Tricks and Traps in MRI of the Pituitary Region

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To my wife
to my sons
to their children
and their family
to Françoise, Sonia, Véro, Julia
to Jean-Louis
to Albert

Preface

This book is neither a textbook nor an up-to-date work exposing the supposed benefits of the use of radiomics analysis or ChatGPT in the diagnosis of pituitary lesions. It is a compendium of the difficulties of MRIs in the pituitary region and of their remedies collected during a long period of time. It offers simple solutions to overcome pitfalls and traps.

The proposed technical protocols and the general way to go will appear to some readers simplistic or provocative or even outrageous. But the exposed philosophy has been proven efficient for decades and has been shared with endocrinologists and neurosurgeons.

A text full of abbreviations becomes boring, annoying, or even unreadable: I tried to keep them to a minimum and I am sure you will accept RCC for Rathke Cleft Cyst without being upset. However, the World Health Organization has recently changed the classification of pituitary adenomas. This change categorized pituitary adenomas as neuroendocrine tumors and proposed the name to be revised to pituitary neuroendocrine tumor or PitNET. But to be sure to be understood and that their work be recorded, most authors have made the choice to append both denominations in their recent papers, or even to use a triple denomination: "Pituitary neuroendocrine tumor (PitNET)/pituitary adenoma," that is certainly neither economical nor ecological. In this book, I use indifferently either pituitary adenoma or PitNET although the repetitive alternating typing of upper and lower case letters made me at first a little bit upset. At the end, however, I came to find the term PitNET rather pleasant to the eye but nobody knows if it will stand the test of time.

I have adopted CE for Contrast Enhanced in the captions of the figures: after you get to the end of this book, I hope you will remember one of my favorite messages which is that gadolinium is not the universal panacea. If you had the curiosity to count the number of figures with gadolinium, you would see that nonenhanced images, particularly T2W images, far exceeds the enhanced ones.

Lastly, I used a few abbreviations you may never have seen just to intrigue you and get your attention on previously undescribed variations or curiosities such as IUO for Infundibular Unidentified Object.

I wish you a pleasant and instructive reading.

Liége, Belgium — Jean-François Bonneville

Contents

Abbreviations

ACTH	Adrenocorticotropic hormone
AVP	Arginine vasopressin
CE T1WI	Contrast-enhanced T1WI
CP	Craniopharyngioma
CSF	Cerebrospinal fluid
CT	Computed tomography
DWI	Diffusion–weighted image
ENT	Ears, nose, and throat
GE	Gradient echo
GH	Growth hormone
GHRH	Growth hormone-releasing hormone
IGF-1	Insulin-like growth factor 1
IPSS	Interrupted pituitary stalk syndrome
PitNET	Pituitary adenoma
RCC	Rathke cleft cyst
SE	Spin echo
T1WI	T1-weighted image
T2WI	T2-weighted image
TSH	Thyroid-stimulating hormone

The (My) Golden Rules

1

Unless you are practicing in a Pituitary Center, you, my dear colleagues radiologists, you did not manage a pituitary MRI every day and probably not one every week: it is a very special examination with possible crucial issues that require your full attention.

If it is the first pituitary MRI of your patient and not a follow-up, some recommendations are welcome.

- Take a short time to greet your patient and ask a few questions: undoubtedly, you will learn more than what you have read on the MRI prescription.
- You must know what you are looking for—for instance, macro (visual field defect), micro (hyperprolactinemia), or possible picoadenoma (Cushing disease), and you have to adapt your technical protocol.
- The localizer image may sometimes tell you in seconds if there is a mass of the sellar region or not: do not neglect its reading to adapt possibly your protocol (Fig. 1.1).
- Be personally present during the examination to modify, if necessary, the choice of the sequences in real time. For instance, deciding to inject gadolinium (it is not compulsory!); adding an axial T1W or a sagittal T2W sequence to elucidate an unexplained intrasellar image; changing the thickness of the reformat to confirm a tiny lesion or understand an artifact; obtaining an additional FLAIR sequence to precise a liquid-looking image. Your presence during a pituitary MRI may seem like a heavy burden but is for me key to best helping the clinician and the patient.
- Allow at least 15–20 min for a pituitary MRI: again, it could be a complex examination.
- If a brain MRI is also ordered or is considered necessary, it will be scheduled in a different session.

The first MRI could be often the first of many follow-up studies: comparison will be easy and accurate if the same rigorous projections are chosen. We perform all coronal

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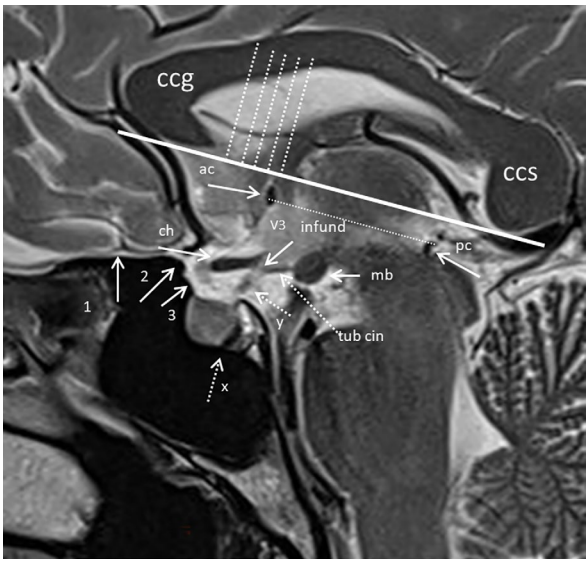

Fig. 1.1 Sagittal T2W image. Main landmarks of the hypothalamic-hypophyseal region. 1: Planum sphenoidale. 2: Tuberculum sellae. 3: Chiasmatic sulcus. x: Pars intermedia/Rathke cleft cyst (anatomical variant). y: Pituitary stalk. *infund* infundibulum, *tub cin* tuber cinereum, *ch* optic chiasm, *ac/pc* anterior and posterior commissures, *ccg/ccs* corpus callosum, genu, and splenium. Coronal sections are obtained perpendicularly to the line joining the inferior border of the genu and of the splenium of the corpus callosum. This line is very close to the classical bicommissural line adopted by the anatomists (thin dotted line), but more easy to draw

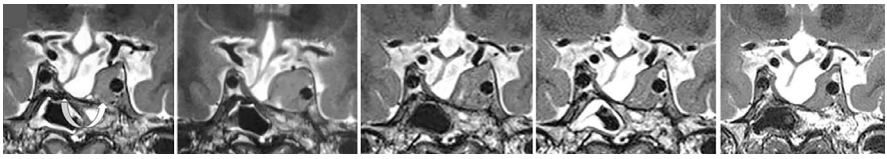

Fig. 1.2 Example of a postoperative MRI follow-up for 10 years. T2W coronal sections according to the subcallosal line

sequences perpendicularly to a line joining the genu and the splenium of the corpus callosum. This line is easier to draw than the classical bicommissural line (Fig. 1.2). Our landmark being distant from the sellar area is immovable at the difference of the sellar floor or the pituitary stalk which could be modified after surgery or medical treatment. It has the advantage to be applicable to any MR scanner whatever the firm.

- The most informative sequence is most of the time T2W, not a gadolinium-enhanced one. Favor a long acquisition time to get the best information.
- Dynamic imaging must never be systematic and reserved for exceptional cases or research purpose.
- Hyperprolactinemia is certainly one of the most frequent indications for pituitary MRI in your practice. Symptomatology is secondary amenorrhea, often after stopping the pill, galactorrhea, or infertility. A lot of "microincidentalomas" can

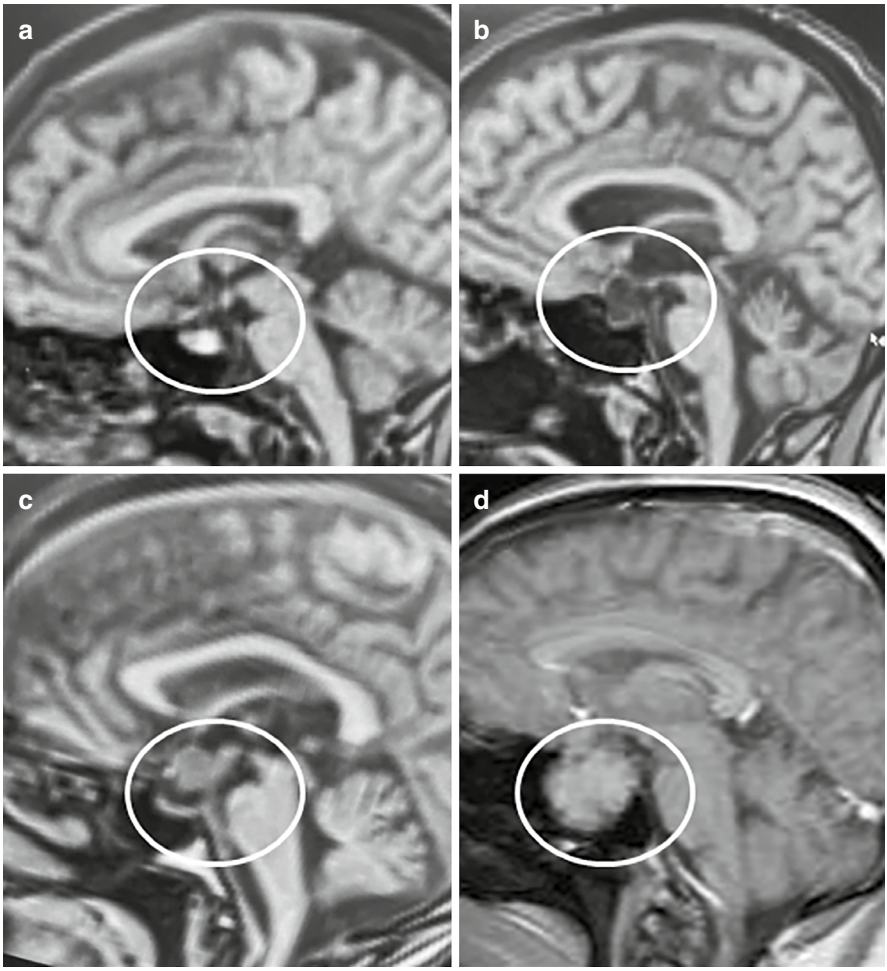

Fig. 1.3 Sagittal localizer images may help to adapt the MRI protocol

mimic microprolactinomas. Fortunately, there is an excellent correlation between prolactin level and pituitary adenoma size—except when the lesion is liquid or hemorrhagic. Most microprolactinomas (less than 10 mm) correspond to a prolactin level between 35 and 120 µg/L, but an intrasellar prolactinoma invading the cavernous sinus can be responsible of a 1000 µg/L prolactinemia. A tiny millimetric image associated with a 100 µg/L prolactin level or more is not a prolactinoma but probably an artifact or an incidentaloma.

- Therefore, knowledge of the prolactin level is essential and must be always requested. If it is not available at the time of the MRI, ask your secretary to call the laboratory.
- Pituitary MRI follow-up is another frequent indication: after medical treatment of prolactinomas, after surgery or radiotherapy, or just for monitoring a non-secreting adenoma. Tumoral volume and signal changes are well seen on T2WI (Fig. 1.3). Gadolinium injection is usually unnecessary.

T2W MRI: The Master Sequence

2

The T2W MRI sequence largely deserves a dedicated chapter. This sequence is curiously neglected in the scientific literature, particularly the endocrinological and neurosurgical literature. For instance, in a journal specifically devoted to the normal and pathological pituitary gland, about nine out of ten figures are post-gadolinium-enhanced. Moreover, T2W images, when present, are frequently of poor quality (Fig. 2.1). The choice of the parameters of this sequence must be managed by a specialist, ideally by an MR engineer. It is undeniable that the image quality is higher with a 3.0 Tesla scanner, but a 1.5 Tesla MR scanner can give excellent results if the T2 sequence is optimized. A long acquisition time is essential, but an excellent T2 sequence often allows the number of sequences to be reduced, especially those obtained after gadolinium injection.

We will briefly list and illustrate several situations where T2W imaging is at least as informative, or more often more informative, than enhanced T1W sequences (Figs. 2.2, 2.3, and 2.4).

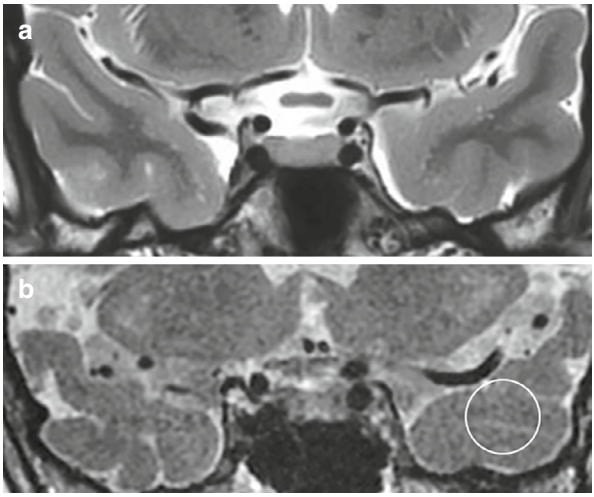

Fig. 2.1 Optimized (**a**) versus unacceptable (**b**) coronal T2WIs. In **b**, the poor signal resolution does not distinguish gray and white matter of the temporal lobe

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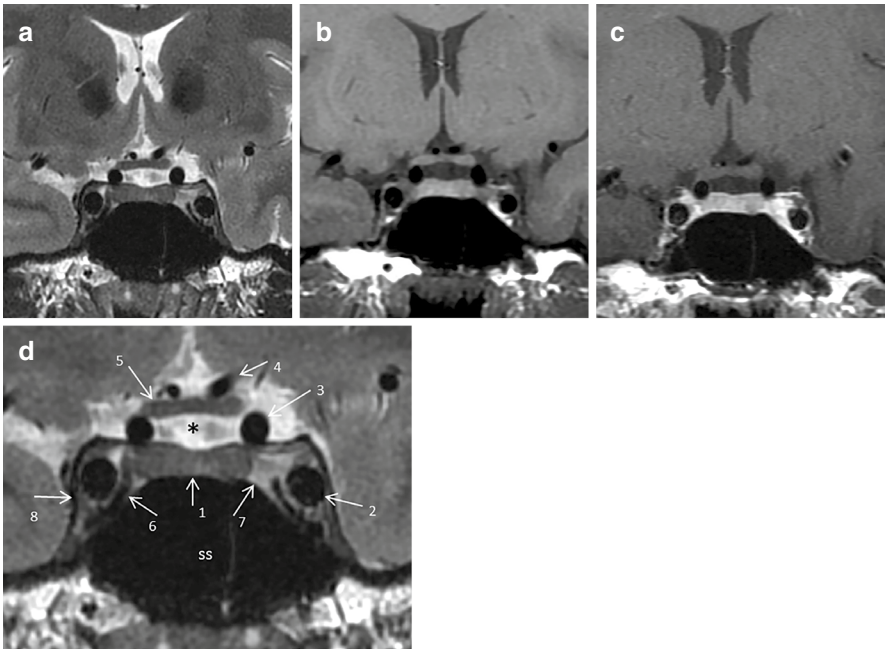

Fig. 2.2 T2W coronal images (**a**, **d**) versus T1W (**b**) and enhanced T1W images (**b**, **c**). 1: Sellar floor. 2: Internal carotid artery. 3: Supra clinoid carotid artery. 4: Anterior cerebral artery. 5: Optic chiasm. 6: Vein of the carotid sulcus. 7: Laterosellar veins. 8: Lateral wall of cavernous sinus

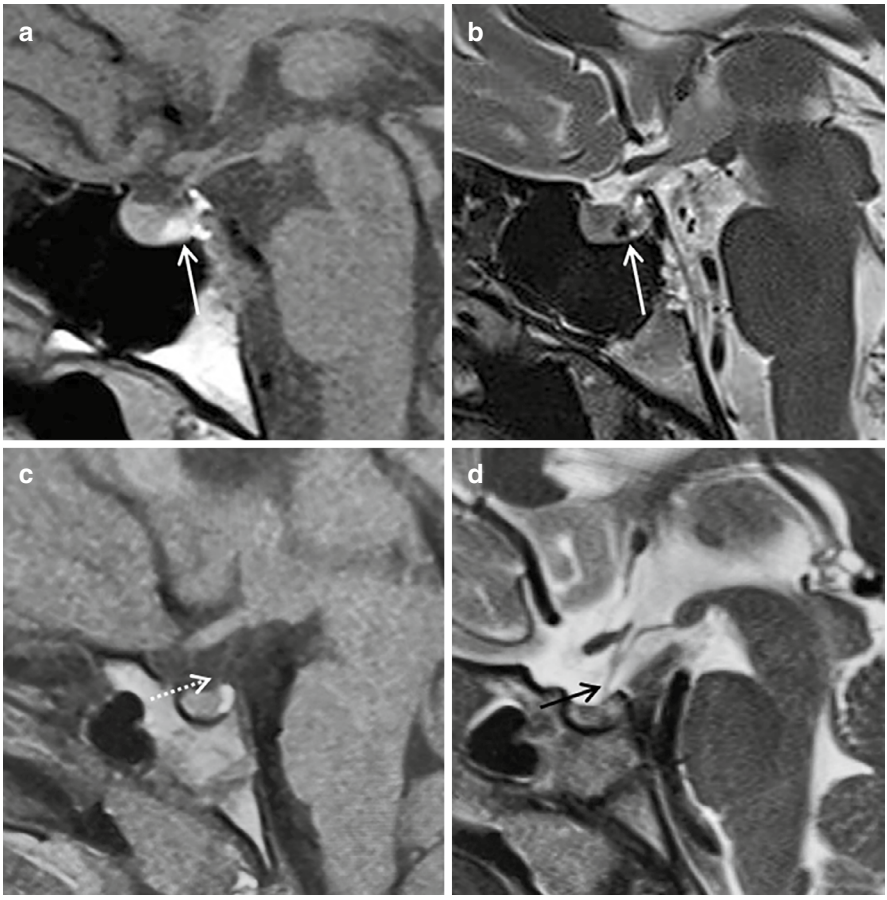

Fig. 2.3 Sagittal unenhanced T1W versus T2WI. (**a**, **b**) The T1W hyperintense nodule (arrow) is not the bright spot of the posterior lobe but a small T2W hypointense Rathke cleft cyst. (**c**, **d**) In this 7-year-old girl with growth hormone deficiency, hypoplasia of the pituitary stalk (arrows) is better shown in **d** T2WI than in **a** sagittal T1WI

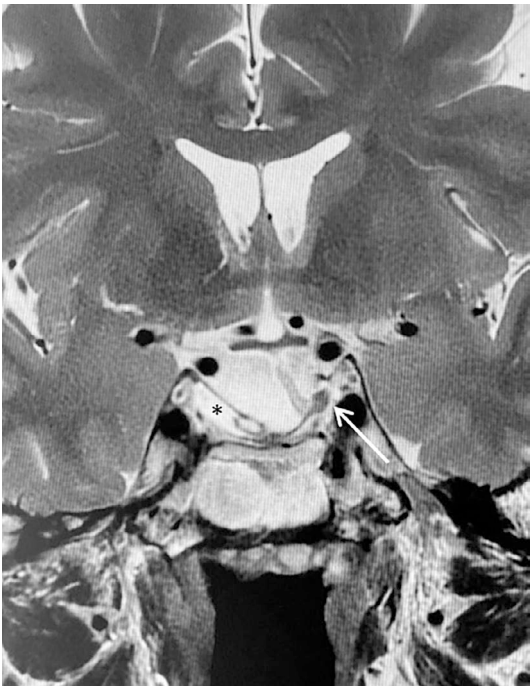

Fig. 2.4 Coronal T2W image 1 year after pituitary surgery. The anterior pituitary is perfectly visible as a small rounded T2 hypointense nodule located at the distal end of the tilted pituitary stalk (arrow). Note that there is no relation between the size of the residual pituitary gland and the severity of a possible deficit. Contralaterally, a triangular T2W hyperintense area (asterisk) reflects here the presence of a sero-hematic residue. Its T2W signal being different from that of the tumor before surgery (not shown) eliminates a tumoral remnant

2.1 Hyperprolactinemia

This is one of the most usual indications of MRI of the pituitary gland. If hyperprolactinemia is symptomatic and greater than 30–35 μg/L, and if macroprolactinemia and an iatrogenic cause have been eliminated, an MRI will show a pituitary adenoma visible from the T2 sequence which must be performed first. Microprolactinomas are more or less hyperintense on T2W images, rarely hypointense or isointense (see Chaps. 12 and 13). The sequences performed after gadolinium injection certainly demonstrate more clearly the contours of the adenoma and allow a more accurate measurement of its diameter or volume. But are these details useful when the treatment is first-line medical? In addition, the enhancement of the surrounding pituitary gland is likely to mask a tiny microadenoma. In my practice, I reserve gadolinium injection to these cases of clear symptomatic hyperprolactinemia when the nonenhanced sequences are negative.

It is common practice to perform a control MRI, in general 6 months after the institution of the treatment by cabergoline. When the treatment is effective, which is the most common case, the adenoma decreases in volume and especially sees its T2W hypersignal more pronounced and thus becomes even more visible. Then, there is no justification for performing a sequence with gadolinium injection in this situation.

2.2 Ratke Cleft Cyst (RCC)

This is one of the most common mistakes: an intrasellar mass discovered by chance is frequently reported as a pituitary adenoma after the reading of T1 and CE T1 WIs when it is a Rathke cleft cyst. However, the coronal T2W sequence will better show a difference of signal between the RCC and the pituitary gland which frequently encircles the cyst bilaterally, what is never the case with PitNET (see Chap. 24). Besides, in more than half of the cases of Rathke cyst, the T2W sequence demonstrates a hypointense intracystic hyperproteinic nodule which is pathognomonic of the diagnosis.

Another frequent mistake in sagittal T1W sequence is the confusion between the bright spot of the posterior lobe and an intrasellar mucoid Rathke cleft cyst; this is immediately clarified by a T2W (Fig. 2.3a, b) or an axial T1W sequence.

2.3 Growth Retardation

The pituitary stalk configuration is an important feature in the setting of growth hormone deficit in children. For decades, gadolinium injection was formally recommended for its precise demonstration. It is today accepted that a high-resolution high contrast millimetric T2W sequence (CISS, FIESTA) is superior to a T1W enhanced sequence to separate total pituitary stalk absence—usually observed in multiple hormone deficit—from hypoplastic or truncated pituitary stalk—usually observed in isolated growth hormone deficit. A 2D 2 mm Fast Spin Echo sagittal sequence gives similar results (Fig. 2.3c, d). In these situations of growth retardation, gadolinium injection must be abolished, making MR examinations quicker, better accepted, without any risk, and less expensive. Unenhanced T1W sequences, sagittal and optionally axial, demonstrate clearly the vasopressin storage in ectopic or eutopic position. A tumoral process can be ruled out without gadolinium injection.

2.4 Diabetes Insipidus and Hypophysitis

Is the pituitary stalk normal, thickened, or atrophic? The question is fundamental when diabetes insipidus or hypophysitis is suspected. In the literature, the diameters of the pituitary stalk have been measured very carefully at the level of the optic chiasma and at the pituitary insertion. The extreme precision of these figures is unfortunately of no help in the borderline cases.

The morphology of the stalk is sometimes more interesting to consider. The pituitary stalk usually has a bulge at the top and tapers below; a cylindrical stalk, of constant thickness from top to bottom, may suggest thickening while the measured diameters are still within the norm. This feature is more obvious on T2W images. Similarly, deepening of the posterior recess of the third ventricle which can mimic a pituitary stalk thickening is better recognized in the same sequence. At last, a

previously undescribed T2 hypointense ring, predominant anteriorly, which encircles the upper part of the stalk, constitutes a new landmark undetectable on T1W- and T1W-enhanced MRI (Fig. 5.2).

2.5 Postoperative Pituitary MRI

After pituitary surgery, an MRI follow-up spreads over years or even decades. The use is still to perform these examinations with gadolinium injection. For early controls, at 3 or 6 months after the intervention, the injected sequences are most often illegible and therefore useless due to an undifferentiated enhancement of the sellar content and/or the presence of surgical packing or sero-hematic suffusion (Fig. 36.2). At 1 year, the T2 sequence is the most likely to separate a possible remnant or a recurrence from normal pituitary tissue. Beyond 1 year, the goal of the examination is strictly to look for an increase in size of an adenoma remnant or for a recurrence. The unenhanced T2W sequence easily answers these questions (Fig. 2.4).

Recent papers have proposed to spare gadolinium injection for MRI surveillance of *unoperated* pituitary macroadenoma: for more than a decade, our team has controlled *operated* adenomas without the use of contrast agents.

In summary, the T2W sequences are by far our favorites (Bonneville JF 2019) and they deserve it (Fig. 2.5). We use largely the coronal T2 sequence in all circumstances and particularly for the research of PitNETS and postoperatively and the

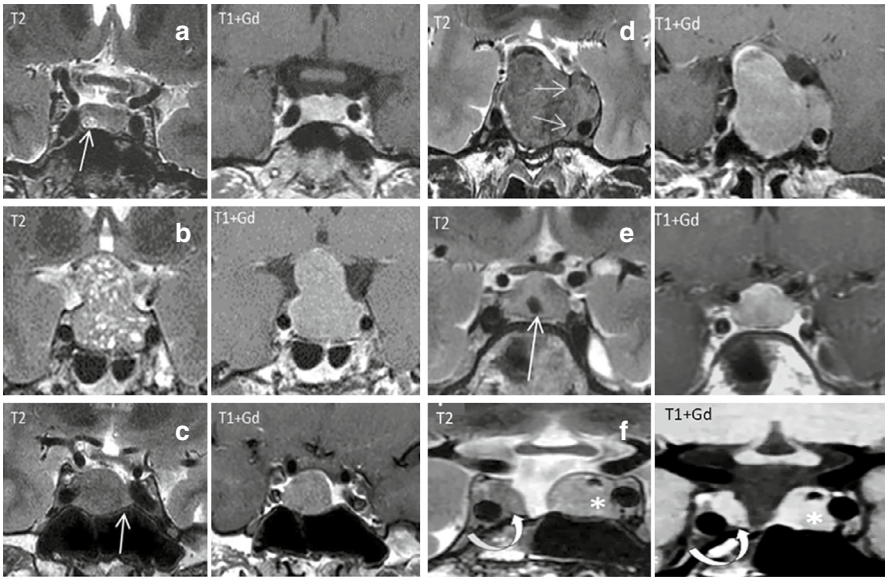

Fig. 2.5 Examples of the efficacy of T2WIs over CE T1W images. (**a**) Microprolactinoma. (**b**) Silent corticotropic adenoma. (**c**) Densely granulated growth hormone-secreting adenoma. (**d**) Invasion of cavernous sinus. (**e**) Hyperproteinic nodule of a Rathke cleft cyst. (**f**) Post-operative tumoral remnant (asterisk) versus normal residual pituitary tissue (arrow)

sagittal T2W sequence systematically in case of diabetes insipidus, in hypogonadotropic hypogonadism, in children with growth retardation or precocious puberty and each time where an optimal image of the hypothalamic-hypophyseal junction is required.

Further Reading

Bonneville JF. A plea for the T2W MR sequence for pituitary imaging. Pituitary. 2019;22(2):195–7. https://doi.org/10.1007/s11102-018-0928-9.

Axial T1: An Underused MRI Sequence

3

An important diagnostic tool for pituitary diseases is incomprehensibly rarely performed in radiologic centers including tertiary centers, the unenhanced axial T1W sequence, preferably with Fat saturation (AxT1W Fatsat). This projection deserves a short but full chapter with convincing illustrations. At the end of this short presentation, you will have at least seven good reasons to keep this weapon ready in your bag.

First, the axial T1W sequence demonstrates at best the vasopressin storage—formerly antidiuretic hormone—stored in the posterior lobe. As the sagittal T1W sequence is said to be unable to detect it in a variable percentage of normal cases, axial T1W Fatsat demonstrates it almost always. The disadvantages of the sagittal sequence for the visualization of vasopressin—anterior concavity, thickness, compact bone or fatty composition of the dorsum sellae—are here eliminated. Thus, AxT1W must be the first sequence to be obtained when a vasopressin deficit is suspected. Fat saturation is highly recommended to avoid chemical shift artifacts from the dorsum (Fig. 3.1).

Second, this statement is even more true in several physiologic or pathologic conditions known to interfere with plasmatic osmolality and then likely to reduce the amount of stored vasopressin, for instance in the elderly, in patients with diabetes mellitus, under dialysis, in stress situation or during pregnancy (Fig. 3.2).

Third, AxT1 is the only sequence able to separate the posterior lobe from an incidental Rathke cleft cyst (RCC). Indeed, the distinction of a normal posterior lobe from a mucinous T1 hyperintense RCC may be impossible on a sagittal view. On AxT1W, the posterior lobe is clearly recognizable as strictly applied to the anterior T1W hypointense surface of the dorsum sellae while an intrasellar mucoid RCC which is usually median is in close contact with the anterior surface of the posterior lobe from which it is separated by a thin line, possibly the wall of the RCC (Fig. 3.3c, d).

Fourth, a lateral imprint of the anterior surface of the posterior lobe, clearly visible on AxT1WI, signals an intrasellar mass effect and can constitute a useful marker, for instance in the presence of an isointense pituitary adenoma (Fig. 3.4).

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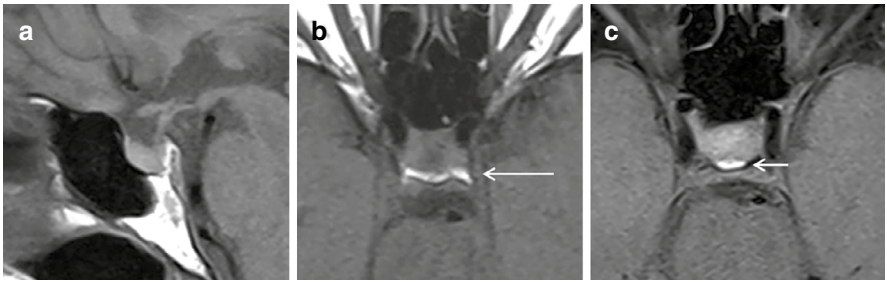

Fig. 3.1 Sagittal T1W (**a**) versus axial T1 (**b**) versus axial T1 Fatsat (**c**) images. The chemical shift artifact from the dorsum (long arrow in **b**) is deleted in **c**. The posterior lobe which is masked in **a** is clearly visible in **c** (short arrow)

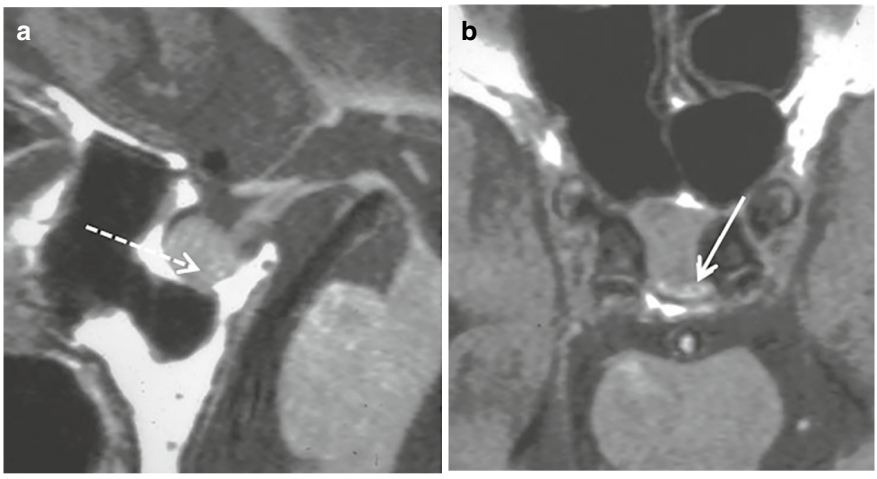

Fig. 3.2 (**a**, **b**) Sagittal and axial T1WIs. The bright spot of the posterior lobe is visible on axial view only in this non symptomatic 75-year-old man

Generally speaking, the research of a mass effect is an important tool to differentiate a pituitary adenoma from a T2W hyperintense cyst. Pituitary adenomas may modify the sellar floor, the upper surface of the gland, the pituitary stalk, the secondary pituitary bed, or the posterior lobe configuration while intrasellar "cysts" whose internal pressure is low do not or less.

Fifth, only axial T1W sequences are able to formally identify posterior lobes cysts (Fig. 3.5 and Chap. 26).

Sixth, in front of a bulging sellar content, visualization of an uncompressed posterior lobe eliminates a mass effect from a sellar mass and permits to refer to an anatomical variant (Fig. 3.6).

Seventh, AxT1W Fatsat, as well as gadolinium enhanced and axial T2W sequences, are very useful for the early diagnosis of a discrete invasion of the posterior part of the cavernous sinus which is illustrated in Chap. 18.

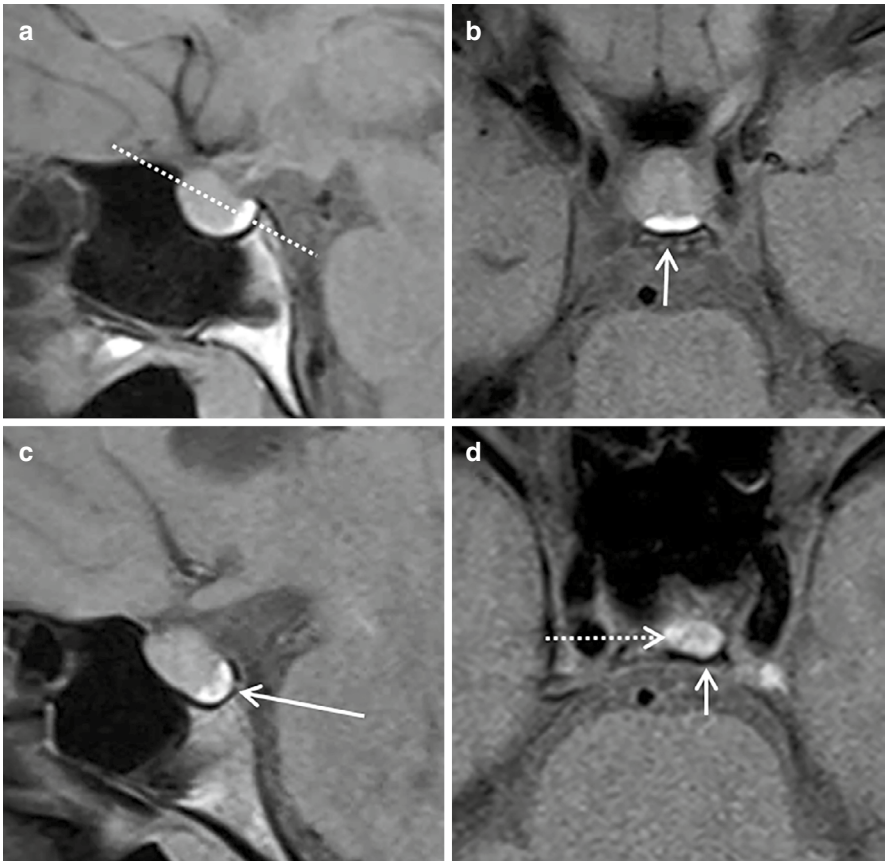

Fig. 3.3 Upper row. Normal posterior lobe on axial T1WI. The orientation of the sequence is marked in **a**. Lower row: Rathke cleft cyst (dotted arrow) separated from the posterior lobe (small arrow) by a thin line in **d**. (**a**, **c**) Sagittal T1WIs. (**b**, **d**) Ax Fatsat T1WIs