

Association of Multiple Sclerosis and Microprolactinoma: Role of Hyperprolactinemia

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Abstract: Prolactin is a pleiotropic hormone, in addition to a wide variety of endocrine effects, it has also immunostimulatory effects. As a result, there is increasing evidence linking prolactin to a large number of systemic and organ-specific autoimmune diseases. We describe the case of a 41-years-old woman diagnosed with multiple sclerosis in the context of a prolactinoma with poorly controlled hyperprolactinemia that has been evolving for 5 years. This raises the question of the involvement of prolactin in the pathogenesis of multiple sclerosis.

Keywords: multiple sclerosis, prolactinoma, hyperprolactinemia, autoimmunity.

INTRODUCTION

Multiple sclerosis (MS) is the most common demyelinating disorder of the central nervous system. The highest incidence is between 20 and 30 years, and women are affected twice as often as men [1]. The etiology of multiple sclerosis is not known, but it probably involves multiple factors, including autoimmunity as a central pathogenic mechanism [2]. The predominance of women in autoimmune diseases suggests that female sex hormones may play a role in the susceptibility of the disease. A possible role for prolactin is suggested by some clinical evidence [3, 4]. Prolactin is a peptide hormone with potent immunomodulatory properties that can stimulate and inhibit the immune response. We describe the case of a 41-years-old woman with a prolactin-induced pituitary adenoma.

She initiated her first MS outbreak five years after a period of uncontrolled hyperprolactinemia, suggesting that it may facilitate the induction of the inflammatory process that triggers the disease.

CASE REPORT

S.A., 41 years old, consults in 2008 for headaches with diplopia. The interrogation finds the notion of temporal headaches of moderate intensity evolving since one year with diplopia without galactorrhea without disorders of the menstrual cycle, without signs of thyrotropic insufficiency nor corticotropic without notion of drug intake. His first consultation was with an ophthalmologist who requested a visual field objectifying a superior homonymous lateral quadrants. Prolactinemia was requested returning high at 298 ng / ml. The hypothalamic-pituitary MRI performed in 2008 showed a 9 mm lateralized pituitary micro-adenoma responsible for tilt of the sellar floor and a sheathing of intracavernous carotid (Figure 1).

The patient was put on cabergoline at a dose of 0.5 mg / week. Prolactinemia control was still moderately elevated between 123-195 ng/ml (4 -23 ng/ml) and radiological monitoring showed a decrease in microadenoma size in 2010 after 2 years of treatment. In 2013, there was a re-increase in the size of the adenoma of 10 * 06 mm versus 8 * 4 mm with multiple lesions of the periventricular white matter in T2 hypersignal (Figure 2), with significant worsening of both fields visuals. Visual evocative potentials show early onset of macular central vision with bilateral conduction disturbance. The electrophoresis of the cerebrospinal fluid proteins notes the absence of the oligoclonal gamma-globulin profile. These arguments evoke an outbreak of multiple sclerosis. The patient was treated with IV boluses of methylprednisolone, with an increase in the dose of cabergoline at 1 mg / week. The patient did not have a relapse of her multiple sclerosis (Table 1).

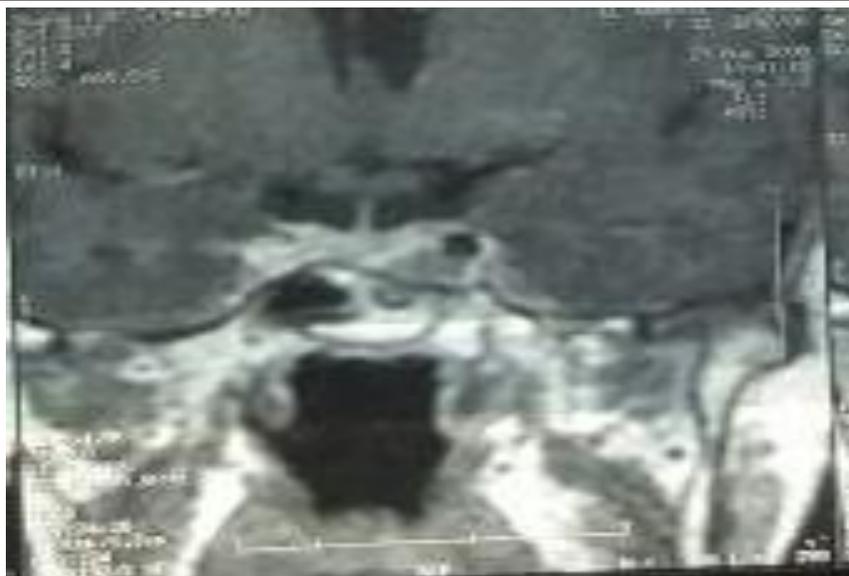


Fig-1: Pituitary MRI, frontal sections: lateralized pituitary microadenoma on the left



Fig-2: Cerebral MRI, multiple periventricular white matter lesions

Table-1: Evolution of the size of adenoma and prolactin

Date	size of the adenoma	prolactin
2008	9 mm	295 ng/ml
2010	5 mm	188 ng/ml
2013	10 mm	123 ng/ml
2016	4 mm	76 ng/ml

DISCUSSION

The pathogenic mechanisms that explain the development of multiple sclerosis are still unclear. However, autoimmunity is considered a central pathogenic mechanism. Th1 and Th17 CD4 + cells are thought to lead to an immune attack against myelin sheath components leading to demyelination and axonal damage [2]. Among the etiological factors, it is suspected that sexual factors influence the incidence and progression of multiple sclerosis [5]. Indeed, epidemiological studies have revealed that this disease is more common in women than in men [5]. In addition,

pregnancy as well as breastfeeding affects significantly the activity of MS. The relationship between prolactin and autoimmune diseases could be explained that the human prolactin gene is located on the short arm of chromosome 6, close to the region of the human leukocyte antigen (HLA). Some antigens of the HLA complex are correlated with a higher frequency of many autoimmune diseases. Indeed, prolactin has been shown to promote the maturation of B lymphocytes and CD4 + T cells and the development of antigen presenting cells, to decrease apoptosis of B cells and to interfere with B cell tolerance, and to improve the production of

autoantibodies, all of which contribute to the degradation of tolerance and the development of autoimmunity [6-8]. In agreement with these experimental observations, several clinical studies highlight the relationship between prolactin and several autoimmune diseases [6, 9]. Thus, hyperprolactinemia has been reported mainly in patients with systemic lupus erythematosus, rheumatoid arthritis, Sjogren's syndrome, systemic sclerosis, Hashimoto's thyroiditis, psoriasis, celiac disease and Behçet's disease. With regard to multiple sclerosis, many clinical studies have been conducted, most of which are analyzed in a recent revision of the literature, including 23 studies [10]. Despite the lack of a randomized study, available data report significantly higher levels of prolactin in serum and cerebrospinal fluid (CSF) in MS patients than in healthy subjects ranging from 16% to 34% [10]. Nociti *et al.* [4] describe the case of a 32-year-old man who experienced the first clinical event of MS and the two subsequent relapses during development and relapses of a prolactin-secreting adenoma. Watad *et al.* [3] report the case of a teenager diagnosed with MS occurring in the context of an untreated prolactinoma that has been evolving since childhood. Kira *et al.* [11] demonstrated that in 9/27 patients with MS, mild to moderate hyperprolactinemia was observed, with half of the patients having prolactin increase during relapse. Moshirzadeh *et al.* [12] reported elevated prolactin levels in patients with MS relapse compared to controls. However, other authors [13, 14, 15] found no correlation of basic prolactin values with disease activity. These studies are often limited (cross-sectional studies, small number of patients) that do not allow a definitive conclusion hence the need to conduct large randomized studies.

CONCLUSION

Clinical and experimental data support the involvement of prolactin in the pathogenesis of MS. Our case report reinforces this hypothesis. In fact, prolonged uncontrolled hyperprolactinemia could facilitate the immune process and trigger the disease.

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