

# PITUITARY PROLACTIN MICROADENOMA WITH, CORTICOTROPIC AND THYREOTROPIC DEFICIENCY: FROM INFERTILITY TO PREGNANCY: ABOUT A CASE

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## ABSTRACT

Pituitary adenomas are benign tumours developed at the expense of different cellular populations of the pituitary gland. Within the pituitary gland, several cell populations may be involved, but the lactotrophic cells remain the most frequently affected by this hyperplasia. For both sexes, the overall frequency of adenomas is 100 per million, of which 40% are prolactinomas. The stimulating effect of oestrogens (combined oral contraceptives and pregnancy) on lactotrophic cells has long been demonstrated, and in general, only large tumours (macroadenomas) have an evolving risk to be feared during pregnancy. The diagnosis rests on the one hand on the evidence of a hormonal hypersecretion of the cell population concerned as well as a hormonal deficiency of the other cell groups which can be compressed by the tumour. On the other hand, this diagnosis uses hypophyseal magnetic resonance imaging (MRI) to distinguish, according to their size, microadenomas (diameter less than 10 mm) from macroadenomas (diameter greater than 10 mm) pituitary. The risk of increasing the volume of the adenoma during pregnancy depends on the initial size of the tumour. This risk is evaluated at 2% for microadenoma and 15-35% for macroadenomas. However, the most severe complication during pregnancy remains acute paroxysmal growth or pituitary apoplexy by necrotic-haemorrhagic phenomena. The management is mainly based on prolactinoma on bromocriptine or cabergoline and sometimes surgery, urgently in the presence of a pituitary apoplexy or the presence of an evolutionary macroadenoma.

**KEYWORDS:** Pituitary microadenoma, infertility, pregnancy, prolactin

## Introduction

Pituitary adenomas are benign tumours developed at the expense of different cellular populations of the pituitary gland. Within the pituitary gland, several cell populations may be involved, but the lactotrophic cells remain the most frequently affected by this hyperplasia. For both sexes, the overall frequency of adenomas is 100 per million [1], of which 40% are prolactinomas. The stimulating effect of oestrogens (combined oral contraceptives and pregnancy) on lactotrophic cells has long been demonstrated, and in general, only large tumours (macroadenomas) have an evolving risk to be feared during pregnancy. A significant aspect is represented by fertility disorders induced in both sexes and which sometimes constitutes the circumstance of

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DOI:10.5455/IJMRCR.pituitary-microadenoma

First Received: March 26, 2017

Accepted: March 30, 2017

Manuscript Associate Editor: George Baitchev (BG)

Editor-in Chief: Cvetanka Hristova (BG)

Reviewers: Derun Taner Ertugrul (TR)

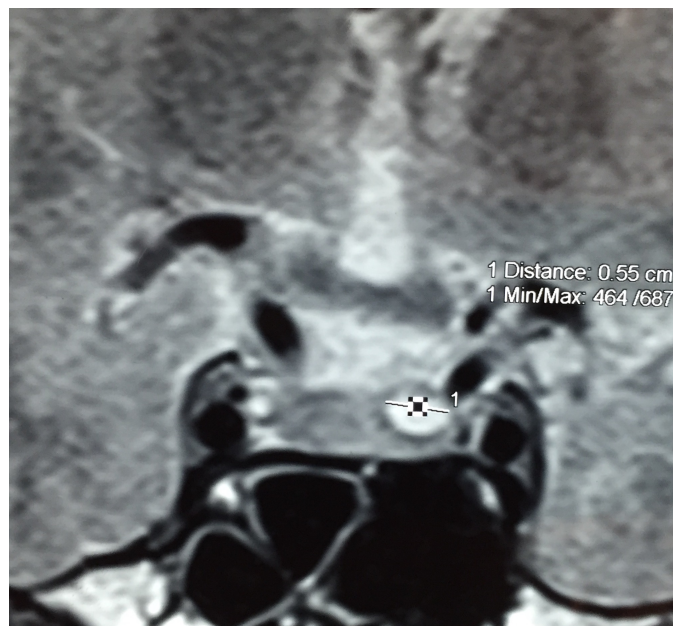
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discovery. The diagnosis rests on the one hand on the evidence of a hormonal hypersecretion of the cell population concerned as well as a hormonal deficiency of the other cell groups which can be compressed by the tumour. On the other hand, this diagnosis uses hypophyseal magnetic resonance imaging (MRI) to distinguish, according to their size, microadenomas (diameter less than 10 mm) from macroadenomas (diameter greater than 10 mm) pituitary. The risk of increasing the volume of the adenoma during pregnancy depends on the initial size of the tumour. This risk is evaluated at 2% for microadenoma and 15-35% for macroadenomas [2]. However, the most severe complication during pregnancy remains acute paroxysmal growth or pituitary apoplexy by necrotic-haemorrhagic phenomena. The management is mainly based on prolactinoma on bromocriptine or cabergoline and sometimes surgery, urgently in the presence of a pituitary apoplexy or the presence of an evolutionary macroadenoma. We reported here a case of microadenoma found during the infertility assessment and followed during pregnancy and childbirth.

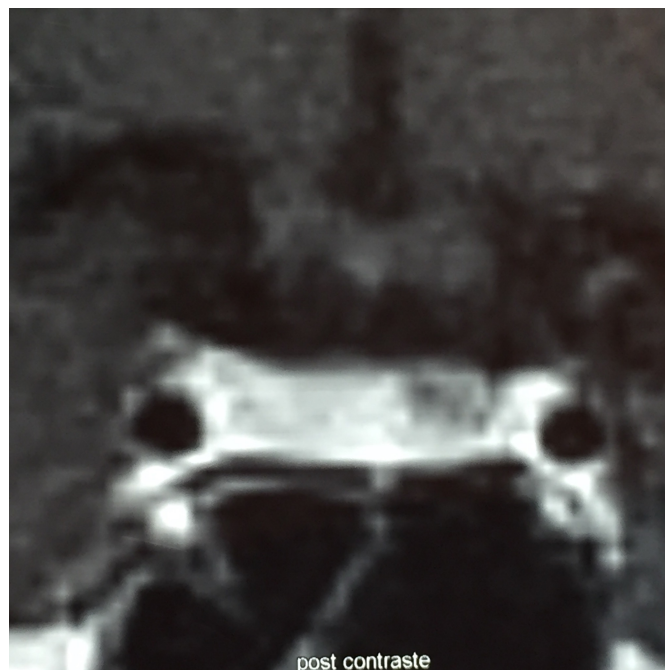
### Observation

Ms K B, 36, nulliparous, was referred the management of a galactorrhoea without amenorrhoea, and primary infertility of the unexplored 10-year-old couple. The interrogation found an age of onset of menars at 12 years, a regular menstrual cycle. We showed a delay in ideation, pubic and axillary depilation and bilateral galactorrhea. Examination of the thyroid gland found a homogeneous goitre without clinical sign of hypothyroidism. There was no evidence of intracranial hypertension. The patient had a body mass index of 27.04. The thyroxine (tetraiodothyronine) level was decreased to 9.96 pmol / L, a level of thyrotropin releasing hormone (usTSH) normal to 1.689 uUI / ml, a prolactin level of 45.42 ng/ml and a cortisol level of 78 ng/ml. Thyroid ultrasound noted a moderate left lobe heteronodular goitre. Pituitary magnetic resonance (MRI) imaging with gadolinium injection resulted in a 5.5 mm left micro-adenoma (Figure 1) with delayed contrast enhancement compared to the



**Figure 1:** Coronal section through the pituitary gland (T2), showing a tumour of 5.5 mm diameter.

rest of the gland (Figure 2). In summary, the diagnosis of pituitary prolactin's microadenoma was retained with corticotropic and thyrotropic insufficiency complicated by primary infertility. She had subsequently benefited from a cabergoline-based treatment at a dosage of 0.25 mg per week, levothyroxine due to 50 mg daily in two doses and 40 mg hydrocortisone. Nineteen months later, the patient, with very irregular follow-up, was admitted to maternity for the management of a pregnancy at 38 weeks of amenorrhoea complicated by severe preeclampsia (blood pressure of 240/130 mmHg). A caesarian was performed in emergency and had resulted in the birth of a female newborn weighing 3100 g. The return home was allowed after 12 days without complications. Three months after the patient was stable with a normal diaper return.



**Figure 2:** Coronal section of the brain passing the pituitary in T1 sequence with a dynamic injection, showing the delayed enhancement of the adenoma

### Discussion

Also known as pituitary hyperplasia, it is defined as an absolute increase in a cell population within the pituitary gland, manifested radiologically by an increase in its size [3]. The overall frequency of adenomas is about 100 patients per million [1]. However, prolactin adenomas (or prolactinomas) remain the most frequent of pituitary tumours. In both sexes, this condition is responsible for impairment of reproductive function. Indeed, hyperprolactinemia is responsible for suppression of the pulsatile secretion of gonadotropin-releasing hormone (GnRH), the positive feedback of oestradiol on gonadotropin secretion and inhibition of progesterone production by The granulosa of the ovary. Moreover, a mere duplication of its primary level (prolactin) is enough to produce these effects [4, 5]. The association with an insufficiency of other hormonal axes is rare [3]. Our patient simultaneously affected three cell populations (hyperprolactinemia, corticotropic insufficiency and thyrotropin) causing galactorrhea without amenorrhoea with infertility of the couple.

## Diagnosis

The diagnosis of adenoma is most often made before pregnancy [6]. The circumstances of the discovery are, in the woman in reproductive period, an amenorrhea-galactorrhea syndrome associated with infertility, a syndrome of Cushing and more rarely a tumour syndrome which makes suspicion a macroadenoma. The pituitary hormone assay, especially prolactin, regains very high levels greater than 30 or 35 mg / L, which are also strongly correlated with the size of the adenoma. Pituitary MRI reveals an increase in the volume of the pituitary, specifies its size and its relationship with adjacent structures (optic chiasm and cavernous sinus) and delayed contrast with the rest of the gland as it was for our patient (Fig. 2). It is classical to distinguish the pituitary microadenomas, whose diameter is less than 10 mm, from macroadenomas more than 10 mm in diameter [7]. Exceptionally, the adenoma is discovered during pregnancy by a tumoral syndrome related to pituitary hyperplasia on a pre-existing adenoma. The latter form provides complications such as apoplexy. The microprolactinoma is usually expressed by a hypointense image T1 and, in 4 cases out of 5, a T2 hyperintense signal. The hypersignal T2 may correspond to only a part of the adenoma [7].

## Management

The management of prolactinomas relies on medical treatment and neurosurgical excision of the tumour. The latter, although assuring the definitive cure, is only a second intention proposed. However, surgery becomes indispensable in the presence of a pituitary apoplexy or acute necrotic-haemorrhagic form and after the failure of the drug treatment. Moreover, the occurrence of pregnancy in these patients is only possible after a medical treatment that allowed standardisation of prolactin. It is based on the dopaminergic antagonist's bromocriptine, cabergoline and quinagolide. These molecules, by stimulating the D2 receptors, are responsible for a cascade inhibiting the lactotrophic cell. Their effectiveness varies between 70 and 90%. With a rate of tumour growth rate of 1.4% of microadenomas during pregnancy, it is recommended to stop antidopaminergic drugs to discover a pregnancy and to propose a simple monitoring [8]. The pregnancy occurred in our patient after one year of treatment, and the treatment could not be interrupted because she had been lost sight of and no malformation was detected at birth.

## Evolution and prognosis

In fact, during pregnancy, we see an increase in the lactotrophic cell population in the pituitary, which can reach half of its total cell population. This phenomenon is mostly observed during the second and third trimesters of pregnancy where oestrogen levels are highest. This suggests, according to its natural history, an aggravation of the symptomatology (intracranial hypertension) of the adenoma during the pregnancy. The evolutionary risk seems more important in the case of macroadenoma [9]. In our case, medical treatment had made it possible to correct the various disorders. It was followed by a pregnancy during which the patient presented no symptoms related to a complication of the adenoma (a headache, vomiting, visual disturbances).

## Conclusion

Pituitary adenomas are rare pathologies and have the particularity of involving several entities or cell groups of the pituitary gland. In women of childbearing age, it most often manifests

as an amenorrhea-galactorrhea syndrome or infertility of the couple. Its association with pregnancy, on the one hand of the good evolution of the pathology, also raises the problem of excessive tumour growth but also exposes these patients to major complications such as pituitary apoplexy.

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