Marked Hyperprolactinemia Caused by Carotid Aneurysm

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ABSTRACT: Background: Pituitary dysfunction caused by intracranial aneurysms is rare. We report a patient with the unique feature of hyperprolactinemia to a degree previously seen only with prolactin-secreting tumours. Method: Case report. Result: A 42-year-old woman had a galactorrhea, left-sided headache, reduced vision in the left eye and a left temporal hemianopsia. Serum prolactin was elevated (365 μg/L). Cranial computed tomography (CT) revealed a suprasellar mass, which carotid angiography showed to be a left internal carotid artery aneurysm. At craniotomy, this aneurysm and a smaller one of the ophthalmic artery were repaired, and the patient's vision returned to normal. The prolactin level fell to normal. Follow-up CT showed no evidence of pituitary adenoma or hypothalamic lesion. Conclusions: Carotid aneurysm can cause reversible pituitary dysfunction. A prolactin level >300 μg/L is not a reliable cut-off for distinguishing prolactin-secreting adenomas from other causes of elevated prolactin. A co-existing prolactinoma was felt to be ruled out by both a normal CT scan and normal prolactin levels following aneurysm repair. Patients with marked hyperprolactinemia should be considered for angiography or MRI to rule out carotid aneurysm, since the consequences of pituitary exploration in this setting are potentially grave.

RESUME: Hyperprolactinemie importante due à un anévrisme de la carotide. Introduction: Une dysfonction pituitaire causée par un anévrisme intracranien est rare. Nous rapportons un cas inusité d’hyperprolactinémie à un niveau décrit antérieurement seulement dans les cas de tumeurs sécrétant de la prolactine. Méthode: Report d’un cas. Résultats: Une femme âgée de 42 ans s’est présentée avec une histoire de galactorrhée, d’hémicranie gauche et de baisse de la vision de l’œil gauche, et une hémiopsie temporaire gauche. La prolactine sèrique était élevée (365 μg/L). La tomodensitométrie cérébrale (CT) a montré une masse suprasellaire et l’angiographie carotidienne a révélé qu’il s’agissait d’un anévrisme prenant naissance sur la carotide interne gauche. À la craniotomie, cet anévrisme et un autre plus petit sur l’artère ophtalmique ont été resserrés et la patiente a recouvré une vision normale par la suite. Le niveau de prolactine s’est abaisssé à normale. Le suivi par CT n’a montré aucun signe d’adénome pituitaire ou de lésion hypothalamique. Conclusions: L’anévrisme de la carotide peut causer une dysfonction pituitaire reversible et qu’un niveau de prolactine >300 μg/L n’est pas un critère fiable pour distinguer l’adénome sécrétant de la prolactine des autres causes d’hyperprolactinémie. Nous avons déterminé que la possibilité d’un prolactinome coexistant était éliminée par le CT scan normal au cours du suivi et par le fait que le niveau de prolactine s’est normalisé suite à la chirurgie. Les cas d’hyperprolactinémie marquée on devraient donc penser à faire une angiographie ou une RMN pour éliminer un anévrisme carotidien parce que les conséquences d’une exploration pituitaire dans une telle situation peuvent être graves.

The general physical exam was unremarkable, except for bilateral expressible galactorrhea. Neurological exam was notable for diminished visual acuity (20/200) and a temporal upper quadrantic hemianopsia in the left eye. Complete blood count and serum biochemistry were normal. Normal values were obtained for serum thyroxine, free thyroxine index, triiodothyronine, thyroid stimulating hormone, luteinizing hormone, follicle stimulating hormone and growth hormone. The 8 a.m. cortisol was low (160 nmol/L; normal 248-690); the 4 p.m. cortisol was normal (165 nmol/L; normal 83-414). Serum prolactin was markedly elevated (365 μg/L; normal < 25).

Dynamic pituitary function testing was performed via injection of thyrotropin releasing hormone (TRH) 200 μg i.v., CII insulin 0.1 μkg i.v., and luteinizing hormone-releasing hormone 100 μg s.c. There was a blunted TSH response to TRH and LH response to LHRH. Prolactin, which was 363 μg/L at baseline, rose to a peak of 499 at 30 min after TRH. Hypoglycemia was not achieved, making the interpretation of the blunted cortisol and growth hormone response impossible.

Skull X-ray revealed enlargement of the sella turcica and chiasmatic groove (Figure 1). Non-contrast CT scanning of the cranium demonstrated a suprasellar mass eroding the posterior clinoid (Figure 2). The history of severe unilateral headaches beginning eighteen months prior to the onset of galactorrhea and the documentation of assymetrical visual changes led to suspicion of a possible cause other than prolactinoma. Carotid angiography was performed and showed a 2 X 2 cm partially thrombosed aneurysm arising from the left internal carotid artery, above the anterior clinoid process (Figure 3). An MRI scan was not performed because of the perceived urgency of performing surgery before aneurysmal rupture.

At craniotomy a large aneurysm arising from the left paracclinoid internal carotid artery above the opthalmic artery was found. The aneurysm ballooned upward and posteriorly, compressing the optic nerve, optic chiasm, and hypothalamus. There was also a smaller aneurysm at the origin of the opthalmic artery which had not been appreciated on angiography. Both aneurysms were clipped without incident.

Post-operatively, the patient noted improved vision in the left eye (20/40). The post-operative angiogram showed two surgical clips at the level of the previous aneurysms and no evidence of residual aneurysm (Figure 4). Three months post-operatively the galactorrhea resolved, but the prolactin level remained elevated (77 μg/L). Eighteen months after the surgery, the prolactin level was still elevated (58 μg/L). The patient did not return for follow-up until four years after surgery, at which time the prolactin level was normal (19 μg/L), as were the TSH and prolactin responses to TRH infusion. A high resolution CT scan of the brain with coronal cuts of the sella done at this time showed no evidence of adenoma of the pituitary or lesions of the hypothalamus (Figure 5). An MRI scan was not performed because of the presence of surgical clips.
Intrasellar carotid aneurysm was in a 74-year-old woman with an intrasellar carotid aneurysm, hypopituitarism, and a serum prolactin of 182 |g/L. Tumours, as were 70% of cases with serum prolactin levels greater than 200 |g/L. A study of 235 patients with galactorrhea of various causes showed that likelihood of pituitary tumour directly correlated with the prolactin level, such that all cases with prolactin concentrations above 300 |g/L were associated with pituitary tumours. A coexisting prolactinoma was ruled out in this patient by a normal high resolution CT scan and a prolactin level which decreased post-operatively and was normal at four years follow-up.

A study of 204 patients with space-occupying sellar lesions and isolated hyperprolactinemia showed that in all cases of non-prolactinoma sellar lesions, the prolactin level was less than 130 |g/L. The highest prolactin previously reported in association with carotid aneurysm was in a 74-year-old woman with an intrasellar carotid aneurysm, hypopituitarism, and a serum prolactin of 182 |g/L. Surgery was not performed, hence a post-operative prolactin level was unavailable. However, in a 59-year-old woman with panhypopituitarism and hyperprolactinemia caused by a giant intracranial aneurysm, the prolactin level returned to normal by the thirteenth post-operative day. This is in contrast with our case, where the prolactin level remained elevated until sometime between eighteen months and four years post-operatively.

The mechanism by which carotid aneurysm produces hyperprolactinemia is likely via hypothalamic or pituitary stalk compression, resulting in interference with the delivery of prolactin-inhibiting factor to the pituitary. Two studies of patients with non-prolactin secreting sellar tumours with secondary hyperprolactinemia have, however, demonstrated a lack of correlation between suprasellar extension with compression of the pituitary stalk and degree of prolactin elevation. In our patient the extremely high level of prolactin suggests an additional stimulating effect by a putative hypothalamic prolactin-stimulating factor. It is not known whether the pulsatility of an aneurysm can stimulate the secretion of such a factor or stimulate the anterior pituitary itself. Studies in experimental animals have shown that irritative lesions of the anterior hypothalamus could potentially cause release of prolactin-stimulating factor. The reason that the prolactin level in our patient normalized only years post-operatively is unclear, but implies reversible stimulation of prolactin-secreting cells.

In summary, our patient illustrates that carotid aneurysm is a cause of reversible pituitary dysfunction, and that a prolactin level greater than 300 |g/L should not be considered to be a safe cut-off in distinguishing pituitary tumour from other causes of elevated prolactin. Thus, even patients with this degree of hyperprolactinemia should be subjected to cerebral angiography or magnetic resonance imaging if there is any clinical suspicion of carotid aneurysm, since CT scanning is not reliable for this purpose and the surgical consequences of pituitary exploration in this setting are potentially grave.

**REFERENCES**