Amyotrophic lateral sclerosis and prolactinoma

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Received: August 2006
Accepted for publication: February 2007

Summary

A 59-year-old male with amyotrophic lateral sclerosis is presented. Investigations revealed the co-existence of a pituitary adenoma of the prolactinoma type. This combination has not been reported before. The possible relation between endocrinological disturbances and this neurological disease is discussed.

KEY WORDS: ALS, amyotrophic lateral sclerosis, prolactinoma, prolactin

Introduction

Different endocrine disorders have been reported in association with central nervous system (CNS) diseases, including amyotrophic lateral sclerosis (ALS) (1,2). In rare cases, hyperinsulinism, hyperthyroidism and hyperparathyroidism are accompanied by an ALS-like syndrome (2-4).

Furthermore, certain observations have highlighted the existence of an islet cell dysfunction in ALS (5). It has also been found that the tissue and cerebrospinal fluid concentration of thyrotropin-releasing hormone (TRH) and corticotropin-releasing factor (CRF) were lower in ALS than in control patients (6,7). Very rarely, the combination of ALS with acromegaly has also been reported (8). There are a few studies reporting prolactin changes in patients with ALS during TRH therapy (9) and an exaggerated prolactin response to metoclopramide in ALS (10), while there are no reports of patients with prolactinoma and ALS.

In this study we describe a patient with diagnosed ALS which was associated with prolactinoma.

Case report

A 59-year-old male was referred to the Neurological Clinic of the University of Athens, presenting progressive weakness in both lower limbs, which had started 20 months earlier. For the past three months, this weakness had also extended to both upper limbs without sensory disturbances or cramps.

Neurological examination revealed a marked reduction of muscle power in both arms and legs with marked weakness when walking. When muscle strength was rated according to the Medical Research Council (MRC) scale, the following scores were recorded: head extension was graded 5 out of 5 (5/5), head flexion 4/5, arm abduction 3/5, arm flexion 3/5, arm extension 3/5, wrist extension and flexion 2/5, finger extension 2/5, abductor pollicis brevis 2/5, first interosseus dorsalis 2/5, hip flexion 3/5, hip extension 3/5, knee flexion 2/5, knee extension 2/5, foot dorsiflexion 1/5 and foot plantar-flexion 2/5. Atrophy was visible only in the small muscles of the distal arms; infrequent fasciculations were present in both shoulder areas. Hyperflexia of both upper and lower limbs and an extensor plantar response were present. Abdominal reflexes were present and there were no sphincter disturbances. No sensory or cranial nerve disturbances were observed during the examination. Control of bladder and bowel was normal, as was autonomic function. The patient’s ALS Functional Rating Scale score was 26 (11). There was no gynecomastia or galactorrhea, or features of acromegaly. The piliation of the pubes and axilla was physiological. The testicles were of normal size. The patient had normal facial pilation, but he reported impotence beginning one year previously. The thyroid gland was not palpable and clinically the patient was normothyroidic. Skin thickness and consistency was normal, without streaks. The patient was thick-skinned with normal distribution of skin thickness.

Complete microbiological, immunological, virological and biochemical blood and cerebrospinal fluid tests did not show any pathological findings. Visual field examination and direct ophthalmoscopy were normal. X-ray of the skull showed an enlarged sella without any erosion. CT scanning and MRI of the brain revealed a tumor in the sella area mainly to right of the middle line extending into the homolateral cavernous sinus. Motor and sensory conduction velocities were normal. The EMG showed widespread fibrillations and fasciculations (active degeneration) in three limbs. The muscles presented a marked reduction of maximum voluntary contraction. The cerebrospinal fluid was normal. The basal gonadotropin values were within the normal range and presented the expected increase after intravenous ingestion of 100mg gonadotropin-releasing hormone (GnRH). Basal thyroid stimulating hormone (TSH) levels...
were normal and showed a normal response to stimulation with TRH. Serum growth hormone (GH) levels were also normal. Serum cortisol levels were within the lower normal limits and showed complete depression in the depression test with 2 mg of dexamethasone. Testosterone values were compatible with hypogonadism (1.24 nmol/L, normal values: 300-1100) while T3 and T4 values were indicative of normal thyroid function. Measurement of serum prolactin levels revealed a significant increase, up to 385 ng/ml (normal values: 0-20). Treatment was started with bromocriptine (starting dose 2.5 mg rising to final daily dose of 7.5 mg) and a considerable reduction of prolactin levels to 4.9 ng/mg was obtained. On follow up of the patient around 3 months later a slight improvement in muscle strength was observed in comparison with the first neurological examination.

Discussion

The pathogenesis of ALS is still unknown. Dietary insufficiency, exposure to toxins or heavy metals, viral infections, defects of the normal DNA repair mechanisms, immune system dysfunction, and metabolic and endocrine disturbances have been suggested as potential causal factors.

It has been hypothesised that ALS could be an illness in which androgen receptors, which are found in high concentrations in the motor neurons of the cranial nerves and the spinal cord, are destroyed or do not function. According to this hypothesis a motor cell dysfunction could be present (12).

In recent years, there has been growing evidence that TRH also acts as a neuroregulator of the voluntary motor system including the alpha motor neurons (13). TRH exists in significant quantities in the terminal endings of anterior horn cells which contain TRH receptors (14). This finding prompted scientists to research the role of TRH in the pathogenesis and treatment of ALS. Even though it is likely that the metabolism of TRH is abnormal in ALS, it seems improbable that the disease is connected with primary insufficiency of TRH (6.9).

It is difficult to clarify the role of the pituitary gland hormones in the nervous system, and this is because the pituitary gland hormones can exert both a direct action on the nervous system, but also a secondary action, through the release of hormones as a result of the stimulation of other distal endocrine glands (8). This is perhaps also the reason why the literature contains few reports dealing with pituitary gland function in patients with ALS.

Endocrinological tests, in our patient, were indicative of prolactinoma in combination with low (hypogonadic) testosterone level as result of hyperprolactinemia. The test results also excluded Cushing syndrome and confirmed the presence of normal thyroid function. The clinical and laboratory findings showed the existence of a central and peripheral nervous system affection, meeting all the original and revised EL Escollar criteria for clinically definite ALS (15,16).

The combination of pituitary gland adenoma and ALS raises fundamental questions that remain unanswered. Does the pituitary gland adenoma simply play a role in the pathogenesis of ALS, is it a part of the disease course, or is the coexistence of these two entities merely coincidental? The improvement of the neurological symptoms in parallel with the endocrinological pathology in two patients reported by McCullagh and Hewelett (1947) led these authors to the opinion that the combination of these two diseases is not accidental (8).

Melmed and Braunstein (1) studied the function of the pituitary gland in 19 patients with ALS, treating them with intravenous TRH and luteinising hormone releasing factor (LRH). Release of TSH in response to injection of TRH injection was decreased in the patients with ALS in comparison with the control group and this difference was more evident in the female patients (1). On the contrary, the TRH-stimulated release of prolactin was considerably increased in the female patients while it was normal in the males. The basal levels of the gonadotropic sex hormones were normal in both the male and the female patients. Finally the gonadotropin response to LRH ingestion was mild in the male patients. These data in combination with the difficulty of interpreting the findings led the writers to conclude that it is unlikely that ALS is associated with primary pituitary gland dysfunction.

In conclusion, we suggest that, in view of the reports of multiple endocrine disturbances in patients with ALS and the relative endocrine hypothesis of the pathogenesis of the disease, further research is called for. Such research should aim to reveal a potential direct association since data show that prolonged critical illness appears to have a neuroendocrine component (17).

References