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Consensus

Non-functioning pituitary adenoma: When and how to operate? What pathologic criteria for typing?☆

Adénomes hypophysaires non fonctionnels : quand et comment opérer ? Quels critères anatomo-pathologiques retenir ?

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Abstract

After diagnosis of non-functioning pituitary adenoma and impact assessment (pituitary deficiency, visual field disorder), the question of management arises between surgery and surveillance. This part of the Consensus document aims to clarify the principal situations encountered in clinical practice (visual disorder, pituitary deficiency, asymptomatic adenoma, etc.), so as to determine which ones indicate surgery and which ones simple surveillance. Particular contexts are also dealt with (elderly patients, young women hoping for pregnancy, etc). The principal surgical techniques (microscopy, endoscopy, etc.) are also considered. Finally, in case of surgery, the principal pathologic criteria are specified (immunolabeling, proliferation markers, etc.).

Keywords: Pituitary adenoma; Pituitary deficiency; Visual field defect; Elderly subject; Pregnancy; Ki67; p53; Silent pituitary adenoma

Résumé

Après l'étape de diagnostic positif d'adénome hypophysaire non sécrétant, et l'étape d'évaluation du retentissement (déficit hypophysaire, altérations campimétriques), se pose la question de la prise en charge : chirurgie ou surveillance. Cette partie du consensus a pour objectif de déterminer quelles situations rencontrées en pratique clinique (altération campimétrique, déficit hypophysaire, absence de retentissement…) justifient d'une prise en charge chirurgicale ou d'une simple surveillance. Les cas particuliers tels que le sujet âgé, la femme jeune avec désir de grossesse… seront également évoqués. Enfin seront précisés les principales techniques chirurgicales, et les renseignements indispensables que devra comporter le compte-rendu anatomo-pathologique.

Mots clés : Adénome hypophysaire ; Déficit hypophysaire ; Anomalie du champ visuel ; Sujet âgé ; Grossesse ; Ki67 ; p53 ; Adénome hypophysaire silencieux

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1. Introduction

After diagnosis of non-functioning pituitary adenoma and impact assessment (pituitary deficiency, visual field disorder), the question of management arises, between surgery and surveillance. This part of the Consensus document aims to clarify the principal situations encountered in clinical practice, and to specify the criteria rendering surgery necessary, possible, or else, debatable with respect to simple surveillance. The principal surgical techniques are specified. Finally, the principle pathologic criteria to be determined on the operative specimen in case of surgery are defined to adapt postoperative treatment in case of remnant.

2. Indications for surgery

2.1. Symptomatic adenoma

2.1.1. Visual disorders

Improved vision is reported in some 80–90% of cases (including both partial and total recovery) [1,2]. Recovery may be progressive, over a period of up to 1 year after surgery. Some studies highlighted a correlation between percentage recovery and duration and severity of campimetric disorder (acuity < 1/10 or optic atrophy being of poor prognosis) [3,4]. In case of demonstrable visual disorder, surgery should therefore not be delayed; the urgency depends on the severity of visual impact. There are no clear data for a threshold time beyond which visual recovery after chiasma decompression is no longer possible. Visual disorders are an indication for surgery, even though complete recovery cannot be guaranteed.

2.1.2. Pituitary deficiency

The risk of onset of further pituitary deficiency associated with macroadenoma is estimated at 12% per year. Arafah et al. correlated preoperative deficiency, headaches and hyperprolactinemia to the potential for postoperative recovery: when all the criteria were met, postoperative recovery of deficiency and improvement in headaches were more frequent [5,6], correlating with intrasellar pressure. Surgery provided recovery of normal anterior pituitary function in about 30% of cases, at a mean of 1-year follow-up [7]; the rate was higher for earlier management. Some teams indeed recommend surgery at the asymptomatic stage of macroadenoma [7]. The risk of postoperative deterioration in pituitary function is about 10% [3]. Postoperative recovery being uncertain, pituitary deficiency is thus probably not the main factor indicating surgery.

2.1.3. Headaches

The involvement of pituitary adenoma in headaches can only be established after ruling out all other possible causes (possibly after referral to a neurologist) and determining time of onset in relation to the natural history of the adenoma.

Headaches are classically due to distension of the dural envelopes [8]. Retro-orbital or vertex locations suggest pituitary etiology. If headaches do indeed implicate adenoma, surgery seems to be effective in relieving symptoms [3,9,10]. Disabling headache implicating adenoma thus seems to be an indication for non-emergency surgery, warning the patient that no direct causal relation can be proven and thus results cannot be guaranteed.

2.2. Asymptomatic adenoma

Surgical indications are founded on several factors:

- patient age. Non-emergency surgery may be considered in young patients without awaiting progression, given the low risk of postoperative visual impairment, the almost inevitable progression of adenoma over the long term, and the risk of definitive postoperative visual impairment if surgery is delayed awaiting onset of a campimetric visual-field effect;
- the natural history of non-functioning adenoma (possible spontaneous increase or decrease in tumor volume). Losa et al. recently stressed that the risk of postoperative recurrence was lower with early surgery [11];
- the risk of onset of campimetric impairment, correlated with the rate of tumor growth and proximity to the optic pathways;
- the risk of onset of pituitary deficiency (12% per year in macroadenoma);
- the risk of apoplexy (estimated at 1% per year in the absence of extra risk factors: see corresponding Consensus article);
- risks inherent to trans-sphenoidal surgery: mortality is less than 1%; the risk of severe adverse events (osteomeningeal breach, meningitis, visual deterioration) is less than 5%; the risk of diabetes insipidus may reach 10%.

Progression is slow in microadenoma and surgery is not indicated. The natural progression of macroadenoma may indicate non-emergency surgery, depending on evolutive status, proximity to the optic pathways, and the patient's age.

2.3. Special cases

2.3.1. Elderly patients

Most studies set a threshold of 65 years for elderliness: physiological age would seem more relevant. There are, however, no data on complications or efficacy in patients aged over 75 years at diagnosis. Most studies combined secreting and non-secreting adenomas, making it difficult to know whether the complications reported relate exclusively to non-secreting adenoma.

Non-functioning adenoma accounts for 60–80% of adenomas in the "elderly", with incidence around 7% [12–14]. Characteristics seem to be identical to those found in "young" subjects, particularly as regards signs at diagnosis: the main presenting symptom is visual impairment, in 50–70% of cases [13]. Most patients present with macroadenoma of 2–4 cm on the long axis [12].

Therapeutic decision-making needs to take account of visual impact, proximity to the chiasm, and comorbidity: 80% of patients have at least 1 comorbidity [12]. Anesthesia risk assessment is crucial, 10% of patients having ASA risk scores contraindicating surgery [15]. One study suggested that non-secreting adenoma growth is slower in elderly subjects [16]. The risk of apoplexy, in the absence of extra risk factors (notably,