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Consensus

# Neuro-ophthalmologic exploration in non-functioning pituitary adenoma<sup>☆</sup>

## *Explorations neuro-ophthalmologiques d'un adénome hypophysaire non fonctionnel*

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### Abstract

Non-functioning pituitary adenoma may lead to blindness and causes visual impairment in 58% of cases and, more rarely, ocular motor disorder. Patients are slow to become aware of their visual dysfunction, vision in one eye compensating the deficit in the other. Assessment of visual function, comprising visual acuity and visual field evaluation and fundus examination, should be performed regularly according to the severity of impairment. Optic nerve optical coherence tomography (OCT) can quantify optic atrophy reproducibly, and is of prognostic value for postoperative visual recovery. Diplopia most often involves decompensation of heterophoria, visual field fusion being hampered by the visual field defect; such diplopia without ocular motor deficit is known as “hemifield slide”. Diplopia associated with ocular motor palsy is caused by tumoral invasion of the cavernous sinus (IIIrd, IVth or VIth nerve palsy); in large impairment, restricted eye movement is easily observed; milder palsies require neuro-ophthalmologic assessment and/or Lancaster test. Pituitary apoplexy induces ocular motor impairment in 70% of cases, strongly guiding diagnosis. Visual impairment is associated in 75% of cases. The degree of neuro-ophthalmologic (visual and ocular motor) impairment is one of the main criteria guiding treatment of pituitary apoplexy (conservative medical and/or surgical treatment) and follow-up.

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**Keywords:** Pituitary adenoma; Non-functioning pituitary adenoma; Visual field defect; Diplopia

### Résumé

Les adénomes hypophysaires non fonctionnels, pathologie potentiellement cécitante, sont responsables d'atteinte visuelle dans 58 % des cas et plus rarement de troubles oculomoteurs. L'atteinte de la fonction visuelle est longtemps asymptomatique, par compensation de l'œil controlatéral. Il est nécessaire d'effectuer une évaluation de l'acuité visuelle, du champ visuel et du fond d'œil de manière régulière, la fréquence dépendant de la sévérité de l'atteinte (entre tous les 3 à 6 mois au début). L'*optical coherence tomography* (OCT) du nerf optique peut compléter le bilan, et comporte une valeur reproductible, de suivi et pronostique, sur la récupération post-opératoire. Les diplopies les plus fréquentes sont en général liées à la décompensation de phories par le déficit du champ visuel, avec une perte de la capacité fusionnelle, sans déficit oculomoteur, et portent le nom de « glissement de l'hémichamp ». En cas de paralysie oculomotrice, l'atteinte est liée à l'envahissement du sinus caverneux par la tumeur (paralysie du III, du IV, ou du VI). Lorsque le déficit est important, une limitation des mouvements de l'œil est facilement observée. Lorsqu'il est minime, il nécessite un bilan orthoptique et/ou un test de Lancaster. En cas d'apoplexie pituitaire, l'atteinte oculomotrice, qui est présente dans

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70 % des cas, prédomine et est fortement évocatrice. Une baisse visuelle associée est observée dans 75 % des cas d'apoplexie. L'importance de l'atteinte neuro-ophthalmologique (visuelle et oculomotrice) est un des éléments essentiels dans le choix du traitement (médical conservateur et/ou chirurgical), ainsi que dans le suivi de cette pathologie.

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*Mots clés* : Adénome hypophysaire ; Adénome hypophysaire non fonctionnel ; Altération du champ visuel ; Diplopie

## 1. Introduction

Non-functioning pituitary adenoma (NFPA) is a major source of visual disorders, and is diagnosed later than functioning adenoma, often with larger tumor volume. Incidence of NFPA was 28–33.2% in pituitary adenoma populations, with or without visual involvement [1,2], but 58% in case of pituitary adenoma specifically with visual involvement [3]. Patients may be unaware of their deficit, especially in case of bitemporal hemianopsia, as functioning visual field in one eye can long compensate for visual field loss in the other.

Ocular motor impairment is mainly due to compression or invasion of the cavernous sinus, and is more frequent in case of large pituitary adenoma.

Finally, neuro-ophthalmologic involvement is critical in pituitary apoplexy, very frequently associating visual disorder, ocular motor disorder and headache of exceptionally sudden onset or with rapid progression.

The present paper will deal successively with visual involvement (acuity and visual field), ocular motor disorder, and neuro-ophthalmologic involvement in pituitary apoplexy.

## 2. Visual impairment

### 2.1. Anatomic bases

The visual impairment is caused by compression of the anterior visual pathways (optic nerves, chiasm, optic tracts) by the adenoma. The anatomic position of the anterior visual pathways with respect to the pituitary gland varies greatly from individual to individual, as does tumor orientation. Thus, while compression is usually chiasmal, it may also involve one or both optic nerves anteriorly or optic tract(s) posteriorly.

The ganglion-cell fibers that constitute the optic nerve change in spatial relation between the origin (in the inner retinal layers) and termination (in the lateral geniculate body).

Their organization in the retina and head of the optic nerve is as follows (Fig. 1): the fibers of the nasal retinal hemifield (temporal visual hemifield) are shown in blue and are distributed over the entire circumference of the optic nerve head when they reach it (blind-spot). The fibers of the temporal retinal hemifield (nasal visual hemifield) are shown in pink and are mainly located at the superior and inferior poles of the optic nerve head.

Along the optic nerve, the fibers gradually shift, bringing together those of a given quadrant of the visual field, with fibers corresponding to the superior and inferior temporal fields on the inside, ready to decussate, and those corresponding to the superior and inferior nasal fields remaining on the outside (Fig. 2).

A simplified diagram of fiber distribution (Fig. 3) is enough to explain the visual disorders induced by pituitary adenoma. At the chiasm, the ganglion cell fibers corresponding to the temporal hemifield of either eye cross the midline into the contralateral optic tract, while those corresponding to the nasal hemifield enter the ipsilateral tract, without decussation. Thus, visual information corresponding to the right hemifield is entirely encoded in the left optic tract, and vice-versa. Fibers encoding the superior temporal hemifield, when they cross over, initially head for the contralateral optic nerve before joining the contralateral tract; damage to these fibers is the source of the junctional Traquair syndrome (junctional scotoma) (cf. “Initial assessment”, below).

### 2.2. Pathophysiology

Contact between a pituitary adenoma and the anterior visual pathways is not in itself of visual impact. It is compression that induces visual disorder; the compression, however, is not measurable and is only indirectly suspected on imaging, as displacement of the visual pathways in contact with the tumor is present.

Several mechanisms are implicated in onset of visual impairment; initially reversible, they become irreversible. Reversible functional mechanisms comprise axoplasmic flow disorder, conduction blockage and demyelination. Irreversible mechanisms consist in axonal fiber degeneration under longer and/or more intense compression. This is seen in the fundus as optic atrophy; the level of redundancy of ganglion cell fibers forming the optic nerve and encoding visual information, however, means that a small degree of atrophy may be without functional impact, leaving visual acuity and the visual field normal. Advanced optic atrophy, on the other hand, induces lasting deficit, even after compression has been relieved by surgery.

### 2.3. Initial assessment

Ophthalmologic assessment includes visual acuity, pupil and fundus examination, ocular motor assessment and examination for ptosis (including cover test  $\pm$  Hess-Weiss coordimetric graph if necessary) and visual field assessment. The rest of the usual ophthalmologic assessment protocol (refraction, intra-ocular pressure, anterior segment slit-lamp examination, retinal examination) is also systematically performed, as other ophthalmic pathologies may interfere with the tumor-induced deficits: notably, severe myopia and tilted disc syndrome may mimic bitemporal visual field defect (Fig. 4A and B), and need to be identified.

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