Letters to the editors

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Amyotrophic lateral sclerosis and thyroid function

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Sirs: We read with interest the paper by Malin et al. [6] on thyroid function in patients with amyotrophic lateral sclerosis (ALS). The authors determined the thyroxine (T_4), triiodothyronine (T_3), and reverse T_3 in cerebrospinal fluid (CSF) and in serum of 12 patients with ALS by radioimmunoassay. In all their patients the serum levels of T_4, T_3 and rT_3 were within normal limits. In CSF, the rT_3 levels were significantly elevated, those of T_4 were not significantly elevated, and T_3 could not be detected. The antithyroid antibody (thyroglobulin antibodies and microsomal antibodies) showed normal titres and the authors did not suggest disturbance of thyroid autoimmunity in the patients with ALS [6]. We elected to study thyroid status in ALS. The diagnosis of ALS was established on the basis of history, clinical and laboratory examination, electrophysiological study, and muscle biospy. The thyroid function tests were carried out in 32 of these patients (20 men and 12 women aged 26–64 years, with a mean of 52.7). The control group consisted of 50 patients with non-neurological conditions [3]. In all patients the serum concentrations of T_3, T_4, thyroid-stimulating hormone (TSH), and free T_4 were measured by radioimmunoassay. All sera were also tested for the presence of antithyroid antibody activity [antithyroglobulin (Tab), antimicrosomal antibody (Mab)] with the commercial haemagglutination tests. No patients were receiving any medication known to influence thyroid function assessment.

With statistical variables as T_3, T_4, TSH, free T_4, Tab, and Mab, the following tests were performed: calculation of mean values (and standard deviation), examination for the normal range, and Student's t test. The limit of significance was $P<0.05$. The results of thyroid function tests and the frequency of the circulating antithyroid antibody titres are summarized in Table 1. The T_3, T_4, TSH and free T_4 levels were found to be within the normal range except in one patient, who exhibited a low level of T_3 (15 ng/dl). This patient did not have hypothyroidism, but was considered to have a low-T_3 syndrome. There were no statistically significant differences between patients with ALS and the normal subjects. Thyroid antibodies were not detectable in the sera of all patients with ALS. No patients exhibited thyroid enlargement. The aetiology of ALS is still obscure. Motor neuron diseases have been associated with immunological disturbances [1].

Offprint requests to: Y. Iwasaki

Table 1. Thyroid function in patients with ALS

Thyroid function tests	Normal range	All ($n=32$) Mean, SD	Male ($n=20$) Mean, SD	Female ($n=12$) Mean, SD
T_3, ng/dl	70 ~ 190	103.9, 39.2	101.2, 41.0	108.7, 38.0
T_4, μg/dl	5.0 ~ 13.0	8.7, 1.5	8.7, 1.5	8.6, 1.8
TSH, μU/ml	~ 10	3.6, 1.8	3.6, 2.5	3.9, 1.0
Free T_4, ng/dl	1.1 ~ 2.0	1.4, 0.1	1.4, 0.1	1.4, 0.1
Antithyroid antibody titres				
Tab-positive		None	None	None
Mab-positive		None	None	None

T_3: triiodothyronine, T_4: thyroxine, TSH: thyroid-stimulating hormone, Tab: antithyroglobulin antibody, Mab: antimicrosomal antibody, ALS: amyotrophic lateral sclerosis, SD: standard deviation

An autoimmune pathogenesis is suggested by the presence of immune system abnormalities in patients with ALS [1]. However, the evidence implicating immunological abnormalities is inconclusive. Hyperthyroidism may cause a variety of neurological disorders, and some of these have to be considered in the differential diagnosis of ALS, but few reports are available of thyroid function studies in patients with ALS [2, 4]. In the literature two patients with ALS and hyperthyroidism have been reported [5]. McMenamin and Croxson [7] reported motor neuron disease with coexisting hyperthyroid Graves' disease, and circulating thyroid autoantibodies were also detected in the same case, suggesting that the nature of motor neuron disease and the detection of circulating autoantibodies warranted speculation on a possible immunological association. Kiessling [4] reported a normal range of thyroid functions and no evidence of thyroid antibodies in 44 patients with ALS. Appel et al. [2] reported that 11 of 58 patients with ALS had evidence of thyroid disease, and 6 had thyroiditis. Unfortunately there was no opportunity to perform a scintillation thyroid scan and a suppression test, which might have provided additional proof of absent thyroid disorder.

In conclusion, we found normal thyroid values in patients with ALS; ALS could not be related to thyroid disorders.

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Almitrine-induced peripheral neuropathy and weight loss

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Sirs: We read with interest the report on 46 cases of almitrine neuropathy by Bouche et al., which appeared in a recent issue of this journal [5]. The authors stated that, in addition to the features of peripheral nerve involvement, an unexpected weight loss (range 2–20 kg) was frequently found. Weight loss cannot be considered "unexpected", as weight loss has been mentioned since the first reports about almitrine neuropathy [2–4, 6, 8–10, 12, 13] and was particularly emphasised as early as 1985 [8, 9]. We have observed 33 cases, including 18 previously published cases [2, 8–10], of typical almitrine sensory neuropathy in patients to whom the compound had been administered for 2–12 months before the onset of neurological symptoms. A 3–15 kg weight loss was found in 30 of the 33 patients. Anamnesis revealed highly variable chronological relationships between weight loss and neurological symptoms. The weight loss was either progressive or rapid. Most patients did not complain of any anorexia or digestive disorder, but a mild depressive syndrome was frequently noted. Weight loss has not been noticed in large series of patients or healthy subjects to whom almitrine had been chronically administered [11]. Therefore, weight loss appears to be a reliable criterion for the diagnosis of almitrine neuropathy.

The mechanisms of both weight loss and peripheral neuropathy in patients treated with almitrine are unclear. Bouche et al. [5] stressed that the role of hypoxaemia in the genesis of peripheral nerve involvement has been a matter of some controversy. The impressive number of large series of almitrine neuropathy in patients with and without hypoxaemia [2, 4, 5, 7, 12, 13] as well as the recent results of long-term, placebo-controlled double-blind studies [1, 14] are definitely consistent with a neurotoxic effect of almitrine. In order to determine whether or not the susceptibility to develop almitrine neuropathy is genetically determined through a polymorphism of hepatic drug oxidation, we have recently studied the oxidation phenotype of 15 patients with almitrine neuropathy with regard to the P-450 iso-enzyme involved in the metabolism of dextromethorphan/debrisoquine [2]. The study revealed that the patients were not "poor metabolizers", which contrasts with what is known about perhexiline neuropathy.

Offprint requests to: R. Gherardi

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