

Management of Giant Prolactinomas: Evaluation of the Role of Surgery and Medical Treatment

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ABSTRACT

Objective: Prolactinomas account for approximately 30% of all pituitary adenomas and 50 to 60% of functional pituitary tumors. Giant prolactinomas are often encountered in surgical practice presenting with hyperprolactinemia, local mass effect and pituitary apoplexy. The aim of this study was to assess the role of surgery and/or medical treatment in the management of giant prolactinomas. **Methods:** Ten cases of giant prolactinomas managed at the neurosurgery department, Alexandria University were reviewed. The different clinical, endocrinological and imaging features before and after treatment were reported and analyzed. **Results:** Following initial surgery for VP shunt placement and craniotomy for tumor resection, headache and symptoms of elevated intracranial pressure disappeared in 67% and were ameliorated in 33%. Following medical treatment, clinical recovery occurred for cranial neuropathies in 100%, visual field defects in 30%, amenorrhea in 57% and galactorrhea in 100%. Tumor volume reduction occurred completely in 60% and partially in 40% with a mean volume reduction of 83.3%. Prolactin levels returned to the normal state in 50%, decreased to less than 100 ng/ml in 30% and between 200-500 ng/ml in 20%. **Conclusion:** Medical treatment with dopamine agonists constitutes a first-line therapy for giant prolactinomas which is effective in controlling hyperprolactinemia and shrinking tumor size. Surgery is indicated for tumor resection in patients with medical failure or medication intolerance as well as for CSF diversion in patients with obstructive hydrocephalus.

INTRODUCTION

PROLACTIN-secreting pituitary adenomas "prolactinomas" account for approximately 30% of all pituitary adenomas and 50 to 60% of functional pituitary tumors.^[41,42] Patients with prolactinomas can present with the clinical sequelae of hyperprolactinemia which causes "Forbes-Albright" syndrome consisting of amenorrhea-galactorrhea in women and impotence and infertility in men, as well as manifestations of local mass effect, and/or pituitary apoplexy.^[6,7]

Treatment of hyperprolactinemia is indicated because of the consequences of infertility, gonadal dysfunction, and osteoporosis. Symptoms from mass effect arise from tumor compression on neighboring structures. Suprasellar extension may cause compression on the optic apparatus, which leads to

visual deficits. Lateral extension into the cavernous sinus can cause cranial nerve palsies. Compression of the normal pituitary gland can result in hypopituitarism. Extensive macroadenomas can obstruct the flow of cerebrospinal fluid, resulting in hydrocephalus. An apoplectic hemorrhage and/or infarction into a prolactinoma (pituitary apoplexy) can cause rapid enlargement of the tumor, resulting in hypopituitarism and acute compression of the sellar, and juxtaseellar structures.^[23,24]

Medical therapy for prolactinomas includes the administration of a dopamine agonist, such as bromocriptine, cabergoline, or pergolide. Dopamine is the primary inhibitory factor for prolactin (PRL), and dopamine receptors are present on normal lactotrophs and prolactinoma cells. More than 90% of patients

respond to this treatment with reduction in the serum PRL level and tumor shrinkage.^[3,4,33]

Surgery is usually indicated in those patients who cannot tolerate medical therapy or for whom medical therapy is ineffective,^[13,39] as well as those who do not wish to receive long-term medical therapy.^[8,43] Surgery may also be indicated in patients who are dependent on antipsychotic medications, because dopamine agonists can precipitate psychotic episodes. The transsphenoidal approach is usually used for microadenomas and most macroadenomas. Both the transsphenoidal and craniotomy approaches have been used for large tumors.^[35]

Predicting pituitary tumor behavior is a challenge, especially given that in many aggressive tumors surgical excision alone does not cure the patient. Invasive pituitary adenomas comprise approximately 40% of all these tumors,^[8,12] and the factors involved in their growth and invasiveness are poorly understood. The appellation "giant" has been reserved for pituitary tumors greater than 4 cm in diameter or those with more than 2 cm of suprasellar extension, or both.^[2,37,44] The aim of this study is to assess the role of surgery and medical treatment in the management of giant prolactinomas.

PATIENTS & METHODS

This series included 10 patients managed for giant prolactinomas between 2003 and 2005 at the department of neurosurgery, Alexandria University.

Patients Evaluation:

All 10 patients underwent a comprehensive clinical evaluation that included thorough neurological, ophthalmological and medical evaluation. All patients were examined

with contrast-enhanced brain computed tomography (CT) scans as the initial imaging study supplemented by contrast-enhanced magnetic resonance imaging (MRI) to verify tumor location and its relationship to the carotid circulation and optic chiasm. Giant pituitary adenomas have been previously defined as those measuring 4 cm or larger in maximum diameter. Cavernous sinus invasion was defined as tumors Grade III or IV according to the classification system of Knosp, et al.^[19] for pituitary adenomas. All patients were subjected to complete laboratory investigations that included, blood chemistry, hematology and neuroendocrine profile including; prolactin, growth hormone, thyroid-stimulating hormone, lutenizing hormone, follicular stimulating hormone, T3 and T4. Inclusion criteria in the present study consisted of the following: 1) tumor size larger than 4 cm in diameter with invasion of the cavernous sinus corresponding to Grade III or IV in the classification system of Knosp and associates, 2) serum PRL level greater than 200 ng/ml, and 3) clinical neurological symptoms of hyperprolactinemia and mass effect.

Surgery:

Three patients were planned to undergo surgery for tumor resection. A unilateral frontal craniotomy was used, and the tumor was reached through an anterior or lateral subfrontal approach. Another 3 patients underwent placement of a ventriculoperitoneal (VP) shunt to treat obstructive hydrocephalus. All 6 patients further received medical treatment postoperatively.

Medical Treatment:

All 10 patients received medical treatment in the form of bromocriptine or combined bromocriptine and cabergoline therapy. Of these 10 patients, 6 patients had previous

surgical intervention for attempted tumor resection or VP shunt insertion and received medical treatment following surgery, whereas 4 patients received medical treatment from the start. Bromocriptine; a D₂ receptor agonist, was initially administered orally before sleep at night at an initial dose of 1.25 mg/day and the dose was slowly increased at increments of 1.25 mg/day being added every week, to reduce the occurrence of adverse side effects. Therapeutic doses were monitored by serum prolactin levels till a normoprolactinemic state, or the maximum therapeutic dose of 15 mg/d were reached, or drug intolerance developed. Cabergoline; a selective D₂ receptor agonist was additionally administered in patients who experienced adverse effects on bromocriptine dosage escalation or those who reached the maximum of 15 mg/day without reaching a normoprolactinemic state. Cabergoline has an extremely long plasma half-life of about 65 hours allowing once- or twice-weekly administration. Therapeutic doses ranged between 0.5-1 mg/week.

Follow-up and Data analysis:

Follow-up examination took place at 3-months, 6-months, and 1-year visits. The follow-up examination included contrast-enhanced cranial CT scans and MR imaging, endocrinological laboratory tests, visual acuity and visual field checks. Tumor volume on posttreatment CT scans and MR images was assessed and compared to the volume before medical treatment.

RESULTS

Patient Population:

The study group included 7 females and 3 male patients, whose ages ranged from 25 to 53 years (mean age 39 years) and whose disease lasted

from 6 month to 4 years (mean course 2.8 years). Three patients were initially treated using craniotomy for attempted gross tumor resection, however, surgical circumstances resulted in partial resection. Another three patients refused surgery for tumor resection and underwent surgery for placement of a ventriculoperitoneal shunt for obstructive hydrocephalus. The other 4 patients showed a giant pituitary tumor with clinical manifestations of hyperprolactinemia and PRL levels above 200 and received medical treatment without any surgical intervention. All patients were followed up between 24 and 56 months posttreatment (mean follow-up of 24.3 months). Six patients received bromocriptine alone at a maximum dose of 7.5 mg/d without recorded adverse effects or medication intolerance. Four patients received combined bromocriptine/cabergoline regimen because they did not reach a normoprolactinemic state with bromocriptine alone. Of these; 2 patients received bromocriptine at a dose of 15 mg/d and cabergoline at a dose of 1 mg/week. The other 2 patients developed bromocriptine intolerance at a dose higher than 7.5 mg/d, thus received a combined bromocriptine/cabergoline regimen of 7.5mg/d and 1 mg/week, respectively. Due to financial reasons, some patients who did not reach a normoprolactinemic state and were on a maximum tolerated bromocriptine dose alone did not receive cabergoline as an adjunctive treatment as well as those on bromocriptine/cabergoline regimen did not increase cabergoline dose beyond 1 mg/week.

Clinical Data:

The presenting clinical manifestations included, visual field defects in all 10 (100%) patients, cranial neuropathies of the oculomotor nerves in 3 (30%)

patients, amenorrhea in all 7 (100%) women, galactorrhea in 4 (57%) females, decreased libido in 2 (67%) men. Headache and manifestations of elevated intracranial pressure occurred in 6 (60%) cases, and epilepsy in 6 (60%) patients. Following initial surgery for VP shunt placement in 3 patients and craniotomy for tumor resection in 3 patients, headache and symptoms of elevated intracranial pressure disappeared in 4 (67%) patients and were ameliorated in the other 2 (33%) patients. Following medical treatment for all 10 patients, visual field impairment recovered completely in 3 (30%) patients and was ameliorated in 7 (70%) patients. Cranial neuropathies in 3 (100%) patients completely recovered. In 7 females with amenorrhea, menstruation resumed in 4 (57%) patients whereas amenorrhea remained in the other 3 (43%) patients. In 4 patients with galactorrhea, the relevant symptoms vanished. In 2 males with sexual dysfunction and a decrease in PRL levels, sexual function improved to various degrees.

Imaging Data:

According to contrast-enhanced brain CT scans and MR images, maximum tumor diameters initially ranged from 41 to 97 mm, with a mean maximal diameter of 62 mm. Invasion of bilateral cavernous sinuses occurred in 6 (60%) cases, of a unilateral cavernous sinus in the other 4 (40%) cases. Following initial craniotomy for tumor resection in 3 patients, tumor

volume reduction ranged between 10-25%. Following medical treatment for all 10 patients, tumor volume decreased significantly with a mean reduction of 83.3% (range 50-100%). The tumor had almost disappeared completely in 6 (60%) patients; whereas for the other 4 (40%) patients residual tumor remained in the cavernous sinus areas and the sphenoid sinus region. In the course of tumor reduction, lesions in the suprasellar area commonly shrank first, followed by those in the sphenoid sinus and the intrasellar region. Tumors in the cavernous sinus area were always the last to shrink.

Endocrinological Data:

All PRL levels were initially greater than 200 ng/ml before treatment. Six patients had a PRL that exceeded 4000 ng/ml and 4 patients had PRL levels that exceeded 10000 ng/ml. Following initial craniotomy for tumor resection in 3 patients, there was no significant change in PRL levels before and after surgery. Following medical treatment for all 10 patients, PRL levels returned to the normal state in 5 (50%) patients, decreased to less than 100 ng/ml in 3 (30%) patients and in 2 (20%) patients, levels continued to exceed 200 ng/ml, yet below 500 ng/ml. Normal pituitary functions other than hyperprolactinemia were preserved in all patients, without evidence of pan-hypopituitarism. No case of diabetes insipidus was observed.

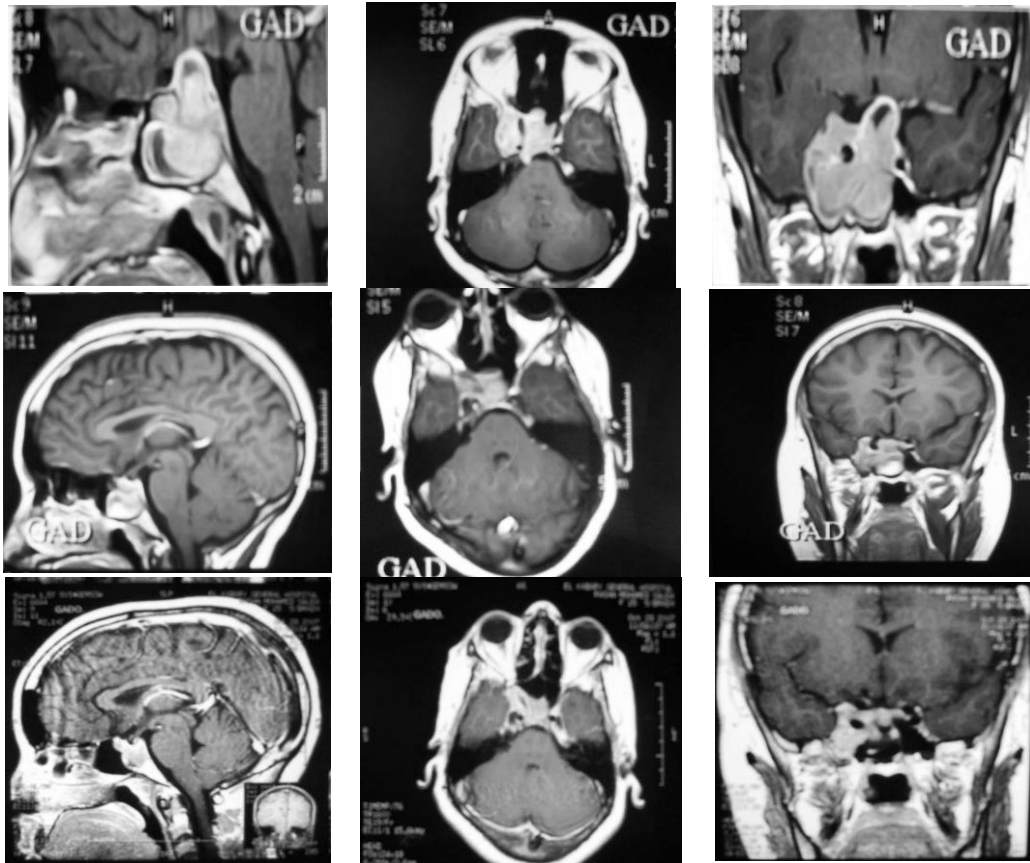


Figure 1: Sagittal, axial and coronal contrast-enhanced T1-wighted brain MR images of a patient with giant prolactinoma showing 90% tumor volume reduction following medical treatment. Upper row: before medical treatment. Middle row: 1-year after medical treatment. Lower row: 2-years after medical treatment.

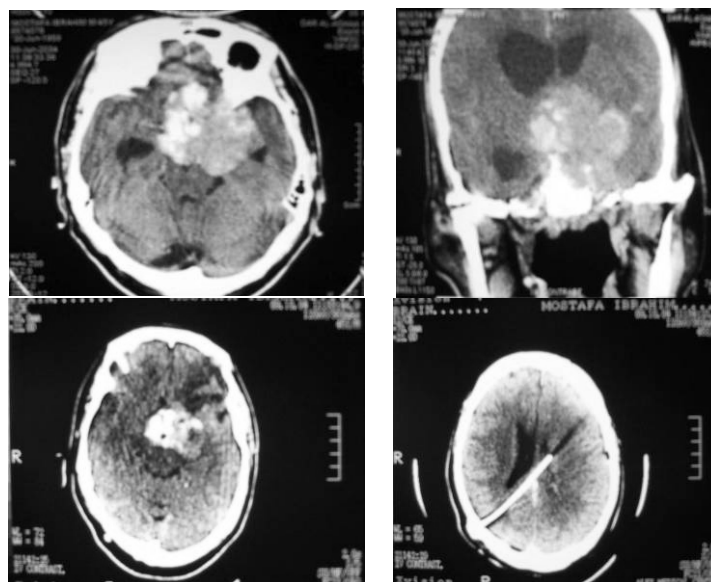


Figure 2: Contrast-enhanced brain CT scans of a patient with giant prolactinoma showing 50% tumor volume reduction following medical treatment. Upper row: before medical treatment. Lower row: 2-years after medical treatment and VP shunt placement.

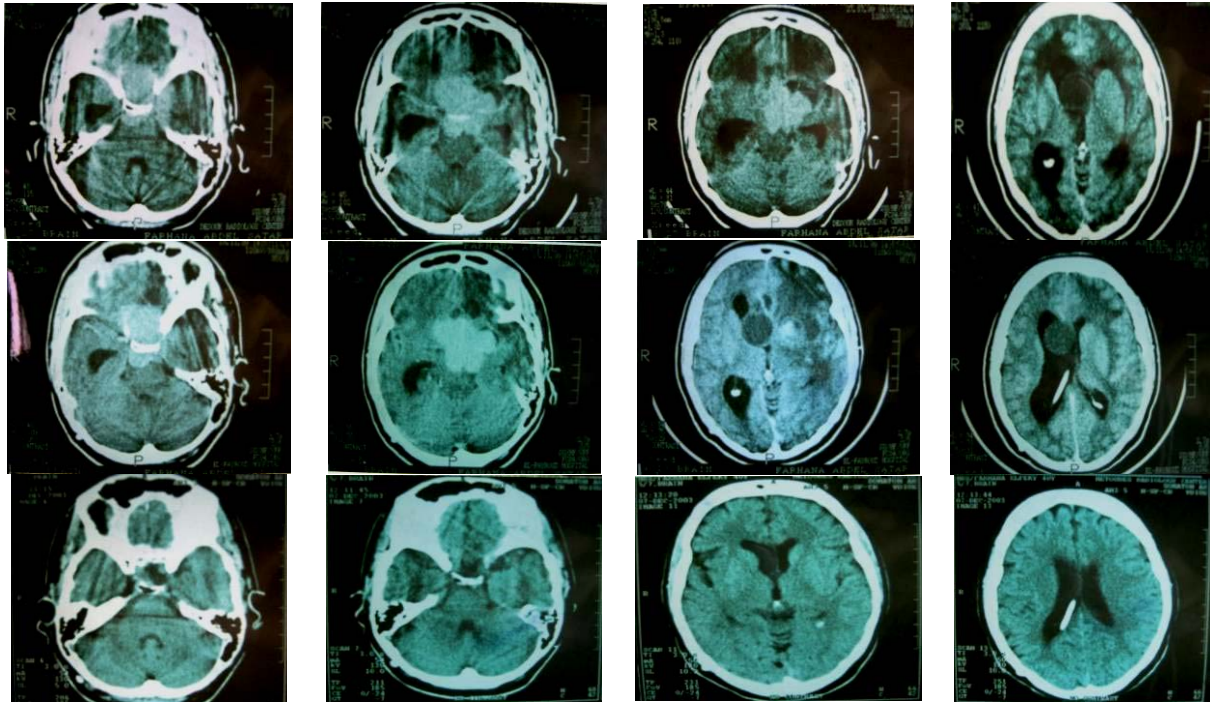


Figure 3: Contrast-enhanced brain CT scans of a patient with giant prolactinoma showing 100% tumor volume reduction following medical treatment. Upper row: before medical treatment. Middle row: 1-month after medical treatment and VP shunt placement. Lower row: 4-years after medical treatment and VP shunt placement.

DISCUSSION

The natural history of untreated prolactinomas remains unclear but the available evidence suggests that the risk of progression from a microprolactinoma to a macroprolactinoma is low, almost certainly under 10%.^[16,29,36] Nishioka, et al.^[31] reported that small prolactinomas (tumor volume <1.0 cm³) with mild hyperprolactinemia (<150 ng/mL) have extremely low growth potential irrespective of age and rarely cause estrogen deficiency. Once the underlying cause of the hyperprolactinemia has been identified, the next step is to determine whether a patient has a definite indication for treatment, such as amenorrhea, infertility, evidence of mass effect, or a macroadenoma (a tumor ≥ 10 mm diameter). Other relative indications for treatment include significant galactorrhea, ovulatory dysfunction,

diminished libido, acne, hirsutism, osteopenia, or headache. The goals of treatment for microprolactinomas are normalization of prolactin level, restoration of gonadal function, and avoidance of the adverse effects of chronic hyperprolactinemia. An additional goal of treatment in macroprolactinoma patients is tumor shrinkage with relief of mass effect symptoms. Current therapeutic options include observation, medical therapy, surgery, and radiotherapy.

Medical treatment using dopamine agonist medications is the first consideration in the treatment of prolactinomas. Bromocriptine can normalize the serum PRL level in more than 90% of cases and reduce tumor volume in approximately 85% of cases.^[3,4,33] Its main mechanism involves the dopamine D₂ receptors on the cell membrane of PRL cells, which is selectively activated; thus, the transcription and expression of the

PRL gene and the metabolism of PRL cells are inhibited, leading to decreased synthesis and secretion of PRL. In addition, the involution of the endoplasmic reticulum and Golgi apparatus and the suppression of cell proliferation cause a reduction in tumor volume.^[38] The most reported adverse effects of bromocriptine are nausea and vomiting, postural hypotension, headache, Raynaud-type syndrome of painless digital vasospasm, drowsiness, fatigue, leg cramps, flushing, nasal congestion, anxiety, depression, confusion, delusions, auditory hallucinations, dysinhibition, insomnia, paranoia, blurred vision, nightmares, and paresthesia. Other authors,^[7,11] have reported that cabergoline is a first-line drug in the treatment of prolactinomas. Cabergoline is more expensive than bromocriptine, but easier to administer, usually better tolerated, and effective in patients who do not have a response to bromocriptine. In our study, however, successful treatment effects were achieved using bromocriptine alone. If the prolactin level does not normalize or if the patient cannot tolerate bromocriptine, a change to cabergoline may be effective. Patients with macroprolactinomas generally require higher doses of bromocriptine or cabergoline than patients with microprolactinomas. Both dopamine agonists decrease the serum prolactin levels within days and result in a decrease in the size of the tumor and restoration of anterior pituitary function. Visual-field testing should be repeated 1 month after initiation of therapy, and MR imaging should be repeated at 6 months and again at 1 year after initiation of treatment. Serum prolactin levels should be monitored yearly. With the reduction in lesion volume and the control of the PRL level, clinical symptoms are ameliorated. Headache and sexual

dysfunction are improved to differing degrees. Most authors have reported that in cases of giant prolactinomas, visual symptoms improve several days to several weeks after treatment with bromocriptine. Posttreatment visual improvement was not significantly different after drug administration compared with that following surgery.^[22,28] If, after drug administration, the tumor had obviously diminished but vision and visual fields had not improved, ocular defects were rarely improved by subsequent surgery.^[13] The blood supply to the optic nerve and chiasm can be impaired during the surgical separation of adhesions between the giant tumor and the optic nerve. Bromocriptine treatment gradually reduces tumor volume and therefore does not contribute to acute damage of the optic nerve and chiasm. Visual improvement usually occurred within several weeks after beginning bromocriptine treatment and has occurred even on the 1st day after commencing treatment.^[28]

The extent and rate of the reduction in tumor volume was remarkable. During a mean follow-up period of 37 months in the present study, tumor volumes decreased by a mean of 83.3% overall and lesions almost disappeared in 6 patients, according to MR imaging studies. During follow-up, after treatment with bromocriptine, we found that tumors growing into the suprasellar area shrank first (for example, tumors protruding into the third ventricle or the temporal lobe). In 4 patients with residual tumors, the remnant always involved the cavernous sinus. Shrivatava and colleagues,^[37] reported on 10 cases of giant prolactinomas that had been treated with bromocriptine, only five of which involved the cavernous sinus. During a mean follow-up period of 6.7 years, tumor volume decreased by a mean of

69%. In three patients tumor volume was reduced within several weeks to several months then as drug therapy was prolonged, the tumor diminished slowly. This condition has been considered as late resistance and may have occurred for the following reasons. 1) After drug administration, tumor fibrosis becomes progressive and, to a certain extent, the tumor can shrink no further. 2) The absence, lower expression level, or a postreceptor defect of the dopamine D2 receptors on the surface of tumor cells.^[32] Caccavelli, et al.^[6] considered drug resistance to be strongly associated with the decrease in D2 receptor gene transcription, resulting in a fourfold decrease in the number of D2 receptors on the cell membrane.

Data in our study showed that in 5 patients the PRL level was normalized (25 ng/ml), whereas in 3 patients the PRL level was lower than 100 ng/ml and in 2 patients the PRL level ranged between 200-500ng/ml. In those 5 patients who continued to demonstrate a high PRL level, tumor disappearance on MR images was partial in 4 patients and complete in 1 patient. For this latter patient, tumor disappearance did not necessarily indicate complete lesion resolution, because the tumor had invaded adjacent bone matrix which may possess a strong ability to excrete PRL. All 5 patients with non-normalized PRL level, did not stop or reduce therapeutic regimen and were closely monitored, to safeguard against tumor regrowth or recurrence. On the other hand, among 5 patients whose PRL levels decreased to normal, the tumor disappeared on MR images in 4 patients and remained partially visible in 1 patient. Those 4 normoprolactinemic patients whose MR images were negative for tumor existence were amenable to medication dose reduction. Our data agree with previous studies,^[31,32] which reported

that tumor volume shrinkage and controlled PRL levels were not equally sensitive to medical treatment, and there was no positive correlation between tumor size reduction and PRL level decrease.

Close monitoring among patients on medical treatment for recurrent hyperprolactinemia and renewed tumor growth has been established. Recent studies suggest that dopamine agonist treatment may be required indefinitely in patients with prolactinomas.^[17,40] Johnston, et al.^[17] reported that withdrawal of bromocriptine treatment after a mean duration of 3.7 years (range of 1.5 to 7 years) resulted in recurrence of hyperprolactinemia in 14 of 15 (93.3%) prolactinoma patients within 5 to 14 weeks of treatment discontinuation. Yet, only one patient had marginal tumor reexpansion at 6 weeks. van't Verlaat and colleagues,^[40] reported bromocriptine withdrawal in 12 macroprolactinoma patients who had been treated for a mean of 4.9 years (range of 3.5 to 7 years), and 11 (92%) patients developed recurrent hyperprolactinemia during a 1-year follow-up period, although only one (8%) had tumor reexpansion. Muratori, et al.^[30] investigated the effects of cabergoline withdrawal in 26 women with microprolactinomas, 25 (96.1%) of whom had achieved symptomatic control and normoprolactinemia while on treatment for 12 months. After stopping cabergoline, normoprolactinemia was maintained at 1 month in 9 of 22 patients (41%), at 2 months in four patients (18%), and two of these patients remained normoprolactinemic at 38 and 60 months. Six of the 25 patients (24%) remained off treatment with normal or near normal prolactin levels, and 8 of the 13 patients (61.5%) whose radiological pituitary abnormalities had disappeared while on treatment did not show any recurrence of their pituitary lesions

after drug withdrawal. These studies suggest that it would be reasonable to consider dose reduction or treatment withdrawal after 2 to 5 years of dopamine agonist treatment. Abrupt treatment withdrawal should probably be reserved for patients with smaller tumors, although gradual dose reduction may be more appropriate in macroprolactinoma patients. Reassessment of the need for dopamine agonist therapy should also be considered in hyperprolactinemic women following the menopause or after pregnancy.^[18]

Surgery is rarely curative in patients with macroprolactinomas and is usually reserved for patients who cannot tolerate medical therapy or for whom medical therapy is ineffective. On the other hand, sustained normoprolactinemia following cessation of medical therapy has not been demonstrated in all cases and, therefore, there may be a role for curative surgery for microprolactinomas in patients who do not wish to receive long-term medical therapy, as well as those patients who are dependent on antipsychotic medications, because dopamine agonists can precipitate psychotic episodes.^[41] Even if surgery is not curative, as is the case with most macroprolactinomas (<50% cure rate) tumor cytoreduction frequently increases the responsiveness of dopamine agonists and thereby lowers the required dosage.^[2,39] Multimodal therapy is often indicated combining surgical debulking and subsequent adjuvant therapy using stereotactic radiosurgery or medical therapy.^[21] The transsphenoidal approach has been the initial preferred surgical route and is associated with low rates of morbidity and mortality.^[27,39] The extended transsphenoidal approach may be used in some cases in which the tumor is located beyond the

confines of the sella turcica.^[9,20,34] Transsphenoidal surgery offers the possibility of achieving complete cure in selected patients, although at the expense of significant risk in terms of morbidity, especially hypopituitarism, and a very low mortality rate. The surgical success rate depends on the skill and experience of the surgeon. In a large meta-analysis of surgical results from 34 published series,^[29] postoperative normoprolactinemia was achieved in 73.7% of microprolactinomas, with a recurrence rate of 21%, usually within the first year following surgery, giving a long-term cure rate of 50 to 60%. In a recent series of 219 women treated surgically for prolactinomas,^[39] higher initial cure rates of up to 91% were achieved in women with intrasellar microadenomas, falling to 83% in women with suprasellar extension, and only 59% when there was cavernous sinus extension, giving an overall remission rate of 82% in women with microadenomas. Cure rates for macroprolactinomas have been much lower than for microprolactinomas, with initial normoprolactinemia being achieved in 32.4% of patients and a recurrence rate of 19.8%, giving a long-term cure in only 25%.^[29] Tyrrell, et al.^[39] reported an initial cure rate of 88% in patients with intrasellar macroadenomas and 86% in those with moderate suprasellar extension but only a minority of women with major suprasellar extension or cavernous sinus invasion. Morbidity and mortality rates of surgery vary considerably among different centers and have improved in recent years, probably as a result of better imaging. Common complications include, hypopituitarism, cerebrospinal fluid leak and postoperative hematoma. The mortality rates for microprolactinomas and macroprolactinomas are in the region of 0.3 and 0.9%,

respectively.^[29] Lower preoperative basal prolactin value and adenoma stage are the best predictors of initial surgical outcome.^[39,42] Initial remission was achieved in 92% of patients with preoperative prolactin values of ≤ 100 ng/mL and in 91% of those with intrasellar microadenomas. Women with preoperative prolactin values of >200 ng/mL and large or invasive adenomas achieved less favorable outcomes. The effect of prior dopamine agonist therapy on surgical results remains contentious. Tyrrell, et al.^[39] found that prior therapy with bromocriptine had no effect on immediate surgical outcome. This contradicts previous reports that continuation of preoperative bromocriptine beyond 6 weeks induces tumor fibrosis and uneven shrinkage, making surgery unproductive. A low postoperative prolactin value measured 1 to 2 days after surgery appears to be the best predictor of long-term remission. An unmeasurable serum prolactin (<2 ng/mL) predicts a cure with more than 90% probability, and higher values within the normal range are inversely related to probability of cure.^[42]

Surgery for giant pituitary tumors with lateral extension into the cavernous sinus poses a formidable surgical challenge. Recently, some authors have sought to modify the standard transsphenoidal approach to resect pituitary adenomas with cavernous sinus invasion.^[9,20,34] However, surgical outcomes were rather unsatisfactory in patients with pituitary adenomas of Grade III or IV, according to the classification of Knosp and colleagues.^[19] Losa, et al.^[25] reported on 19 PRL-secreting pituitary adenomas with cavernous sinus invasion; the disease was cured in just one patient through early surgery. Increasingly, many investigators have chosen to perform

selective tumor removal with subsequent radiosurgical treatment of residual adenoma within the cavernous sinus to avoid complications of cranial neuropathies. In treating PRL-secreting adenomas, shrinking the tumor volume and controlling the PRL level are equally important. As a result of the tumor's intrusive growth and cavernous sinus invasion, it is usually impossible to achieve complete resection through a single operation. Similarly, controlling the PRL level by using a biological cure cannot usually be achieved through a single operation.^[14] As mentioned earlier, bromocriptine first shrinks the part of a tumor that aggressively extends into the suprasellar space and compresses the optic nerve therefore, bromocriptine treatment, as a first-line therapy for invasive giant prolactinomas, can reduce the necessity for surgery and associated risks and costs.^[15] The following conditions are still indications for surgery: 1) intolerance or resistance to bromocriptine; 2) occurrence of CSF leakage while taking bromocriptine which cannot be conservatively treated; and 3) tumor apoplexy causing significant clinical symptoms, such as sudden severely decreased vision.^[1,10] If the clinical symptoms in a patient with tumor apoplexy are not prominent, bromocriptine treatment can still be effective.^[5]

CONCLUSION

Treatment for giant prolactinomas poses a surgical challenge. First-line therapy with dopamine agonists is effective in normalizing hyperprolactinemia and shrinking tumor size. Surgery is indicated for tumor resection in patients with medical failure or medication intolerance as well as for CSF diversion in patients with obstructive hydrocephalus.

Multimodal treatment may be required for patients with residual tumor in order to achieve a normoprolactinemic state. Following medical treatment, intrasellar or sphenoid sinus residual tumor may be removed surgically through a transsphenoidal approach, whereas, residual tumor within the cavernous sinus may be extirpated using radiosurgery.

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