The Journal of Laryngology and Otology
December 1999, Vol. **113,** pp. 1109–1111

Pituitary adenomas with infra-sellar extension into the nasopharynx

Benoit Godey, M.D.*, Xavier Morandi, M.D.†, François Le Gall, M.D.‡, Stephane Feat, M.D.*, Gilles Brassier, M.D., Ph.D.†, Guy Le Clech, M.D.*

Abstract
Three cases of pituitary adenomas with infra-sellar extension into the nasopharynx and the nasal cavities are reported. The clinical signs were epistaxis, nasal obstruction, painful sinuses and purulent rhinorrhoea. The initial diagnostic hypothesis was that of a carcinoma of the nasopharynx or the sinuses in all three cases. The diagnosis was made by histological examination and measurement of plasma hormone levels. These cases highlight the difficulty in the diagnosis of such tumours due to their misleading clinical, radiological and histological features.

Key words: Pituitary neoplasms; Nasopharynx; Diagnosis, otorhinolaryngological

Introduction

Pituitary adenomas presenting with infra-sellar extension into the sphenoidal sinus are frequent, but extension to the nasal cavity and the nasopharynx is very rare, accounting for only 0.8 per cent of pituitary adenomas (Pia *et al.*, 1985). We report here three cases of pituitary adenomas in which the initial clinical signs were rhinopharyngeal in nature and were suggestive of a carcinoma of the sinuses. The aim of this study is to show the various misleading clinical, radiological and histological features of pituitary adenomas with infra-sellar extension which can give rise to diagnostic errors.

Case reports

Case 1

A 62-year-old patient presented with a two-year history of recurrent minor epistaxis mainly on the right side and progressive nasal obstruction. A nasal fibrescopy revealed a soft, well-demarcated, pinkish mass which was obstructing the nasal cavity and herniating into the left choana. The rest of the clinical examination was unremarkable. A computed tomography (CT) scan showed a sphenoido-sellar tumour extending to the nasal cavity and eroding the clivus, the vomer and the floor of the sphenoidal sinus. There was a homogeneous uptake of contrast by the tumour. A magnetic resonance image MRI (Figure 1) showed that the extension into the nasal cavity was lifting up the nasopharyngeal mucosa. The appearance was that of a nasopharyngeal carcinoma.

A biopsy showed tissue composed of cells with a well-defined cytoplasm and rounded, regular nuclei. Immuno-phenotyping revealed that 10 to 20 per cent of the tumour cells were positive for anti-luteinizing hormone (LH) and anti-follicle-stimulating hormone (FSH) antibodies, while markers for growth hormone, thyroid-stimulating hormone (TSH), prolactin and adrenocorticotropic hormone (ACTH) were negative. Blood hormone levels showed a small increase in FSH-prolactin, GH, LH, free tri-iodothyronine (FT3) free thyroxine (FT4) and TSH blood levels were all normal. Thus, the diagnosis was made of a poorly secretory (gonadotrophin) pituitary adenoma.

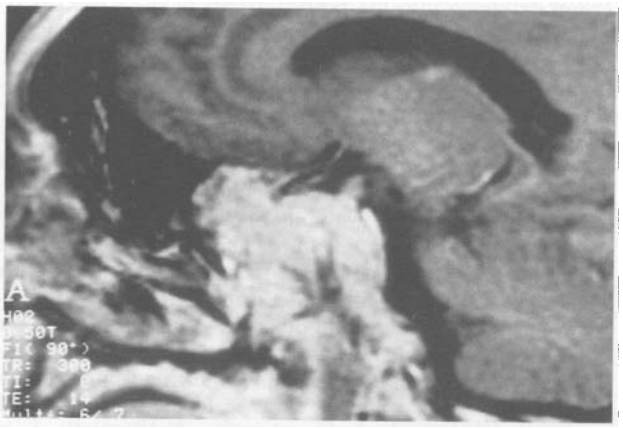

Fig. 1

(Case 1) MRI with gadolinium enhancement. Left parasagittal section showing anterior extension to the cavum and the nasal cavity.

Surgical treatment by the transseptal transsphenoidal approach was performed. The post-operative period was uncomplicated. Five years after the diagnosis, there were no MRI signs of relapse and the blood hormone levels remain normal.

Case 2

A 45-year-old man presented with a one-year history of increasing nasal obstruction and frequent, epistaxis. There was no visual disturbance. The nasal fibrescopy showed a

From the Departments of ENT and Maxillo-Facial Surgery*, Neurosurgery† and Histopathology‡, Rennes University Hospital, Pontchaillou, France.
Accepted for publication: 12 August 1999.

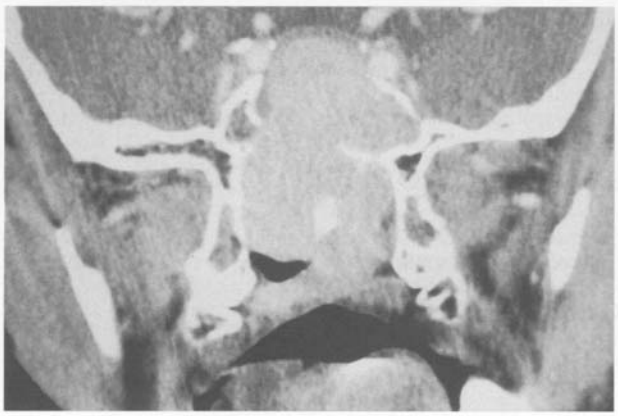

FIG. 2

(Case 2) Contrast-enhanced CT scan. Coronal section showing infrasellar extension to the cavum and the choanae, destroying the floor of the sella turcica and the sphenoidal sinus.

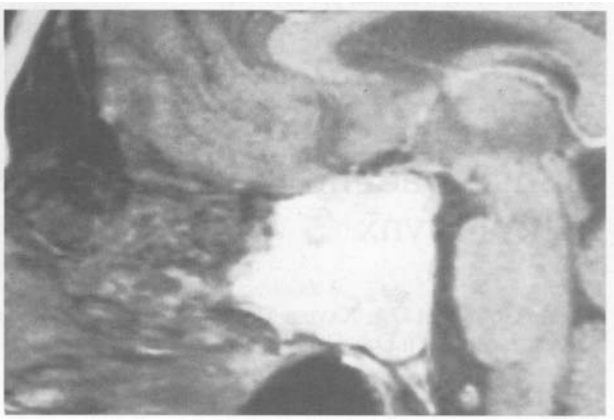

FIG. 3

(Case 3) MRI with gadolinium enhancement. Sagittal section showing anterior extension to the sphenoidal sinus, ethmoidal sinus, and superior part of the nasal cavity.

rhinopharyngeal tumour presenting as a highly vascular outgrowth which was completely obstructing the right choana. A computed tomography (CT) scan (Figure 2) revealed a massive spread of the tumour which was centred on the sphenoidal sinus and invading laterally the cavernous sinus and above, having penetrated the diaphragma sellae, the cisterna chiasmatis. Anteriorly, the lesion extended into the posterior part of the nasal cavity and choanae. On MRI, the mass had an isointense signal on T1-weighted images and showed an intense and homogeneous uptake of gadolinium. The working diagnosis was that of a carcinoma of the ethmoid.

A biopsy performed under general anaesthesia showed a tumour composed of large clumps of uniform, rounded cells, separated by delicate vascular-connective stroma. The cells had a relatively abundant cytoplasm, with a finely granular appearance, and uniform round nuclei without mitotic figures. These neuroendocrine features, along with the positive staining with anti-chromogranin A and anti-neuron specific enolase antibodies, suggested the diagnosis of a chemodectoma. However, this diagnosis was undermined by the unusual localization for such a tumour. New immunophenotyping studies were performed and revealed a strong positivity with anti-prolactin antibodies and weak positivity for FSH and LH. Blood prolactin levels were significantly raised and thereby confirmed the diagnosis of a prolactin-secreting pituitary adenoma.

Treatment was commenced with bromocriptine. Three years after the diagnosis, there were no signs of the rhinopharyngeal tumour on nasal fibrescopy. The MRI confirmed the regression of the tumour, which was confined to the sella turcica. The prolactinaemia was stable at a level only slightly above normal. Surgery was not considered necessary for this patient.

Case 3

A 39-year-old man presented with a four-month history of intermittent pain over the maxillary and frontal sinuses, associated with a fever and purulent rhinorrhoea. He also complained of a recent decrease in his visual acuity on the left side. Rhinoscopy showed the presence of a mass located postero-superiorly in the left side of the nasal cavity and in front of the left sphenoidal sinus. Macroscopically, the lesion appeared to be malignant. The nasal cavity was not obstructed and the nasopharynx was also patent. A CT scan confirmed the existence of an invasive lesion which appeared to be arising from the nasal cavity and extending upwards via the sella turcica towards the optic chiasma, anteriorly, towards the ethmoidal air cells and laterally towards the cavernous sinus. On MRI, the tumour was isointense on T1-weighted images and showed strong uptake of gadolinium (Figure 3). These findings were suggestive of carcinoma of the sinuses.

A biopsy was performed under local anaesthesia. The histological examination and immunophenotyping with anti-prolactin antibodies allowed the diagnosis of a pituitary adenoma. The plasma prolactin levels were elevated. The patient was treated with a combination of bromocriptine and dexamethasone which led to a rapid resolution of his painful symptoms and an improvement in the visual acuity. A MRI performed three months after the start of treatment showed that the tumour had decreased in size by 50 per cent and this was associated with a virtually normal blood prolactin level. Five years after the diagnosis, surgery was not considered necessary for this patient.

Discussion

Extra-sellar extension of pituitary adenomas is frequent, 35 per cent according to Scheithauer *et al.*, (1986) with extension to the sphenoidal sinus occurring in 4.6 per cent of cases (Pia *et al.*, 1985). However, extension to the nasal cavities remains rare and the incidence would appear to have regressed with time: 2.3 per cent of pituitary adenomas in 1939 (Henderson, 1939) and 0.8 per cent in 1985 (Pia *et al.*, 1985). In 1989, Van der Mey *et al.* (1989) cited 24 cases in the literature and reported three further cases. Since that time, 11 new cases have been reported in the English literature (Dent and Rickhuss, 1989; Iwai *et al.*, 1992; Van der Lely *et al.*, 1992; Luk *et al.*, 1996, Ravichandran *et al.*, 1999).

The problem posed by these tumours is that the diagnosis requires a high degree of suspicion in the face of a misleading presentation. None of our three patients had any endocrine signs. Apart from *Case 3*, who had diminished visual acuity, no clinical signs indicated a tumour of pituitary origin in these patients. The clinical presentation of these tumours was highly suggestive of pathology of the sinuses or nasal cavity. The main symptoms were nasal obstruction, epistaxis and painful sinuses, features compatible with a neoplastic lesion, in particular if they were associated with signs of ocular or frontal compression. The rhinoscopy showed a protruding, vascular, pinkish mass that bled easily on contact, also

https://doi.org/10.1017/S0022215100158037 Published online by Cambridge University Press

suggestive of a malignant lesion. In our three cases, the working diagnosis after the rhinoscopy was that of a carcinoma of the sinuses.

The diagnosis can be made easily from CT and MRI scans if the tumour is centred on the sella turcica and when there is supra-sellar extension. The diagnosis is more difficult when the extension is uniquely into the nasal cavities. It is difficult to be certain of the site of origin of the tumour based on radiology alone. The tumour appeared to be centred in the sphenoidal sinus in *Case 2*, and in the nasopharynx in *Case 3*. The destruction of the floor of the sella turcica can be seen in both pituitary adenomas and malignant tumours of the nasopharynx and sinuses, and these pathologies have the same density both before and after injection of contrast material on CT and MRI images.

The histological features can also be misleading. In the absence of endocrine markers, the neuroendocrine appearances can suggest a chemodectoma (*Case 2*). If the tumour is poorly differentiated, a misdiagnosis as an aesthesioneuroblastoma, an undifferentiated carcinoma or a malignant lymphoma can be made (Van der Mey *et al.*, 1989; Luk *et al.*, 1996). Van der Lely *et al.* (1992) reported on four nasal tumours, two diagnosed as being undifferentiated carcinoma and two as aesthesioneuroblastomas, where the histological material was re-examined in view of the excellent outcome. All four cases were pituitary adenomas. Nevertheless, the diagnosis can be made with certainty using antibodies detected against prolactin, FSH, LH, GH and TSH on immunohistochemistry, combined with the measurement of plasma levels of the pituitary hormones. Thus, a high degree of suspicion is required based on the clinical and radiological findings in order to direct the histopathologist to perform the appropriate marker studies.

The differential diagnoses are aesthesioneuroblastomas, chordomas, craniopharyngiomas, neuroblastomas, and carcinoma of the sinuses. Aspergillosis can present as a pseudo-tumour of the sphenoidal sinus producing identical radiological images, in particular, with respect to the bone erosion. Ectopic pituitary tumours must also be distinguished. They are most commonly located in the sphenoidal sinus (Anand *et al.*, 1993; Kikuchi *et al.*, 1994; Langford and Batsakis, 1995). They arise from embryonic remnants of the pharyngo-pituitary tract which are found in the pharyngeal mucosa and the posterior articulation between the sphenoid and vomer (Hori, 1985; Anand *et al.*, 1993). Radiological imaging can sometimes help differentiate between these ectopic adenomas and pituitary adenomas with infra-sellar extension by showing that the floor of the sella turcica is intact. However, ectopic pituitary adenomas can also erode the most inferior part of the sella turcica and invade the pituitary fossa. In such cases, the surgical observations during the operation, in particular, the integrity of the dura mater of the floor of the sella turcica, allow the diagnosis to be established (Kikuchi *et al.*, 1994).

Invasive prolactinomas are treated by bromocriptine as first line treatment (Van der Mey *et al.*, 1989; Van der Lely *et al.*, 1992; Anand *et al.*, 1993; Cook *et al.*, 1994). The effect of bromocriptine increases with the size of the tumour. If the reduction in the size of the tumour is inadequate, surgical excision can subsequently be performed. Follow-up is by monitoring the plasma prolactin levels and by MRI. The other secretory or non-secretory adenomas are treated by surgical excision which should be complete, if possible. However, complete surgical excision is difficult to achieve when there is significant superior extension. Post-operative radiotherapy at a dose of 45 to 50 Grays is reserved for cases of incomplete excision (Dent and Rickhuss, 1989; Iwai *et al.*, 1992; Anand *et al.*, 1993).

Conclusion

The clinical examination did not lead to the diagnosis in any of the three cases reported here. It is important in cases of persistent nasal obstruction, rhinorrhoea and epistaxis, to look for evidence of neoplastic and endocrine disorders which can suggest the presence of a pituitary adenoma. CT and MRI imaging allow the exact delineation of the spread of the tumour and sometimes even the aetiology. The diagnosis must be confirmed by a rhinoscopic biopsy and plasma hormone levels. The otorhinolaryngologist has an important role to play in alerting the histopathologist to the suspected diagnosis, otherwise without the appropriate hormone markers a misdiagnosis of an undifferentiated carcinoma or an esthesioneuroblastoma can be made.

References

Anand, V. K., Osborne, M., Harkey, H. L. (1993) Infiltrative clival pituitary adenoma of ectopic origin. *Otolaryngology – Head and Neck Surgery* **108:** 178–183.

Cook, R. J., Uttley, D., Wilkins, P. R., Archer, D. J., Bell, B. A. (1994) Prolactinomas in men masquerading as invasive skull base tumours. *British Journal of Neurosurgery* **8:** 51–55.

Dent, J. A., Rickhuss, P. K. (1989) Invasive pituitary adenoma presenting with nasal obstruction. *Journal of Laryngology and Otology* **103:** 605–609.

Henderson, W. R. (1939) The pituitary adenomata. A follow-up study of the surgical results in 338 cases. (Dr Harvey Cusching's Series). *British Journal of Surgery* **26:** 811–921.

Hori, A. (1985) Suprasellar peri-infundibular ectopic adenohypophysis in fetal and adult brains. *Journal of Neurosurgery* **63:** 113–115.

Iwai, Y., Hakuba, A., Klosla, V. (1992) Giant basal prolactinoma extending into nasal cavity. *Surgical Neurology* **37:** 280–283.

Kikuchi, K., Kowada, M., Sasaki, J., Sagheshima, M. (1994) Large pituitary adenoma of the sphenoid sinus and the nasopharynx. Report of a case with ultrastructural evaluations. *Surgical Neurology* **42:** 330–334.

Langford, L., Batsakis, J. G. (1995) Pituitary gland involvement of the sinonasal tract. *Annals of Otology, Rhinology and Laryngology* **104:** 167–169.

Luk, I. S., Chan, J. K., Chow, S. M., Leung, S. (1996) Pituitary adenoma presenting as sinonasal tumour: pitfalls in diagnosis. *Human Pathology* **27:** 605–609.

Pia, H. W., Grote, E., Hildebrandt, G. (1985) Giant pituitary adenomas. *Neurosurgical Review* **8:** 207–220.

Ravichandran, T. P., Bakshi, R., Heffner, R. R., Gibbons, K. J., Bates, V. E., Durante, D. J., Kinkel, W. R. (1999) Aggressive giant pituitary adenoma presenting as nasopharyngeal mass. Magnetic pathologic findings. *Journal of Neurooncology* **41:** 71–75.

Scheithauer, B. W., Koracs, K. T., Laws, E. R., Randall, R. V. (1986) Pathology of invasive pituitary tumours with special reference to functional classification. *Journal of Neurosurgery* **65:** 733–744.

Van der Lely, A. J., Knegt, P. P. M., Stefanko, S. Z., Tanghe, H. L. J., Singh, R., Lamberts, S. W. J. (1992) Nasopharyngeal presentation of pituitary tumours. Differential diagnosis and treatment. *Journal of Clinical Endocrinology and Metabolism* **74:** 811–813.

Van der Mey, A. G. L., Van Seters, A. P., Van Krieken, J. H. J. M., Vielvoye, J., Dulken, H. V., Hulshof, J. H. (1989) Large pituitary adenomas with extension into the nasopharynx. Report of three cases and a review of the literature. *Annals of Otology, Rhinology and Laryngology* **98:** 618–624.

Address for correspondence:
Benoit Godey, M.D.,
service ORL, CHU de Rennes,
2 rue Henri le Guillou,
35033 Rennes Cedex 9,
France.

Fax: 02.99.28.41.94
e-mail: benoit.godey@univ-rennes1.fr