine (75 mg/day) and pimozide (2 mg/day).

CGI and HDRS scores during the follow-up period are shown in Table I. The average reductions in the CGI and HDRS scores after 9 months were 27.8% and 36.4%, respectively. It is worth noticing that the improvement was not immediate: the CGI and HDRS scores were substantially unmodified at the first month after the titration conclusion and one patient worsened at the 3rd month. The CGI and HDRS improvement became statistically significant comparing the baseline scores with the scores at 9th month.

Moreover, at the 9th month all patients reported a subjective reduction of pain. This may be explained by the central analgesic action of GBP and the improvement in depressive symptomatology previously demonstrated by Brown *et al.* (10). In conclusion, the present report suggests the potential efficacy of GBP in the treatment of bipolar depression in patients with SLE. Further randomized controlled studies will be necessary to confirm the utility of GBP suggested by the present report.

Table I. Clinical Global Impression Severity scale (CGI) and Hamilton Depression Rating Scale (HDRS) scores during the follow-up period.

Patient	Baseline		1st Month	3rd Month	9th Month	
	CGI	HDRS	CGI	CGI	CGI	HDRS
A	5	27	5	5	4	18
B	5	23	5	4	3	15
C	4	19	4	5	3	13
D	4	21	4	3	2	11

M.G. CARTA[1], *MD*
M.C. HARDOY[2], *MD*
F. DUCCI[2], *MD*
M. CATENA[2], *MD*
L. DELL'OSSO[2], *MD*
B. CARPINIELLO[1], *MD*

[1]Division of Psychiatry, Department of Public Health, University of Cagliari; [2]Department of Psychiatry, Neurobiology, Pharmacology, Biotechnology, University of Pisa, Italy.

Address correspondence to: Mauro Giovanni Carta, MD, Division of Psychiatry, Department of Public Health, University of Cagliari, Via Liguria n° 13, 09127, Cagliari, Italy. E-mail: mgcarta@tiscali.it

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