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EDITORIAL

Clinical significance of pituitary adenoma consistency in patients undergoing endoscopic transsphenoidal surgery

Significación clínica de la consistencia del adenoma hipofisario en pacientes sometidos a cirugía transesfenoidal endoscópica

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Pituitary adenomas or pituitary neuroendocrine tumors (PitNETs) are, according to the latest classification,[1] one of the most common intracranial neoplasms, with a prevalence in the general population, according to imaging modalities and autopsies, of 10% up to 15%.[2] The vast majority are benign, slow-growing tumors. However, they can have significant clinical repercussions and cause a significantly impaired quality of life, even at very young ages, by causing symptoms due to hormonal excess (acromegaly, Cushing's disease) or deficiency (hypopituitarism), or compressing neighboring structures (loss of vision or oculomotor nerve involvement).[2]

Currently, the first-choice therapy for most of these tumors (except prolactinomas) is surgical excision, primarily through an endonasal endoscopic approach, which achieves very good results, especially in expert hands.[3] Although most PitNETs (85% up to 90%) are soft tumors—which greatly facilitates their removal—there is a 10% up to 15% of hard or fibrous tumors that can significantly complicate the surgical procedure and increase the morbidity and mortality associated with the procedure.[4,5]

The concept of consistency or hardness in a pituitary tumor is usually subjective and can be difficult to define and standardize. However, in recent years, there has been some consensus on its classification based on well-defined parameters. One of the most detailed categorizations is that of Rutkowski et al.,[6] who categorize tumors into 5 different groups: cystic, soft, intermediate, hard, and calcified. However, in our view, and more commonly in the literature, tumors can be categorized into 2 equally discriminative groups (mainly soft vs fibrous). Soft tumors are those easily aspirated with a conventional 10-Fr aspiration system, while fibrous/hard tumors require pre-fragmentation and dissection with curettes or extracapsular dissection.[4,7]

It is still to be elucidated which factor or factors determine an increased consistency in these tumors. Primarily, an increase in collagen fibers (types I, III, and IV) has been associated, as well as a higher expression of transforming growth factor beta-1 (TGF-β1).[8,9] Certain histological subtypes have been associated with softer (corticotropinomas) or fibrous/hard (thyrotropinomas) consistencies.[10] Previous medical therapies (dopaminergic agonists, somatostatin analogs, or even temozolomide) have been associated with

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changes in tumor consistency with controversial results. Some studies have linked the preoperative administration of bromocriptine in the management of prolactinomas with more fibrosis of the adenoma.[11]

Regardless of the cause, this increased consistency in some tumors seems to influence their clinical presentation. Hard tumors have been more frequently associated with hormonal deficiency, larger size, and visual deficit, although this can be difficult to separate from other tumor characteristics.[12]

Regarding surgical treatment, it also seems evident that a more fibrous consistency of the adenoma could influence both the outcomes and prognosis. The surgical technique varies in these cases, often requiring tumor fragmentation and extraglandular dissection, thus leading to greater manipulation of the normal gland. Recent reports have shown that more fibrous consistency is associated with lower rates of complete resection vs soft tumors (48.7% vs 76.3%),[4,8] implying that patients usually receive adjuvant therapies after surgery up to 3 times more frequently. Moreover, these fibrous tumors are associated with a higher probability of surgical complications, such as the intraoperative rupture of the sellar diaphragm with cerebrospinal fluid (CSF) leakage, which is 5 times more common in fibrous tumors—requiring more complex reconstructive techniques during closure—or postoperative panhypopituitarism and permanent diabetes insipidus, both being up to 10 times more common in surgical procedures of fibrous tumors. This is due to the above-mentioned glandular and tumor manipulation.[4] While it is true that analyzing these results in isolation is complex due to factors such as tumor size, cavernous sinus invasion, or age,[13] these findings persist after performing multivariable statistical analyses to control for these confounding factors.

It seems logical that, in this context, if the subgroup of patients with hard or fibrous tumors could be preoperatively identified, they could theoretically be referred to highly experienced surgeons in the management of this disease within multidisciplinary reference units.[14]

Therefore, in the last 10 to 15 years, efforts have been made to predict the consistency of these pituitary tumors based on preoperative radiological imaging modalities—mainly brain MRI—which have experienced significant advancements in recent years. The goal is to inform patients more precisely and individually about their tumor expectations and management and plan surgery more accurately. However, attempts to predict tumor consistency have been unsuccessful, often yielding contradictory results. Analyses of diffusion sequences, perfusion, T1 contrast uptake, T2 behavior, and even more complex analyses—elastography—have shown multiple inconsistent results. Therefore, we believe that, probably, and, at least, for now, using radiology as a standalone method to predict tumor consistency will not fully resolve the issue.[15] Recently, we have proposed a predictive model that considers not only preoperative radiological characteristics but also other clinical and biochemical criteria that have proven effective in predicting tumor consistency.[16] Additionally, to simplify its application, we have designed and published a scale to facilitate its use—the pituitary tumor consistency [PiTCon] score— (Table 1).[1] It is obvious that although this is just a first step that needs to be validated through multicentric studies with a larger number of patients, we believe it may be a step in the right direction.

Table 1 Estimate and interpretation of the PiTCon score (pituitary tumor consistency).

Characteristic	PiTCon score
Age (years)	
≥ 40	0
< 40	1
*Compression symptoms**	
No	0
Yes	1
Panhypopituitarism	
No	0
Yes	1
Craniocaudal extent (mm)	
< 20	0
≥ 20	1
Previous surgery	
No	0
Yes	2
PiTCon score	**Probability of fibrous adenoma**
0	< 10%
1	10% up to 25%
2	25% up to 45%
3	45% up to 65%
4	65% up to 80%
5	80% up to 95%
6	> 95%

* Clinical presentation with headache or visual symptoms.

Consistency, cavernous sinus invasion, tumor size, and previous treatments—whether surgery or radiotherapy—are, therefore, variables that determine the difficulty of surgical removal, affecting outcomes and marking patient progression. Except for the first-mentioned variable, the rest are easily identifiable in our office via radiology and the patient's health record. Therefore, we believe it is important to try to predict PitNET consistency as well, thus completing a sort of screening of complex patient cases, which could be individually referred to specialized units and reference centers (SURF) to maximize the chances of cure and minimize complications, thereby improving these patients' quality of life.

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