Prolactinoma and Dopamine Agonists

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Jean-François Bonneville

The long-acting dopamine agonist cabergoline is considered the first line therapy for both microprolactinomas and for macroprolactinomas. Tumor shrinkage starts very early (days or weeks) after initiation of medical treatment (Fig. 6.1). Therefore, cabergoline can be prescribed even for macroprolactinomas abutting the optic chiasm, but in such cases an early MR follow-up, for instance after 2 weeks, is strongly recommended to check that the optic chiasm is not further compromised. Importance of tumor shrinkage is variable and cannot be predicted in individual cases. Usually if a significant shrinkage of about 50 % is demonstrated in the first weeks after initiation of medical treatment, the maximum shrinkage of macroprolactinomas can be observed after 6 months or 1 year (Fig. 6.2). Conversely, observations of quick and complete tumoral shrinkage have been described, with a risk of rhinorrhea, meningitis, or abscess after opening a meningeal breach in macroprolactinomas invading the sphenoid sinus (Fig. 42.1). It is thus recommended to start cabergoline treatment at low dosage, and strictly assess tumoral shrinkage with MRI in those cases of macroprolactinomas invading the sphenoid sinus with skull base erosion. More frequently, shrinkage of macroprolactinoma leads to a partial or, more rarely, complete secondary empty sella with ptosis of the optic chiasm (Fig. 6.3). Tumoral shrinkage is mostly accompanied by MRI signal changes: accentuation of T2 hyperintensity of the adenoma is commonly observed (Fig. 6.4). Nevertheless, no T1 signal change is noted with hemorrhagic adenomas (Fig. 6.5) or T2 markedly hyperintense adenomas (Fig. 6.6). In these situations, tumoral shrinkage is less important than is generally seen in the more common T1 hypointense/T2 slightly hyperintense microprolactinomas.

Late changes of microprolactinomas with prolonged dopamine agonist treatment are variable (Fig. 6.7). Complete disappearance of the prolactinoma image is rare: when stabilization is obtained, it generally remains a T2-hyperintense, laterally located image, with no correlation with the prolactin level. A pathognomonic V-shaped appearance of the upper surface of the pituitary gland sometimes represents the late memory of the treated microprolactinoma (Fig. 6.8). Remodeling of the bony contours is often remarkable. Silent pituitary hemorrhage is frequently observed with medical treatment, but dopamine agonists do not seem to be a risk factor for true pituitary apoplexy. An increased T1 hyperintensity of the normal residual anterior pituitary has been noted in rare cases (Fig. 6.9); we have advanced the hypothesis of a compensatory mechanism of a localized increased hormonal synthesis of the residual anterior pituitary gland. Decision making of a therapeutic window may be proposed after 2 years of dopamine

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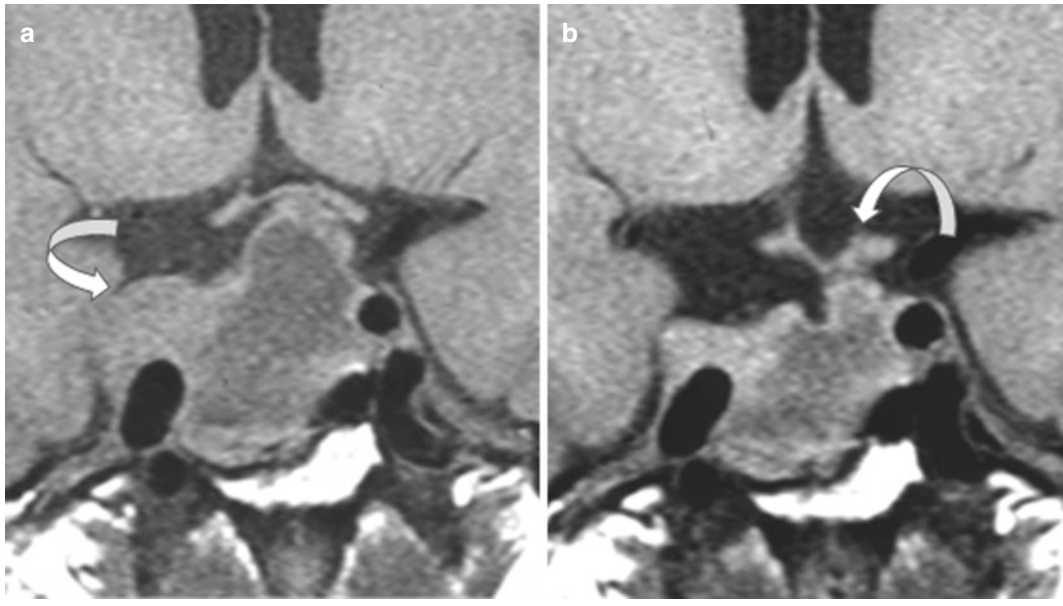

Fig. 6.1 Macroprolactinoma abutting the optic chiasm and invading right cavernous sinus (*arrow*). (**a**, **b**) Coronal T1WIs. Rapid shrinkage is visualized 10 days after cabergoline treatment initiation (**b**). Note that the shape of the optic chiasm is reversed (*arrow*)

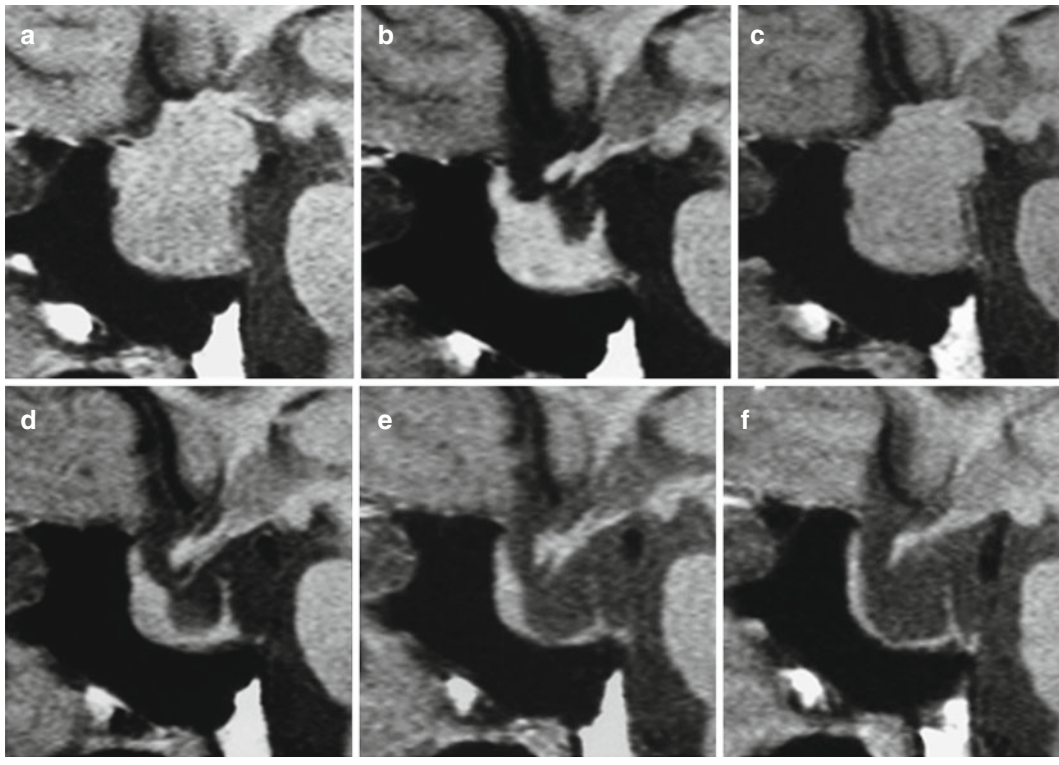

Fig. 6.2 Macroprolactinoma with suprasellar extension. (**a**–**f**) Sagittal T1WIs. (**a**) Before treatment. (**b**) Six weeks after dopamine agonist treatment. (**c**) The patient has stopped treatment: re-expansion of the tumor. (**d**–**f**) Shrinkage of the adenoma after reinstitution of medical treatment on sequential MRIs at 2 months, 1 year, and 2 years, respectively. Secondary empty sella

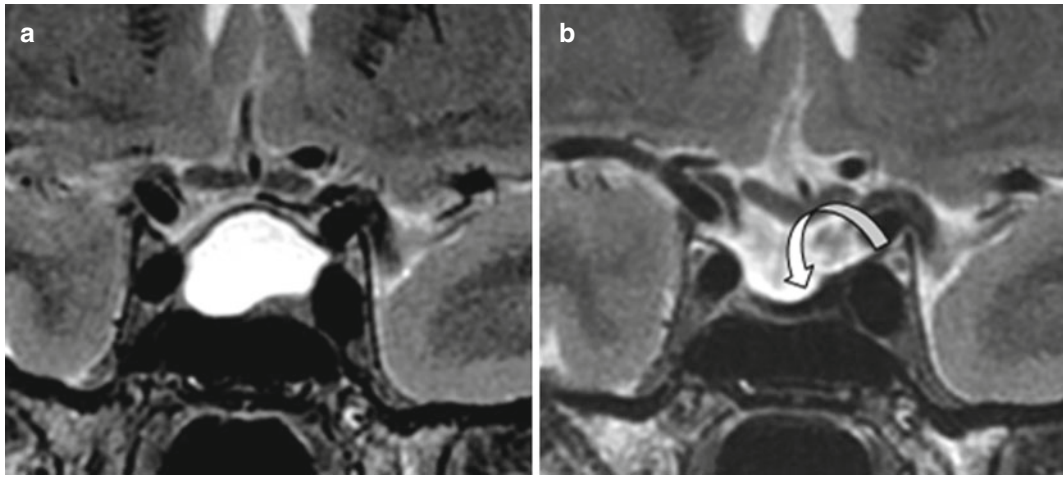

Fig. 6.3 Macroprolactinoma with old hemorrhage. (**a**, **b**) Coronal T2WIs. T2 tumoral hyperintensity. Six months after dopamine agonist treatment (**b**), complete shrinkage of the tumor is seen. A thin dark band doubling the sellar diaphragm is related to hemosiderin deposit (*arrow*)

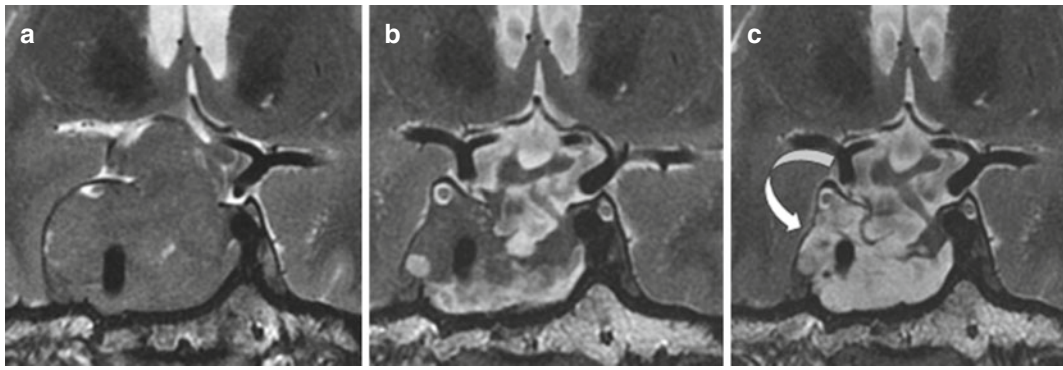

Fig. 6.4 Macroprolactinoma invading right cavernous sinus. (**a**–**c**) Coronal T2WIs. (**a**) Before treatment. Shrinkage and progressive T2 hyperintensity at 3 months (**b**) and 1 year (**c**) of dopamine agonist treatment. Shrinkage and signal changes affect cavernous sinus tumoral compartment (*arrow*) and intrasellar compartment

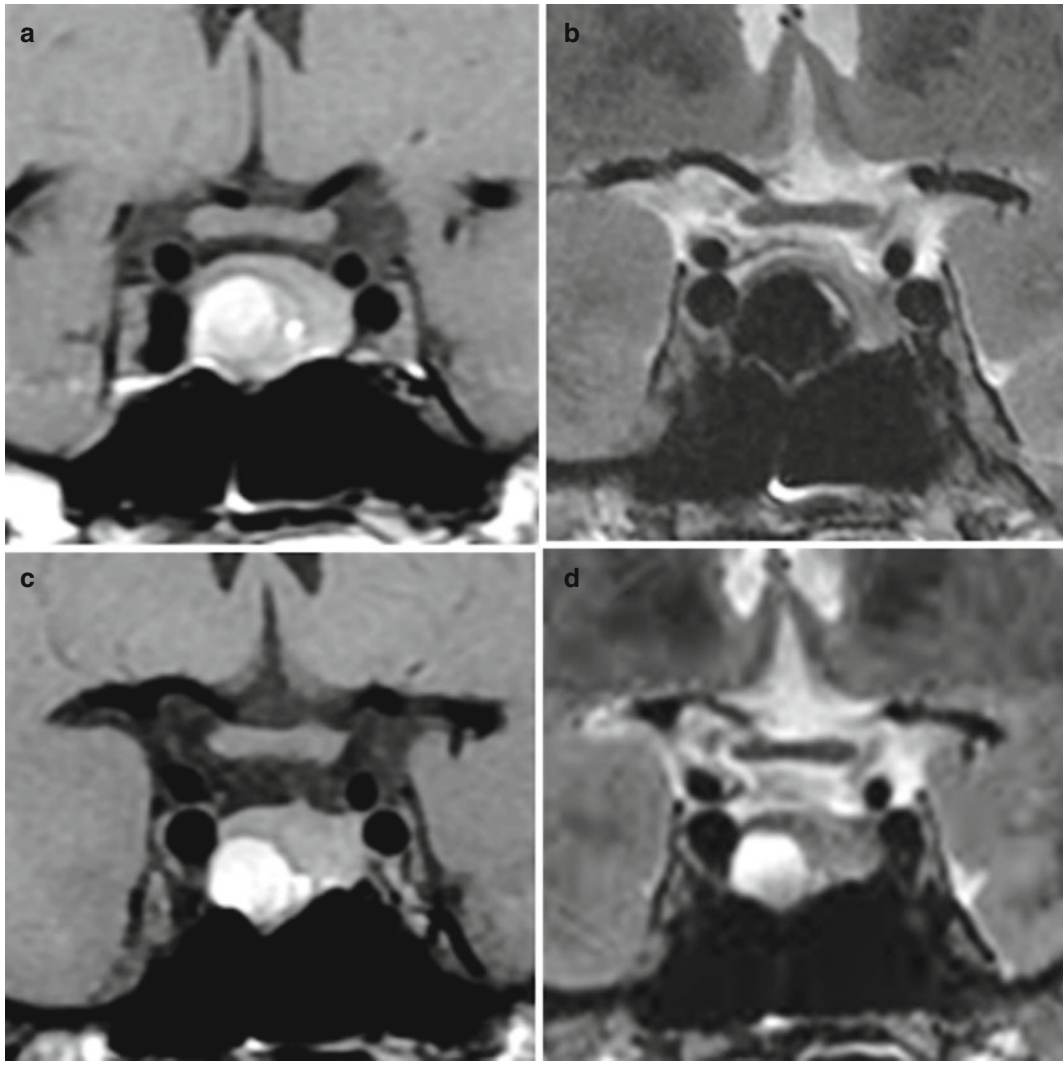

Fig. 6.5 Macroprolactinoma with fresh hemorrhage. (**a**, **c**) Coronal T1WIs. (**b**, **d**) Coronal T2WIs. Four months after treatment with dopamine agonists (**c**, **d**), T1 and T2 hyperintensity of the mass is observed. Mild tumoral shrinkage

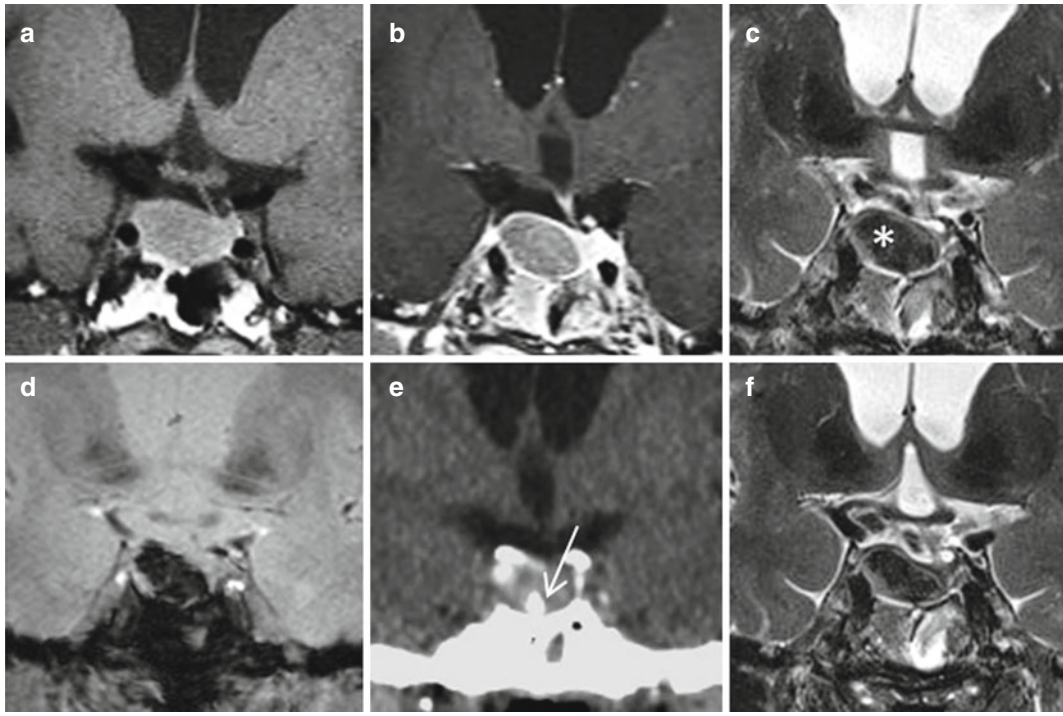

Fig. 6.6 Rare calcified prolactinoma in a 66-year-old woman before and after 6 months of cabergoline treatment. Prolactin level is 60 and 7 ng/ml, respectively. (**a**–**d**) Coronal T1, CE T1, T2, and T2* WIs. Marked T2 hypointensity of the intrasellar adenoma (*asterisk*). (**e**) Coronal CT. Confirmation of intrasellar calcifications (*arrow*). (**f**) Coronal T2WI. Moderate shrinkage after treatment

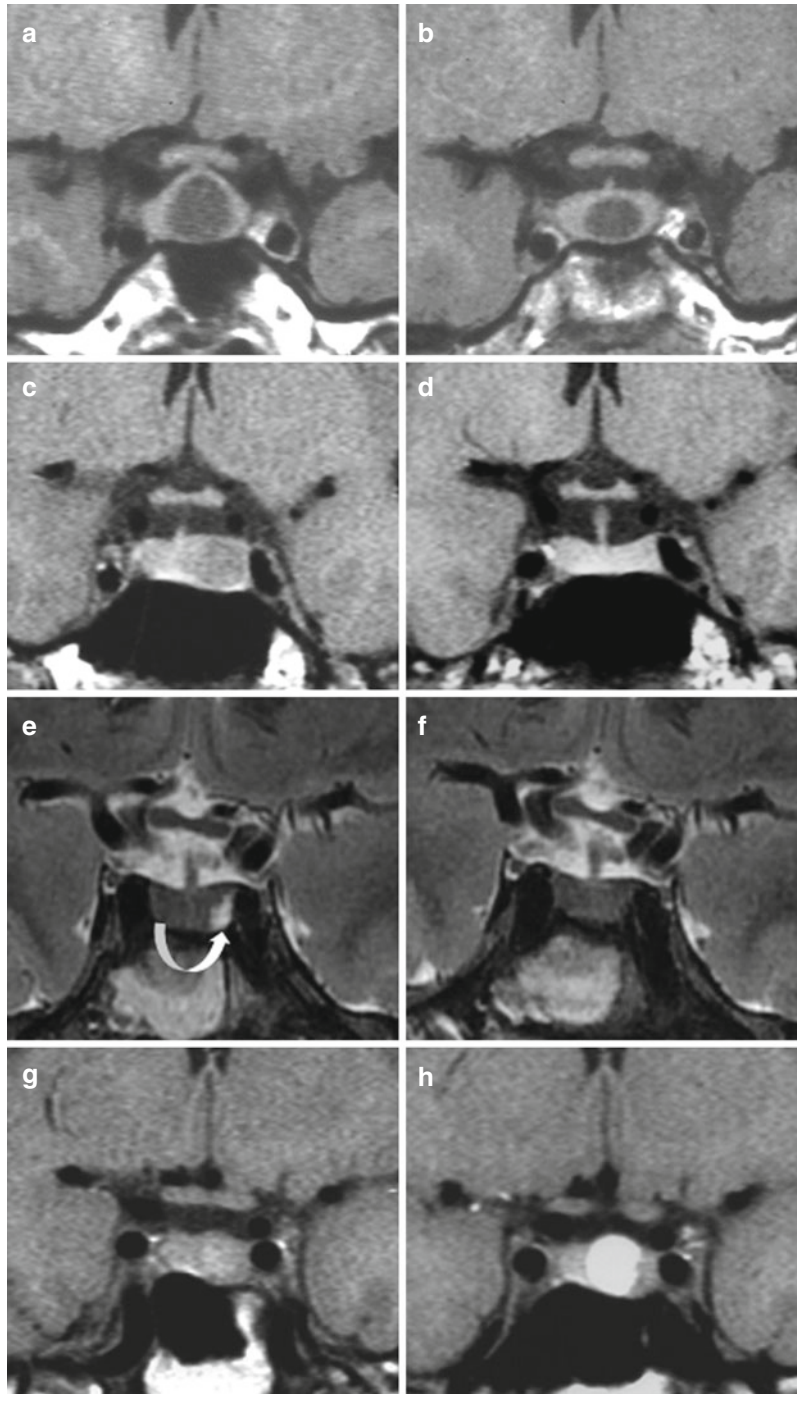

Fig. 6.7 Usual patterns of microprolactinomas before (*left column*) and a few months after dopamine agonist treatment (*right column*). (**a**–**d**) Coronal T1WIs. (**e**, **f**) Coronal T2WIs. (**g**, **h**) Coronal T1WIs. 50 % shrinkage in (**b**). Complete disappearance of the adenoma image and normalization of the sellar floor (rare) in (**d**). Disappearance of the prolactinoma on T2WI in (**f**): this evolution does not preclude the cure of the prolactinoma if cabergoline treatment is suspended. Hemorrhagic transformation (asymptomatic) in (**h**)

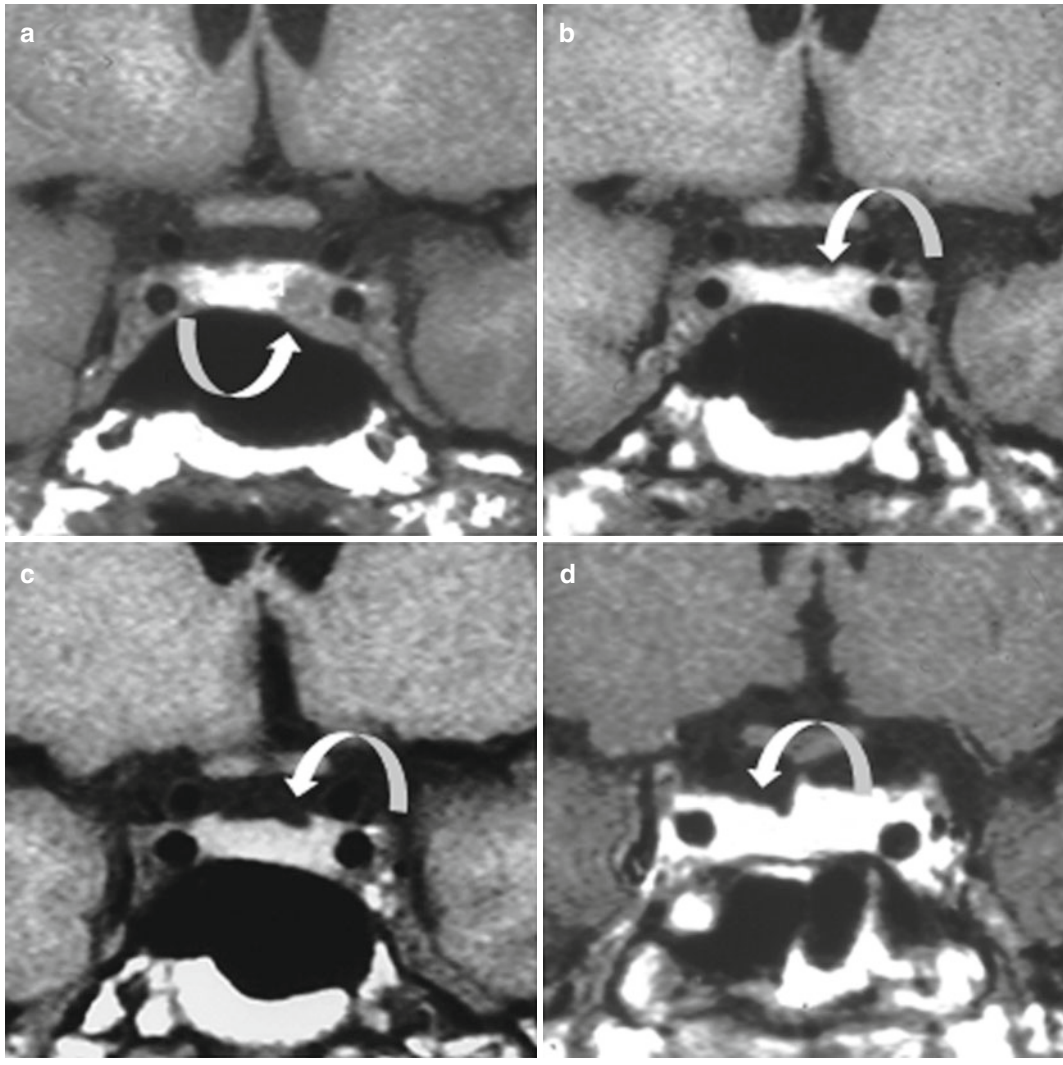

Fig. 6.8 V-shaped appearance of the upper surface of the pituitary gland in treated microprolactinomas. (**a**–**c**) Coronal T1WIs and (**d**) CE T1WI. (**a**) Left-sided prolactinoma invading left cavernous sinus (*arrow*). (**b**) Prolactinoma shrinkage and small indentation of the upper surface of the gland after cabergoline treatment (*arrow*). (**c**, **d**) V-shaped indentation of the upper surface of the pituitary gland in two patients with treated prolactinomas (*arrows*)

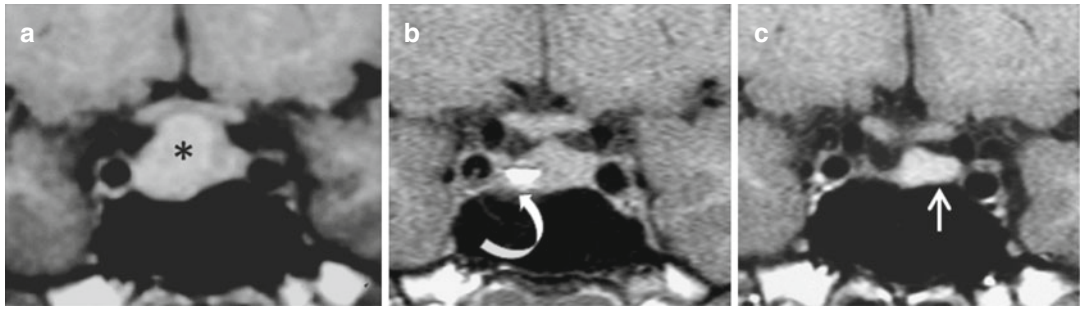

Fig. 6.9 T1W hyperintensity of normal residual anterior pituitary. (**a**–**c**) Coronal T1WIs. (**a**) Right-sided hemorrhagic macroprolactinoma (*asterisk*) deforming the sellar floor and abutting the optic chiasm; prolactin level is 520 ng/ml. (**b**) Six months after treatment there is tumor shrinkage, remodeling of the sellar floor, and small residual hemorrhagic component (*curved arrow*). Prolactin level is now 6 ng/ml. (**c**) One year later, there is marked atrophy of the sellar content on the right side with upward bulging of the sellar floor; T1 hyperintensity of the normal pituitary tissue on the left side (*straight arrow*) indicates possibly of compensatory increased hormonal activity

agonist treatment, especially if a pregnancy has been obtained or is not desired. Recurrence of hyperprolactinemia and tumor regrowth following discontinuation of dopamine agonist therapy in patients with prolactinoma occur on average at 6 months, and more commonly in macroprolactinoma (93 %) than in microprolactinoma (64 %). True resistance to dopamine agonist therapy is rare. It has been said that cavernous sinus invasion is a predictable factor of such resistance, but we do not share this assertion.

Further Reading

Barber TM, Kenkre J, Garnett C et al (2011) Recurrence of hyperprolactinaemia following discontinuation of dopamine agonist therapy in patients with prolactinoma occurs commonly especially in macroprolactinoma. Clin Endocrinol (Oxf) 75(6):819–824

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