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CASE REPORT

Rapid improvement in visual loss with cabergoline treatment in a giant prolactinoma case: 5 years survey

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Abstract

Giant prolactinoma is a rare subset of macroadenomas. Limited studies demonstrated which therapy could be successfully used in the first-line therapy of giant prolactinoma. We presented a case with a 54×40×40 mm pituitary adenoma and optic chiasmatic compression with left sphenoid sinus invasion. The tumor caused a loss of visual field of the right side. Cabergoline treatment was started with dose of 1.5 mg/week. Fifteen days later, the clinical visual acuity examination showed a significant improvement in the patient with visual field defect. After the five years follow-up magnetic resonance imagining showed reduction of the adenoma size (17×12 mm) was significant. Our findings suggest that, cabergoline can be used as a first-line therapy in giant prolactinomas because tumoral shrinkage without a surgical procedure and rapid improvement in visual field defect is achieved with this medical treatment.

INTRODUCTION

Prolactinomas are almost always benign prolactin-secreting pituitary tumors with an incidence of 40% in all patients with pituitary adenomas. In general, prolactinomas have a female predominance. Microadenomas (<1cm) are common more often in women, whereas macroadenomas (>1cm) are common in men (Shimon *et al.* 2007). Larger prolactin-secreting adenomas may exist, especially in younger and in male patients, causing symptoms due to mass effect (Moraes *et al.* 2013).

Giant prolactinoma is characterized by large size (>40mm in diameter), massive extrasellar involvement and usually associated with high serum prolactin levels (>1000 ng/ml). They are a rare subset of macroadenomas, accounting for approximately 3% of all prolactin-secreting pituitary tumors and the pathogeny of them are not clarified yet. (Shrivastava *et al.* 2002; Corsello *et al.* 2003). Although large series and evidence-based treatment recommendations are lacking, limited studies demonstrated that cabergoline should be effective as a first-line therapy and successfully

used in giant prolactinomas (Colao *et al.* 2004; Verhelst *et al.* 1999; Maiter & Delgrange 2014).

The aim of this case report was to evaluate the efficacy of cabergoline treatment on rapid improvement in visual field defects, tumor shrinkage, and prolactin level normalization in a patient with giant prolactinoma during the 5-year follow-up.

CLINICAL CASE

33 year-old male patient applied for occasional headaches and impairment of the sense of sight. Hormonal investigations showed hyperprolactinemia (prolactin: 3735600 ng/mL, normal range (NR): 4.6–21.4 ng/mL). Growth hormone (GH), adrenocorticotropin hormone (ACTH), thyroid stimulating hormone (TSH), follicle stimulating hormone (FSH) and luteinizing hormone (LH) levels were normal. Magnetic resonance imaging (MRI) of the pituitary gland showed a 54x40x40 mm pituitary adenoma with optic chiasmatic compression and left sphenoid sinus invasion. The tumor caused a loss of visual field of the right side (Figure 1).

The patient diagnosed with a giant prolactinoma and therapy was initiated with cabergoline given at a dose of 1.5 mg per week (0.5 mg three times a week). Clinical visual acuity examination showed a significant improvement on the 15th day of the treatment (Figure1b). Tumor size was 40×25×35 on MRI and prominent shrinkage was obtained in quick response to cabergoline. Prolactin level was normal at the second month of follow-up. MRI-measured tumor size was 35×25×30 mm and significant tumor shrinkage continued three months after onset of the treatment. Tumor size at diagnosis ranged from 54 to 17 mm at the end of 5-year follow-up. During the 5-year follow-up of the patient, regular examination of visual field was performed at month 1 and 3, radiological controls with MRI were performed at 6-month intervals after a year (Figure 1).

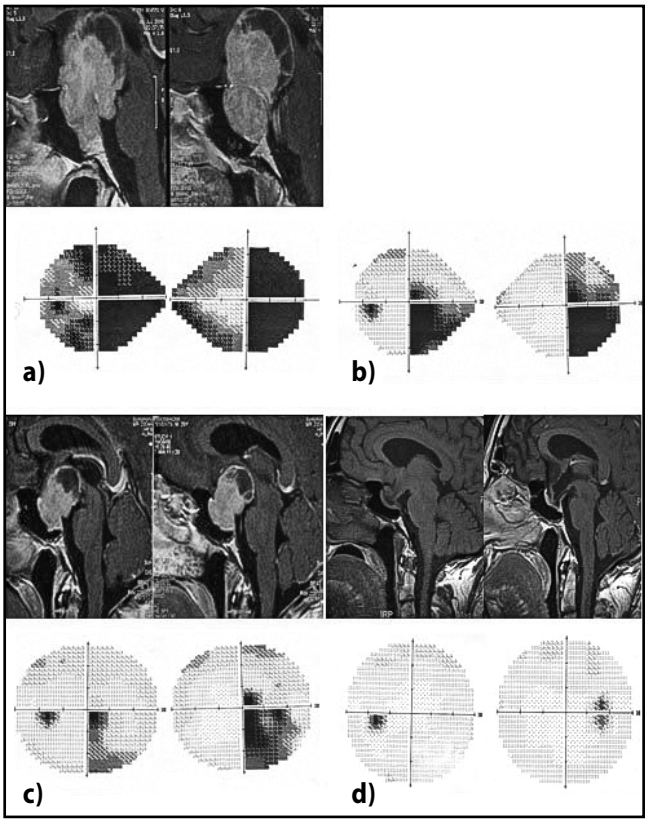

Fig. 1. MRG and visual area development of a 5-year mass, 2008-2012 (a, first diagnosis in 2008; b, 15th day; c, 1st month; d, 60th month.

DISCUSSION

While the vast majority of symptoms in prolactinomas are associated with hyperprolactinemia; hypopituitarism, headache, visual impairment at different degrees and severe neurological complications such as impaired hearing, unilateral hemiparesis, temporal epilepsy or dementia depend on the pressure of hypothalamus-hypophysis pedical or other parts of brain (Ahmed & Al-Nozha 2010; Deepak *et al.* 2007; Brisman *et al.* 1993). Surgery was considered as the primary treatment in the past, due to the first goal of treatment is generally to obtain a rapid relief of these neurological complications. However, it has been shown that surgery has significant mortality and morbidity in the eighties (Pia *et al.* 1985). Therefore, medical treatment has increasingly become the main and preliminary treatment since it resulted rapid tumor shrinkage in most cases with giant prolactinomas (Maiter & Delgrange 2014). Nowadays, almost all prolactinoma patients are treated initially with a dopamine agonist. Surgical treatment can be considered in cases which medical treatment cannot be tolerated or failed (Gillam *et al.* 2006). Long-acting selective cabergoline is an alternative to bromocriptine, D1 and D2 receptor agonist, during the preliminary treatment. Cabergoline treatment as a first preference in macroprolactinoma has been demonstrated to be effective on shrinkage of tumor size and decreasing prolactin levels (Shimon *et al.* 2007; Colao *et al.* 2004; Colao *et al.* 1998; Colao *et al.* 1997; Acharya *et al.* 2010).

The rate of prolactin normalization by the cabergoline treatment was found to be different in various studies. In the study of Colao *et al.* (Colao *et al.* 1998), a decrease in prolactin levels was observed in 69.9% of the patients after 3-month cabergoline treatment with dose of 1 mg/week. In the same study, normalization of visual field defect was determined in 4 of the 10 patients after 3 months and in 5 patients between 6 and 12 months, who have giant prolactinoma and visual defect. A prospective study made by Ono *et al.* (2008) in which impact of cabergoline was reviewed comprehensively in the literature, some patients showed an improvement in the visual field defect after a 1 to 3 month treatment period, and 50% of a 60-patient prolactinoma group showed normal prolactin levels in 1 month and 84% in

3 months, who were not given any treatment previously but 0.5 mg/week primarily (Ono *et al.* 2008). Cho *et al.* investigated the efficacy and safety of cabergoline in 10 male patients with invasive giant prolactinoma and they showed that cabergoline induced a profound reduction (>95%) in serum prolactin levels within 3 months in 7 among 10 patients. Tumor shrinkage was significant (86% reduction) within 6 months although a further decrease (97%) in tumor size was observed after >12 months of cabergoline treatment (Cho *et al.* 2009). The rate of prolactin normalization can vary from a couple of months to 2 years or more. These variations cannot be explained by the tumor size, initial prolactin level or the amount of reduction in tumor size and any implication towards the effect of cabergoline treatment in giant prolactinoma cannot be made.

The time course of visual field recovery differs among patients receiving cabergoline treatment. It has been discussed whether this recovery can be associated with the tumor size, initial prolactin level and treatment dose or, irrespective of all, can depend on such instances as a separate activity of cabergoline, sensitivity of patients to cabergoline treatment, probable expression of D2 dopamine receptor gene in prolactin-secreting pituitary adenomas or isoform ratios. In the light of these findings, a possible mutation or polymorphism in D2 gene may be the reason for variations of treatment response in patients with giant prolactinoma. In the study of Shimon *et al.* (2007), 12 men patients were evaluated according to the degree of effectiveness of long term cabergoline treatment, 9 patients had visual field impairments at diagnosis; and visual field normalized in 3 patients and improved in five patients in 1–3 months (Moraes *et al.* 2013). While prolactin levels normalized in 5 patients after 6 months, 7 patients returned to normal or close to normal values within 12 months. In the study of Corselo *et al.* (2003), while visual area impairment was detected in 7 of 10 patients, normalization of visual field defect was observed after a 1–3 month cabergoline treatment in 6 patients. Normalization of visual field defect in all these patients was correlated with the shrinkage of tumor size.

The remarkable improvement of the visual field in patient, presented in our case, was found on 15th day of cabergoline treatment (Figure 1b). Prolactin level was found to be normal at the 2-month follow-up, significant shrinkage in tumor size was observed (40x25x35 mm) and normalization of visual field defect was monitored at 1 month. While tumor shrinkage continued throughout the 5-year follow up of the patient (figure 1a–d), prolactin levels remained in normal ranges.

A rapid improvement of visual field defects and significant shrinkage in tumor size without any requirement of a surgical treatment support the effectiveness of cabergoline treatment also in patients with giant prolactinoma. Determination of new indicators for these giant prolactinomas should help to better understand their origin and progression and to find new treatment options. Further investigations and prospective studies with larger patient groups should be conducted to clarify the differences in response rates towards similar cabergoline treatment protocols when compared to other cases.

REFERENCES

1 Acharya SV, Gopal RA, Menon PS, Bandgar TR, Shah NS (2010). Giant prolactinoma and effectiveness of medical management. Endocrine practice : official journal of the American College of Endocrinology and the American Association of Clinical Endocrinologists **16**: 42–46.

2 Ahmed M, Al-Nozha O (2010). Images in clinical medicine. Large prolactinoma. The New England journal of medicine **363**: 177.

3 Brisman MH, Fetell MR, Post KD (1993). Reversible dementia due to macroprolactinoma. Case report. Journal of neurosurgery **79**: 135–137.

4 Cho EH, Lee SA, Chung JY, Koh EH, Cho YH, Kim JH, Kim CJ, Kim MS (2009). Efficacy and safety of cabergoline as first line treatment for invasive giant prolactinoma. Journal of Korean medical science **24**: 874–878.

5 Colao A, Annunziato L, Lombardi G (1998). Treatment of prolactinomas. Annals of medicine **30**: 452–459.

6 Colao A, Di Sarno A, Landi ML, Cirillo S, Sarnacchiaro F, Facciolli G, Pivonello R, Cataldi M, *et al.* (1997). Long-term and low-dose treatment with cabergoline induces macroprolactinoma shrinkage. The Journal of clinical endocrinology and metabolism **82**: 3574–3579.

7 Colao A, Vitale G, Cappabianca P, Briganti F, Ciccarelli A, De Rosa M, Zarrilli S, Lombardi G (2004). Outcome of cabergoline treatment in men with prolactinoma: effects of a 24-month treatment on prolactin levels, tumor mass, recovery of pituitary function, and semen analysis. The Journal of clinical endocrinology and metabolism **89**: 1704–1711.

8 Corsello SM, Ubertini G, Altomare M, Lovicu RM, Migneco MG, Rota CA, Colosimo C (2003). Giant prolactinomas in men: efficacy of cabergoline treatment. Clinical endocrinology **58**: 662–670.

9 Deepak D, Daousi C, Javadpour M, Macfarlane IA (2007). Macroprolactinomas and epilepsy. Clinical endocrinology **66**: 503–507.

10 Gillam MP, Molitch ME, Lombardi G, Colao A (2006). Advances in the treatment of prolactinomas. Endocrine reviews **27**: 485–534.

11 Maiter D, Delgrange E (2014). The challenges in managing giant prolactinomas. European journal of endocrinology / European Federation of Endocrine Societies.

12 Moraes AB, Silva CM, Vieira Neto L, Gadelha MR (2013). Giant prolactinomas: the therapeutic approach. Clinical endocrinology **79**: 447–456.

13 Ono M, Miki N, Kawamata T, Makino R, Amano K, Seki T, Kubo O, Hori T, *et al.* (2008). Prospective study of high-dose cabergoline treatment of prolactinomas in 150 patients. The Journal of clinical endocrinology and metabolism **93**: 4721–4727.

14 Pia HW, Grote E, Hildebrandt G (1985). Giant pituitary adenomas. Neurosurgical review **8**: 207–220.

15 Shimon I, Benbassat C, Hadani M (2007). Effectiveness of long-term cabergoline treatment for giant prolactinoma: study of 12 men. European journal of endocrinology / European Federation of Endocrine Societies **156**: 225–231.

16 Shrivastava RK, Arginteanu MS, King WA, Post KD (2002). Giant prolactinomas: clinical management and long-term follow up. Journal of neurosurgery **97**: 299–306.

17 Verhelst J, Abs R, Maiter D, Van Den Bruel A, Vandeweghe M, Velkeniers B, Mockel J, Lamberigts G, *et al.* (1999). Cabergoline in the treatment of hyperprolactinemia: a study in 455 patients. The Journal of clinical endocrinology and metabolism **84**: 2518–2522.