CLINICAL CASE

THE MULTIMODAL MANAGEMENT OF GROWTH HORMONE-SECRETING PITUITARY MACROADENOMA

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Abstract

The expansive processes of the sellar region include tumors of mesenchymal, neural or epithelial origin, along with cystic and inflammatory processes. From the epithelial sellar tumors, almost 90 % are represented by pituitary adenomata – benign tumors which develop from the adenohypophyseal cells, accounting for approximately 10–15% of all intracranial expansive processes. According to the clinical criteria, the pituitary adenomata can be classified as endocrine-inactive or non-producing adenomata, and endocrine-active or producing adenomata. The non-producing adenomata represent approximately 39–50% of all pituitary tumors; the prolactinomata represent approximately 6.1%; the growth hormone producing adenomata approximately 27.9%; the adenocorticotrophic hormone producing adenomata 6%; the thyrotropic producing hormone adenomata 0.4%; and the follicle-stimulating or luteinizing producing hormone adenomata are extremely rare. The surgical approach used on a large scale today in pituitary and suprasellar tumors is the transnasal transsphenoidal approach, which is less invasive compared to the standard transcranial approach and has got excellent results so far. The purpose of this article is to illustrate the main data about pituitary tumors, based on a case report presentation. At the same time, we aim to keep track of the latest information in the specialty literature, and focus on the neurosurgical aspects. The therapeutic strategy in the case of a 24-year-old female patient diagnosed with a growth hormone-secreting pituitary macroadenoma, with a suprasellar extension and an infrasellar one in the sphenoidal sinus and with invasion in the right cavernous sinus..

Keywords: cranial basis, transnasal transsphenoidal approach, sellar tumors, hypophysis, growth hormone (GH), acromegaly, gamma knife.

Introduction

We will next present the case of a female patient diagnosed with a growth hormone-secreting pituitary macroadenoma, with a suprasellar extension and an infrasellar one in the sphenoidal sinus and with invasion in the right cavernous sinus. The tumor was

successfully ablated through a transnasal transsphenoidal microscopic approach, while gamma knife radiotherapy was done for the portion at the level of the cavernous sinus.

Case presentation

A 24-year-old woman, from an urban residence, diagnosed four years ago with acromegaly and pituitary failure (on a thyreotropic and gonadotropic line), on a substitutive treatment with Prednisone (5mg/day), Euthyrox (100mg/day) and Lanreotid (30mg every fortnight for three months, which the patient gave up out for personal reasons), is admitted due to the increasing of the extremities, headaches, and the narrowing of the visual field.

The patient's history reveals menstrual cycle disturbances (normal menstrual cycle until the age of 18, followed by oligomenorrhea alternating with hypomenorrhea for a year, and further with secondary amenorrhea non-responsive to progesterone) and infertility. Moreover, the patient also mentioned that 7 years before she had noticed an increase of the extremities and bilateral galactorrhea to pressure.

Two years ago, the patient went to the endocrinologist where she underwent all general investigations along with a dosage of hormonal markers.

The hormonal biomarkers revealed at the moment pituitary failure on a gonadotropic and thyreotropic line (secondary hypothyroidism), along with an inadequate growth hormone secretion. The prolactin levels closer to the upper normal limit may be a consequence of pituitary stalk compression ("stalk effect") by the tumor therefore affecting the secretion of the prolactin-inhibiting factor (PRLIF).

▪ Cortisol 5.59 µg/dl (normal range: 7–10 a.m.- 5–25 µg/dl, 4–8 p.m. <10 µg/dl)

▪ FSH 2.8 mIU / ml (normal range - follicular: 5–30 mIU/mL)

▪ LH 1.19 IU/l (normal range - follicular 5–30 IU/l)

▪ Estradiol 17.7pg/ml (normal range - follicular 19–140 pg/ml)

▪ Prolactin 28.35 ng / ml (normal range: 2.8–29.2 ng / ml)

▪ TSH 0.9 µIU / mL (normal range: 0.5–3.5 µU/ml)

▪ T3 206 ng/ml (normal range: 80–200 ng/ml)

▪ FT4 8.4 pmol/l (normal range: 12–22 pmol/l)

▪ IGF-1: 1487 ng / ml (normal range: 116–358 ng / ml)

OGTT	0	30	60	120
Glycemia (mg/dl)	91.8	158.8	105.3	111.7
GH (ng/ml)	141	208	186	143

Tabel 1 – Preoperative results of Oral Glucose Tolerance Test showing a very high level of GH

The Synacten stimulation test with 1mg of intramuscular injection revealed a normal response of cortisol, thus indicating the absence of corticotrope failure.

The endocrinological examination showed a homogenous, normal-sized thyroid gland, mobile with deglutition. The patient did not present signs of galactorrhea.

The CT scan showed an expansive perisellar process replacing the pituitary space (at the level of the right cavernous sinus), infrasellar (at the level of the sphenoid sinus which it occupies in a ratio of 2/3) and suprasellar (at the level of the suprasellar and optochiasmatic cisterns, in the floor of the third ventricle).

The ophthalmological examination revealed a right central scotoma, along with visual field narrowing (superior-temporal in the right eye and inferior-temporal in the left eye). The optic fundus examination showed pupils with well-defined borders, hyperemic coloration, retina and vessels with no pathological modifications.

After all the investigations, the patient was diagnosed with GH-secreting pituitary macroadenoma. The patient was referred to the neurosurgical department for further investigations and, presumably, the ablation of the pituitary tumor.

In the same year, the patient was admitted to the neurosurgical department.

The general clinical systemic examination revealed normal values. The patient was conscious, cooperative, with a good general state, blood pressure = 130/80 mm Hg, and the heart rate = 88 beats/min. The acromegalic facies, the prognathism, the reversed occlusion and diastema ought to be noticed, along with the pale, wet and thickened integuments. Moreover,

widened and infiltrated extremities were noticed, but with no arthralgias.

The clinical neurological examination indicated a conscious patient, with no focal, motor or sensory deficits except headaches, no cranial nerves deficits, no signs of intracranial hypertension.

At the ophthalmological examination, the patient showed signs of optochiasmatic syndrome: relatively central right scotoma, visual field narrowing (superior-temporal in the right eye and inferior-temporal in the left eye). The optic fundus examination revealed an incipient bilateral papillary edema.

ENT examination revealed normal values.

Paraclinical investigations: the EKG and the pulmonary X-ray revealed normal values.

The X-ray of the *sella turcica* showed an enlarged sella turcica of 30/25 mm, balloon-like, with an interrupted contour. (Figures 1 and 2)

Figure 1 – X-ray of the sella turcica: enlarged, balloon-like sella turcica with an interrupted contour. From the personal collection of Dr. Dan Păunescu.

Figure 2 – An enlarged sella turcica on X-ray: balloon-like, with discontinuous contours. From the personal collection of Dr. Dan Paunescu.

The cerebral MRI examination (native and with gadolinium) revealed an expansive bulky intrasellar tumoral mass in the sphenoid sinus

and the suprasellar cistern, invading the right cavernous sinus, whose dimensions were 33/ 36/ 42 mm (Figures 3, 4, 5).

Figure 3 – Cerebral MRI: sagittal view reveals an intrasellar mass measuring 33/36/42 mm with a relatively homogeneous structure, with extension in the sphenoid sinus and suprasellar cistern, with invasion of the right cavernous sinus. From the personal collection of Dr. Dan Păunescu.

Figure 4 – Cerebral MRI - axial view

Figure 5 – Cerebral MRI - coronal view

Taking into account the patient's symptoms, the clinical and paraclinical investigations, the diagnosis made was "sellar and suprasellar tumor expanded to the right cavernous sinus and the sphenoid one (probably growth hormone-secreting pituitary macroadenoma)".

An elective surgical procedure was suggested to the patient, namely the surgical treatment of the tumor by means of a transnasal transsphenoidal approach.

Description of the surgery

The patient under general anesthesia was placed in the supine position with the head in extension at 10-15 degrees.

The nasal and buccal mucosae were disinfected with alcohol. The hydro-detachment of the nasal mucosa at the level of the septum through the infiltration of the submucosa with 1% xyline solution in order to decrease bleeding and facilitate the dissection of the septal mucosa.

A linear incision was made in the nasal mucosa, at the level of the nasal septum (at the junction between the bony and the cartilaginous nasal septum). The dissection of the nasal mucosa was continued with a decollator until the level of the junction between the bony and the cartilaginous septum. A conical nasal speculum was inserted which sprained laterally the cartilaginous nasal septum and the bony one arising in the mid-line. The paraseptal dissection of the mucosa at the level of the bony septum was continued until the level of the anterior wall of the sphenoid sinus. The resection of the vomer was done by pinching with a pinching clamp. The sphenoid ostium was identified. The resection of the anterior wall of the sphenoid sinus was made, along with the intra-sphenoid septa with the help of a Kerrison forceps. The speculum was replaced by a divergent one (the Hardy speculum). The mucosa of the sphenoid sinus was removed, an intra-sphenoid tumor was identified – a relatively homogeneous, white-reddish, gelatinous and encapsulated mass with fluid texture, occupying two-thirds of the sphenoid sinus. The tumor's capsule was incised and the intrasinus part of the tumor was removed using bayoneted ring curettes, irrigation, and suction. Thus prepared, the sinus was covered with cotton soaked in oxygenated

water for hemostasis and disinfection. Some anatomical parts were identified (the sella turcica, the clivus, the carotic canals) and the X-ray of the sella turcica was revised. The partially eroded floor of the sella turcica is highlighted and then resected. The intrasinus portion of the tumor is identified and the dura mater is incised in a cross. The tumoral content was voided, avoiding damage to the sellar diaphragm and to the elements at the level of the cavernous sinuses. The remaining empty cavity was filled with fat. After removing the speculum, the nasal septum was returned to the midline and the ipsilateral out-fractured middle turbinate was moved toward the midline. The hemostasis was made and eventually the anatomical planes were brought together. A dressing soaked in gomenol alcohol was inserted in both nasal fossae for 24 hours.

Figure 6. Microphotogram. Hematoxylin Eosin (H&E, 40x). Acidophilic, growth hormone-secreting pituitary macroadenoma. . From the personal collection of Dr. Dan Paunescu.

The histopathological examination confirmed the diagnosis of Acidophilic, growth hormone-secreting pituitary adenoma (Figures 6 and 7).

Figure 7 - Microphotogram. Hematoxylin Eosin (H&E, 10x).

Postoperative evolution

In the following days, the patient was kept under observation in order to detect a possible occurrence of diabetes insipidus and hyponatremia, but also to assess the function of the pituitary gland, of vision and of the patient's neurological state.

The postoperative clinical evolution was favorable and the patient was discharged three days after surgery.

Figure 8 – The postoperative cerebral CT scan showed: a residual tumor in the right cavernous sinus. From the personal collection of Dr. Dan Paunescu

Figure 9 – The postoperative cerebral CT

At the neurosurgical re-evaluation 3 months later, the patient was conscious and cooperative, with no focal, motor or sensory deficits, with no

cranial nerves deficits, and showed no signs of intracranial hypertension. Still, the optochiasmatic syndrome was still persistent. The cerebral CT scan revealed: a residual tumor in the right cavernous sinus (with maximal coronal diameters of 1.05/1.44 cm, sagittal diameters of 2.42/1.23 cm and axial intrasellar diameters 1.33/2.24 cm). The pituitary stalk was displaced to the left with 0.44 cm (Figures 8 and 9).

The endocrinological visit 3 months after surgery revealed the persistence of GH secretion (but with diminished values compared to the preoperative ones) and also decreased prolactin values. Treatment with somatostatin was recommended, but the patient refused the treatment.

OGTT	0	30	60	120
Glycemia (mg/dl)	96	168	126	83
GH (ng/ml)	75.3	70.2	74.2	45.2

Tabel 2 – Postoperative results of Oral Glucose Tolerance Test showing diminuation in GH level

- IGF-1: 968 ng / ml (normal range: 116-358 ng / ml)
- Cortisol 7.59 µg/dl (normal range: 7–10 a.m.- 5–25 µg/dl, 4–8 p.m. <10 µg/dl)
- Prolactin 11.12 ng / ml (normal range: 2.8–29.2 ng / ml)
- TSH 1.19 µIU / mL (normal range: 0.5–3.5 µU/ml)
- FT4 14.4 pmol/l (normal range: 12–22 pmol/l)

Gamma knife radiotherapy was suggested for the residual tumor at the level of the right cavernous sinus. Four months after surgery, the patient was admitted to the radiosurgical unit, where she was given a dose of 17 Gray/ 4.4 cmc target volume.

Treatment	17 Gy on isodose of 50%
Target volume	4.4 cmc
Overall dose	0.7-1.2 Gy (2.3 J)

Tabel 3 – Gamma Knife radiotherapy. A dose of 17 Gray/4.4 cmc target volume was given to the patient

At the neurosurgical visit this year, the patient did no longer present an optochiasmatic syndrome, and the hormonal dosages revealed the significant decrease in the GH level.

OGTT	0	30	60	120
Glycemia (mg/dl)	99	190	213	90
GH (ng/ml)	15.3	29.6	33.9	20.1

Tabel 4 – Results of Oral Glucose Tolerance Test (this year) showing significant decrease in GH level

- FSH 5.64 mIU / ml (normal range - follicular: 5–30 mIU/ml)
- LH 3.61 IU/l (normal range - follicular 5–30 IU/l)
- Estradiol 19.7pg/ml (normal range - follicular 19–140 pg/ml)
- Prolactin 18.35 ng / ml (normal range: 2.8–29.2 ng / ml)
- TSH 0.41 μ IU / mL (normal range: 0.5–3.5 μ IU/ml)
- FT4 7.4 pmol/l (normal range: 12–22 pmol/l)

A treatment with Somatostatin analogues was recommended which the patient accepted.

Discussions

Pituitary adenomata are benign tumors which grow from the adenohypophyseal cells, representing approximately 10-15% of all intracranial expansive processes.

They initially grow, expanding at the level of the sella turcica whose volume they increase, displacing and compressing at the same time the normal pituitary tissue. Thus specific endocrine disturbances appear in the case of secreting adenomata, partial pituitary failures of various hormonal lines, panhypopituitarism or the absence of endocrine signs in the non-secreting ones. The presence of headache is explained through the distension of the pituitary dura mater and sellar modifications (increased volume, modifications in the form of the sella turcica which seems eroded, globular, balloon-like, modifications in the vertical and the anterior posterior axes).

Further on, the tumor's growth can occur by means of suprasellar expansion which leads to the destruction of the clinoid processes and the sellar tuberculum and the break of the quadrilateral blade of the sphenoid. The expansion outside the sella turcica causes the compression of the nervous and vascular formations in the vicinity (nerves and optic

chiasm) or it can invade the 3rd or the lateral ventricles, thus leading to intracranial hypertension and secondary obstructive hydrocephalus.

Then the tumor may grow para or laterosellary, leading to the compression or invasion of the cavernous sinus with the embedment and compression of the internal carotid artery. When the tumor expands infrasellary, the fundus of the sella becomes thinner, being then eroded and destructed and the sphenoid sinus invaded.

At first, there appear dysfunctions affecting the optic nerve, the characteristic bitemporal hemionopsia, the decrease of visual acuity, discoloration of the optic papillae or primitive optic atrophy. Then there may also appear signs of intracranial hypertension (headaches, vomiting, papillary edema), psychic disorders (asthenia, bradypsychia, apathy) and altered states of consciousness (coma) and rarely epilepsy (through the expansion at the level of the temporal lobe). Diabetes insipidus may appear through to the progressive compression of the pituitary stalk. The invasion of the cavernous sinus causes damage to the nerves that pass through it: oculomotor, trochlear, ophthalmic and abducens nerves, along with the occurrence of palpebral ptosis, facial pain and diplopia.

In the case of active endocrine tumors, the endocrine syndrome occurs with clinical manifestations specific to each excessively secreted hormone. Thus, growth hormone-secreting adenomata lead to gigantism in children (when the tumor is formed before the closure of the growth cartilages) and acromegaly in adults. The incidence of acromegaly is 3-4 cases in a million, with a prevalence of 40-60% cases in a million. Acromegaly is characterized by: acromegalic facies (with mandibular prognathism, reversed occlusion, diastema, macroglossia), increase of the extremities, kyphosis, thickened skin, rheumatologic complications (with peripheral and spinal arthropathy), peripheral neuropathy and radicular syndromes or carpal tunnel syndrome (due to the nervous compression by narrowing the nerve emergence foramina), cardiovascular manifestations (HTN in 35% of the cases, acromagalic cardiomyopathy), visceral hypertrophy (affecting especially the

liver, the heart and the spleen), metabolic disorders (type II insulin-resistant diabetes) and respiratory complications (sleep apnea, drowsiness).

In the evolution of pituitary tumors, there may appear pituitary apoplexy which represents a neurosurgical emergency.

Intraoperatively, the invasion of the pituitary tumors is not constantly highlighted. From a histological point of view, they can be observed when they infiltrate the basal dura mater, the base of the cranial bony structures, the pituitary lodge and the arachnoid of the optochiasmatic cistern.

The invasion is positively correlated with the dimension of the tumor (which is lower in the case of secreting adenomata), with the type of endocrine secretion and the immune-histochemical type of the tumor. Therefore, polyhormonal adenomata as well as the tumors with acidophilic cells are the most aggressive.

The accurate assessment of the pituitary function through hormonal dosages is necessary both for the diagnosis of pituitary tumors and for the postoperative monitoring. A seric concentration of prolactin is determined, along with cortisol, free tyrosine (free T4), TSH, estradiol/testosterone, LH, FSH, somatomedin C (insulin-like growth factor IGF-1).

The set of imagistic investigation must comprise the X-ray of the sella turcica (which highlights the degree of pneumatization of the sphenoid sinus and assesses the aspect of the sella turcica). The investigation of choice in sellar pathology is the native cerebral MRI (pituitary tumors can be either hypo or isointense in T1 sequence and hyperintense in T2 sequence) and contrast MRI. The contrast media is not homogeneously fixed on the pituitary tumors. Postoperative MRI images (in the first 24 hours) may indicate the presence of a residual tumor.

The purposes of treating pituitary tumors are tumor ablation, decompression of nervous and vascular structures, normal state of the hormonal secretion, making a histopathological diagnosis and avoidance of tumor recurrence. At the same time, we aim to maintain the normal pituitary function and tissue, but also to avoid postoperative complications.

At the moment, the treatment of pituitary adenomata is multimodal. In growth hormone

and ACTH-secreting pituitary adenomata, the treatment of choice is by means of surgery, while medication and radiotherapy are seen as adjuvant treatments.

Transsphenoidal microsurgery represents nowadays the approach of choice in more than 95% of the pituitary tumors including ectopic pituitary adenomata, macroadenoma and tumors invading the sphenoid sinus, as well as pituitary apoplexy with quick decompression of the optic chiasm. It comprises considerably other sellar pathologies: chordomas, craniopharyngiomas, Rathke's cleft cysts or CSF fistulae. The contraindications include especially the suprasellar tumors with a normal sella turcica, the tumors with predominant cranial invasion and the infections of the sphenoid sinus. In all these cases, the classical transcranial approaches are preferred: pterional, subfrontal, expansive subfrontal, orbitozygomatic, bifrontal interhemispheric, anterior transcallosal. In other cases, mixed approaches are also convenient: transcranial and transsphenoidal.

In deciding upon the most appropriate approach, a few basic principles must be taken into consideration: the size of the sella turcica, the size and the pneumatization degree of the sphenoid sinus, the position of carotid arteries, the presence and the intracranial expansion of the tumor, histological uncertainty of the lesion, the surgeon's experience.

In choosing the treatment of sellar tumors, one must also take into account the efficiency of this microscopic transnasal transsphenoidal approach for the patient especially from the point of view of the morbidity rate (0.5%) and mortality rate (2.2%), which are lower than in case of transcranial approach. Moreover, this approach represents a less labored and traumatizing experience for the patient with a favorable postoperative recovery, thus avoiding the manipulation and trauma through traction or compression of the optic nerves, optic chiasm and brain. At the same time, this approach offers a direct view of the sella turcica and its content, avoids the opening of the cranium, frontal sinuses and subarachnoid space. Therefore, the risk of septic complications is lower and the risk of accidentally damaging the cavernous sinuses and carotid arteries is minimal.

Complications of the transsphenoidal approach : The most important complications of the transnasal transsphenoidal approach are the cerebrospinal fluid fistulae and meningitis which appear in less than 1% of the cases. If the cerebrospinal fluid fistula persists for more than 3-4 days under lumbar drainage, re-intervention is necessary with direct visualization of the fistula and correction of the defect with fascia lata and fat tissue. Meningitides are treated with antibiotics. Another complication is further bleeding inside the tumoral bed, suspected when the patient shows signs of headaches and visual function impairment. The evacuation of the hematoma and precise hemostasis solve this complication. Ocular palsies are rare and usually reversible. Diabetes insipidus persists at the check-up three months after surgery in only 1.5% of the cases. Other rare complications are the lesions of the carotid artery: hemorrhages, pseudo-aneurysms, arteriovenous fistulae, lesions of the cavernous sinus, optic nerve or chiasm, secondary empty sella syndrome, deterioration of the pituitary function.

Disadvantages of the transsphenoidal approach: Adjacent structures in large tumors cannot be visualized, the approach passes through unsterile fields, and also suprasellar sub frontal expansions, in the middle fossa or retroclival area which cannot be ablated.

Results

The transsphenoidal approach has increased the recovery rate up to 80-90% in case of microadenomata and 50-60% in case of noninvasive macroadenoma. Mortality appears in approximately 1-2% of the cases.

Recurrence in case of microadenomata are likely after 5 years, the ratio for prolactinomata being 40-50%, while for macroadenoma the recurrence period is 10 years, and the ratio in case of prolactinomata is 100%.

Radiotherapy is indicated after the surgical resection in patients whose imaging investigations reveal the presence of a residual tumor, especially if it has the tendency to grow or if the pathological hormonal hypersecretion persists. In case of residual tumors, radiotherapy is indicated after having taken into consideration the surgical re-intervention as a

first option (we must state that, in the reported case, radiotherapy was chosen due to the location of the residual tumor in the cavernous sinus, which made it surgically unapproachable). The purpose of radiotherapy was to reduce the size of the residual tumor without destroying the anatomical structure nearby, as well as to bring the pathological GH secretion to normal.

At present, radiotherapeutic techniques comprise radiotherapy using linearly accelerated particles, conformational or stereotactic, irradiation in a single dose or fractioned doses (LINAC) and stereotactic radiosurgery with gamma radiation, applied in a single dose through Gamma Knife.

Still, it is worth mentioning that in case of pituitary adenomata the radiotherapeutical effect doesn't appear immediately, and the maximal reduction of the tumoral volume is obvious 3 years after radiotherapy. In case of Gamma Knife radiosurgery, the control rate of the tumor's growth is 97% after 5 years; the biochemical remission occurs approximately in two years' time, being present in 60-80% of the patients 3 years after radiation. The occurrence of new hormonal failures is noticed in 34% of the patients after an average interval of 1.5 years from radiation.

Regarding the treatment with medication, somatostatin and its long-term effect analogues (Octreotide, Lanreotide) are indicated in the treatment of growth hormone-secreting tumors, as an adjuvant treatment after a surgical resection and radiation if the pathological hypersecretion persists. Their administration leads to bringing to normal the values of the GH in 80% of the cases along with IGF-1 in 70% of the cases. The reduction of the tumoral volume is not constant. The agonists of growth hormone receptors (Pegvisomant) inhibit the peripheral action of the growth hormone, normalizing the IGF-1 in 97% of the patients after 1-5 years of therapy.

Conclusions

Given the case presented along with the update of the information found in the specialty literature, we have reached the conclusion that the management of pituitary tumors has to be multimodal. Each patient needs to have an

individualized therapeutic scheme, which usually begins with transsphenoidal surgery, but may sometimes include other therapeutic options depending on the evolution of the patient.

Although in most cases of pituitary tumors the surgical approach may seem sufficient, there are also cases in which adjuvant therapy is necessary. It is indicated especially in the presence of a residual tumor that has the tendency to grow, or if the pathological hormonal hypersecretion persists.

In somatotropic hormone-secreting pituitary tumors, transsphenoidal surgery represents the gold standard. Depending on the size of the tumor and the degree of invasion, surgery may lead to remission in 50-70% of the cases. Patients for whom postoperative remission was not possible and the level of the growth hormone continues to be high, adjuvant therapy with somatostatin analogues, antagonists of growth hormone receptors, radiosurgery or conventional radiation are to be taken into consideration.

It is worth mentioning that in our case the option after the approach was the transnasal transsphenoidal radiotherapy due to the location of the residual tumor in the cavernous sinus, situation in which the tumor was surgically unapproachable. Together, the transsphenoidal approach and radiosurgery lead to the reduction of the tumoral mass and to the improvement of hormonal secretion. It is expected that in the future the GH secretion will be brought back to normal by introducing somatostatin analogues in the patient's treatment scheme.

In conclusion, in actively endocrine pituitary tumors, in sellar tumors with suprasellar and infrasellar expansions and invasion in the cavernous sinus it is necessary to appeal to a multimodal therapy: the surgical removal

through a transnasal transsphenoidal approach and adjuvant therapy afterwards, depending on the patients' evolution

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