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# CT follow-up of microprolactinomas during bromocriptine-induced pregnancy*

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**Summary.** In the last few years complete or partial regression of prolactinomas has been demonstrated in nonpregnant women treated by bromocriptine. Thus bromocriptine therapy appears as an attractive alternative to surgery for management of infertility related to hyperprolactinemia. However, numerous reports emphasized the possibility of an excessive growth of the pituitary adenoma with visual field defects during the last 3 months of pregnancy. To avoid these complications, the authors followed with serial CT scans the growth of microprolactinoma at the 5th or 6th month of pregnancy. Among six pregnant women, one patient presented a marked upward extension of the adenoma. Bromocriptine was then reintroduced and the effectiveness in reducing tumor growth was proved by CT scan at the 7th month. Regarding low risk of using intravenous iodinated contrast medium in pregnant women and of fetal radiation damage, the authors emphasize the value of CT in the follow-up of bromocriptine-induced pregnancies.

**Key words:** Prolactinoma – CT – bromocriptine – pregnancy

In the last few years many authors reported size reduction of pituitary macroprolactinomas in patients treated with bromocriptine [1–5]. Most of the computed tomographic studies have only demonstrated size reduction in huge prolactinomas with suprasellar extension [6–9]. Using a high-resolution CT scanner the authors demonstrated volume reduction in intrasellar microprolactinomas following bromocriptine therapy [10]. Treatment of infertile women with bromocriptine now makes pregnancy possible. Thus bromocriptine therapy appears as an attractive alternative to surgery [11] for management of anovulatory women related to hyperprolactinemia. However an excessive growth of the tumor with visual field defects may appear during the pregnancy [12–13]. To avoid these complications the authors suggest a CT follow-up at the 5th or 6th month of the pregnancy, so that bromocritpine therapy may be reintroduced if an excessive upward growth of the prolactinoma is noted.

## Material and methods

Since January 1980 more than 50 strictly intrasellar microprolactinomas have been studied with a GE CT/T 8800 scanner. Six women became pregnant after bromocriptine therapy and the tumor could be followed by a CT scan at the 5th or 6th month of the pregnancy. Before pregnancy each patient had a CT examination consisting of a scout view and 1.5 mm axial and direct coronal sections. Sagittal and frontal reformations were then carried out. The CT study immediately followed a bolus intravenous injection of 60 ml of 32% iodinated contrast medium (Hexabrix: sodium and meglumine ioxaglate, Laboratoires Guerbet, Aulnay-Sous-Bois, France) followed by a 100 ml perfusion during the examination [10, 14]. At the 5th or 6th month of pregnancy the CT study consisted of only six 1.5 mm direct coronal sections. The examination was performed after a bolus intravenous injection of 60 ml of Hexabrix followed by a 100 ml perfusion. In one patient the CT study was repeated at the seventh month of the pregnancy in order to follow the suprasellar expansion of the tumor. Pregnant women were protected with a lead rubber apron.

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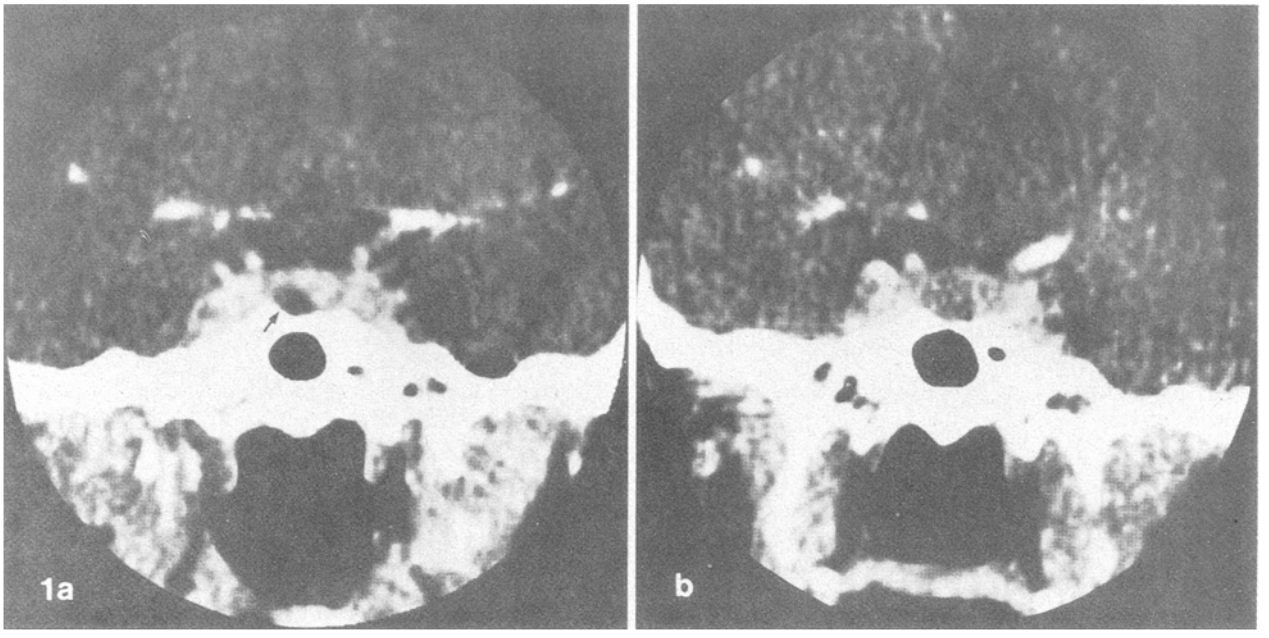


**Fig. 1 a and b.** Case 4. Microprolactinoma located in the right part of the pituitary gland. **a** July 1981, before bromocriptine therapy. Post contrast coronal section. 3 mm in diameter defect in enhancement *(arrow)* associated with a mild upward bulge of the sellar diaphragm. **b** March 1982, at the 6th month of the bromocriptine-induced pregnancy. Post contrast coronal section. An increased defect in enhancement (6 mm in diameter) and bulging of the sellar diaphragm are observed

## Results

Before pregnancy the nontreated intrasellar prolactinoma appears as a low attenuation area within the normal pituitary gland [10, 14, 15]. This low attenuation area corresponds to a defect in enhancement of the microadenoma: the average density of a nontreated microprolactinoma ranges from 15 to 25 HU, whereas the density of the normal enhanced surrounding pituitary gland is between 40 to 45 HU [10]. In some cases the microprolactinoma produces a heterogeneous low attenuation appearance of the pituitary gland. In adenomas greater than 4 mm in diameter, erosion and/or depression of the sellar floor, bulging of the sellar diaphragm and contralateral deviation of the pituitary stalk are usually associated [10, 16]. Among the 6 women studied, 4 presented a defect in enhancement ranging from 3 to 9 mm in diameter, and 2 presented a heterogeneous enhancement. An upward bulging of the sellar diaphragm could be observed before bromocriptine therapy and before pregnancy in all patients (Fig. 1). At the 5th or 6th month of the bromocriptine-induced pregnancy, CT examination demonstrated heterogeneous enhancement of the pituitary gland in 4 patients, a nonincreased defect in enhancement in one patient and an increased defect in enhancement in one patient (Fig. 1). An increased bulging of the sellar diaphragm associated with a visual field defect could be observed in one patient (Fig. 2, Table 1), in whom bromocriptine therapy was reintroduced at the 5th month of the pregnancy. A marked reduction of the tumor size associated with disappearance of the visual disturbances was noted 2 months later at the 7th month (Fig. 2, Table 1). All women delivered at term and all pregnancies resulted in normal children.

## Discussion

Because of the low risk of using intravenous iodinated contrast medium in pregnant women, and the negligible irradiation of the fetus, CT survey of microprolactinomas in bromocriptine-induced pregnancies seems valuable. Placental transfer of iodinated drugs is however well known: iodine crosses the placenta and amniotic fluid becomes highly iodinated [17]. Fetal hypothyroidism related to amniography with a ligo-soluble contrast medium has been reported. No thyroid defect was observed after amniography with a watersoluble contrast medium or after intravenous urography. Liposoluble contrast media appear to be more dangerous because they are less easily excreted [18]. The International Commission on Radiological Protection has recommended that the radiation dose to the fetus should not exceed

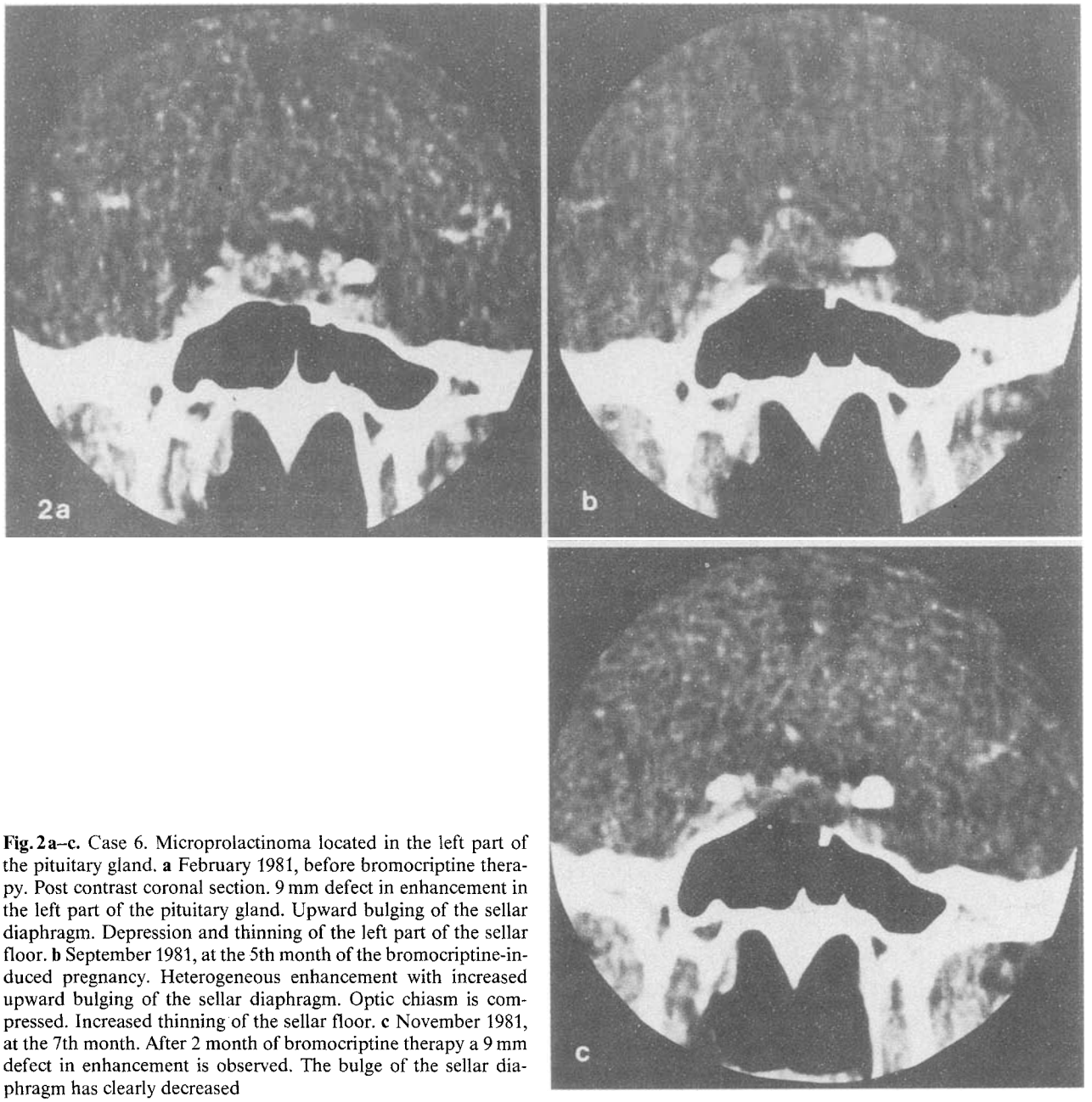


**Fig. 2a–c.** Case 6. Microprolactinoma located in the left part of the pituitary gland. **a** February 1981, before bromocriptine therapy. Post contrast coronal section. 9 mm defect in enhancement in the left part of the pituitary gland. Upward bulging of the sellar diaphragm. Depression and thinning of the left part of the sellar floor. **b** September 1981, at the 5th month of the bromocriptine-induced pregnancy. Heterogeneous enhancement with increased upward bulging of the sellar diaphragm. Optic chiasm is compressed. Increased thinning of the sellar floor. **c** November 1981, at the 7th month. After 2 month of bromocriptine therapy a 9 mm defect in enhancement is observed. The bulge of the sellar diaphragm has clearly decreased

1 rad during the known pregnancy [19]. Ovarian doses for head sections are less than 1 mrad per scan: 0.066 mrads without lead apron, and 0.006 mrads with a lead apron above and below the patient [20].

Low density areas in the contrast-enhanced pituitary gland are observed in pituitary microadenomas [10, 14, 16], but may also be observed in other normal and pathologic processes such as Rathke's pouch cysts (pars intermedia cysts), metastases, infarcts, abscesses or epidermoid cysts [15].

Nonsymptomatic Rathke's pouch cysts may alone be encountered in young infertile women, while the other lesions are observed in older patients. Rathke's pouch cysts are usually in the midline; their density ranges from that of CSF to normal pituitary gland levels. When smaller than 1 cm in diameter, these cysts have no clinical significance [15, 21]. Larger cysts may be symptomatic, however hypopituitarism is encountered rather than the amenorrhea and galactorrhea related to hyperprolactinemia [22].

During pregnancy the weight of the normal pituitary gland may double [16, 23]. Coronal sections at the 6th month may reveal homogeneous enhancement of the normal pituitary gland associated with

**Table 1.** Clinical and biological findings, and treatment

| Cases | Clinical symptoms | | | Plasma prolactin levels (mUI/l) before treatment | Bromocriptine therapy | | Before pregnancy | | | During pregnancy (at the 5th or 6th month) | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Age (years) | Amen-orrhea | Galact-orrhea | | Before pregnancy | During pregnancy | | Defect in enhancement | Bulging of the sellar diaphragm | | Defect in enhance-ment or heteroge-neous enhancement | Bulging of the sellar diaphragm |
| Case 1 | 28 | + | – | 1500 | 5 mg/day during 6 months | 0 | Feb. 1980 May 1981 (before treatment) | 9 mm | ++ | May 1982 6th month | defect of 4 mm | – |
| Case 2 | 24 | + | + | 1150 | 5 mg/day during 6 months | 0 | Oct. 1980 (before bromocriptine therapy) | 5 mm | + | Sept. 1981 6th month | heterogeneous enhancement comparable to CT scan of Feb. 1981 | – |
| | | | | | | | Feb. 1981 (after bromocriptine therapy) | heterogeneous enhancement | – | | | |
| Case 3 | 23 | + | + | 1500 | 5 mg/day during 7 months | 5 mg/day | May 1980 (before treatment) | 4 mm | + | June 1981 6th month | heterogeneous enhancement | + |
| Case 4 | 29 | + | + | 2170 | 5 mg/day during 5 months | 0 | July 1981 (before treatment) | 3 mm | + | Mar. 1982 6th month | defect of 6 mm | ++ |
| Case 5 | 26 | + | – | 1400 | 5 mg/day during 3 months | 0 | Sept. 1980 (before treatment) | heterogeneous enhancement | + | May 1981 6th month | heterogenous enhancement | + |
| Case 6 | 32 | + | + | 1840 | 5 mg/day during 5 months | 5 mg/day during the 3 first months and 5 mg/day from the 5th to the 9th month | Feb. 1981 (before treatment) | 9 mm | ++ | Sept. 1981 5th month | heterogeneous enhancement | ++++ |
| | | | | | | | | | | Nov. 1981 7th month | defect in enhance-ment of 9 mm | ++ |

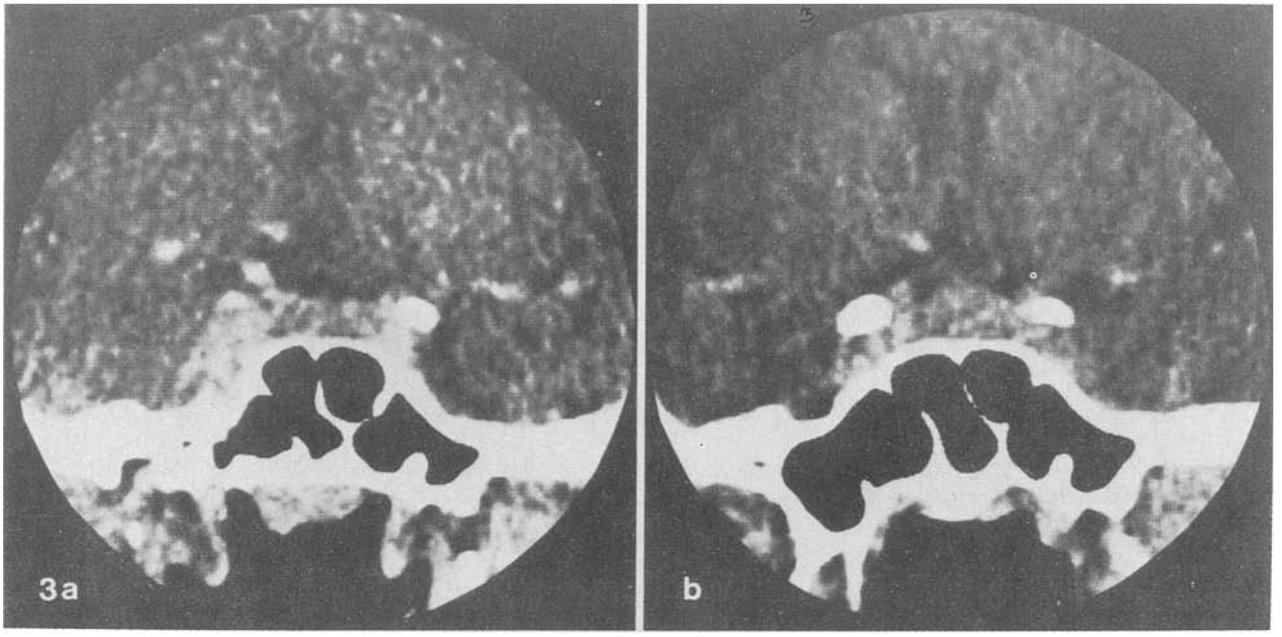


**Fig. 3a and b.** Pituitary gland without prolactinoma during pregnancy. **a** Before pregnancy the sellar diaphragm appears flat. **b** At the 6th month of pregnancy a heterogeneous enhancement of the pituitary gland and an upward bulging of the sellar diaphragm are observed

an upward bulging of the sellar diaphragm without deviation of the pituitary stalk (Fig. 3).

Enlargement of symptomatic pituitary prolactinomas may be observed after bromocriptine-induced pregnancy [12, 13, 24–27]. Gemzell and Wang [26] studied the outcome of pregnancy in women with pituitary adenomas: 25% of the patients with previously untreated microprolactinomas presented complications (headache and visual disturbances), usually during the first and second trimester; only 2% of the women with previously untreated microprolactinomas presented headache and visual disturbances and usually during the 2nd and 3rd trimester of the pregnancy. Gemzell and Wang proposed the following protocal for management of pregnant women with microprolactinomas: measurement of prolactin levels and visual field examination at monthly intervals and, if a visual field defect appears, the possible use of bromocriptine [26]. We suggest adding to the clinical and biological survey, a CT survey at the 5th or 6th month or earlier if a visual field defect appears. Effectiveness on the tumor size of the reintroduced bromocriptine therapy may be appreciated on a repeated CT examination 1 month later.

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