ORIGINAL ARTICLE

Distortion of Normal Pituitary Structures in Sellar Pathologies on MRI

Burak Sade, Gérard Mohr, Jean Lorrain Vézina

ABSTRACT: ***Objective:*** This study was undertaken to assess the displacement patterns and shifts of the normal pituitary gland in sellar pathologies on MRI and to determine if the position of the bright spot (BS) represents a predicting factor for the position of the residual adenohypophysis (RAH) in pathological conditions. ***Methods:*** In a control group of 102 patients without any pituitary pathology, the presence of the BS was evaluated. In 100 patients with intra- or suprasellar pathologies, presence and respective topography of BS and RAH were scrutinized on MRI, according to lesion type, size, endocrine status and intra-operative findings in the surgical group. ***Results:*** The BS was visible in 91.2% of 102 cases in the control group, as compared to 75 of the 100 patients with sellar lesions. Location of RAH was identified in 58% of the patients, and RAH enhanced more than the lesion in all cases after contrast infusion. The RAH was identified in 65.3% of the 75 "BS positive" patients, as compared to 36% of the 25 "BS negative". The normal residual gland was visualized intra-operatively in 63.5% of the 52 operated patients: in 37 "BS positive" patients, it was visualized intra-operatively in 81.1% and in 28 "RAH positive" patients, it was identified in 82.1%. ***Conclusions:*** The BS can be identified in the majority and RAH in more than half of the cases with pituitary lesions on MRI. Positions of both the BS and RAH help predict the location of the normal residual gland during surgery and, therefore, may contribute to preserving the pituitary function.

RÉSUMÉ: Distorsion des structures hypophysaires normales à l'IRM de pathologies de la selle turcique. ***Objectif :*** Le but de cette étude était d'évaluer les signes de distortion et de déplacement de l'hypophyse normale dans les pathologies de la selle turcique à l'IRM et de déterminer si la position de l'image en hyper signal, ou bright spot (BS), peut être considérée comme un facteur de prédiction de la position de l'adénohypophyse résiduelle (AHR) dans les états pathologiques. ***Méthodes :*** La présence du BS a été déterminée chez un groupe témoin composé de 102 patients sans pathologie hypophysaire. Chez 100 patients porteurs de pathologies intra ou suprasellaires, nous avons examiné minutieusement l'IRM pour détecter la présence et la topographie respective du BS et de l'AHR, selon le type de lésion, sa taille, le statut endocrinien et les constatations opératoires dans le groupe ayant subi une chirurgie. ***Résultats :*** Le BS était visible chez 91,2% des 102 patients du groupe témoin comparé à 75 des 100 patients ayant une lésion sellaire. La localisation de l'AHR a été identifiée chez 58% des patients et, après infusion de substance de contraste, le rehaussement de l'AHR était supérieur à celui de la lésion chez tous les cas. L'AHR a été identifiée chez 65,3% des 75 patients BS positifs par rapport à 36% des 25 patients BS négatifs. La glande résiduelle normale a été visualisée à la chirurgie chez 63,5% des 52 patients ayant subi une chirurgie, soit chez 81,1% des 37 patients BS positifs et chez 82,1% des 28 patients AHR positifs. ***Conclusions :*** Le BS peut être identifié chez la majorité des patients et l'AHR chez plus de la moitié des cas ayant une lésion hypophysaire à l'IRM. La position du BS et de l'AHR aide à prédire la localisation de la glande résiduelle normale pendant la chirurgie et peut ainsi contribuer à préserver la fonction hypophysaire.

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The use of magnetic resonance imaging (MRI) enhanced the distinction between the normal residual pituitary parenchyma and sellar lesions and even made the differentiation of the neurohypophysis from the adenohypophysis possible.

In plain T1-weighted MRI images, the neurohypophysis can be located as the "bright spot" (BS) by its spontaneous hyperintense appearance.[1,2] Gadopentate-dimeglumine (Gd-DTPA) injection not only increases the sensitivity of the examination by an average of 15%, but also makes it possible to clearly delineate the lesion and the residual adenohypophysis (RAH).[3-5] This is of special significance from a surgical point of view since pre-operative identification of the normal pituitary structures may facilitate intra-operative visualization and preservation of the normal residual gland. However, the

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distinction between these structures may become at times difficult, particularly in macroadenomas, despite contrast injection, since both enhance with contrast.

The purpose of this study was to assess the radiological displacement patterns and shifts of the normal pituitary gland (both anterior adenohypophysis and posterior neurohypophysis) and to determine if the position of the BS represents a predicting factor for the position of the RAH in pathological conditions.

Materials and methods

Between 1990 and 2002, 161 patients who were treated in the Sir Mortimer B. Davis-Jewish General Hospital with a diagnosis of intra- or suprasellar lesion, were evaluated retrospectively. One hundred patients with adequate MRI documentation were included in this study. The presence and respective topography of the BS and the RAH were scrutinized on MRI according to lesion type, size, and pre-operative endocrine status. Intra-operative identification of the normal residual gland was also recorded in the surgically treated group.

Magnetic resonance examinations were performed using 1.5T imagers (Gyroscan, Philips, Netherlands and Signa, General Electrics, Milwaukee, WI). T1-weighted images (372-548/16-20 [TR/TE]) were obtained before and after Gd-DTPA. Section thickness was 2.0 mm with a matrix size of 256x256. Field of view was 16-18cm.

In all patients, sagittal and coronal series were evaluated and presence of the BS and the RAH were detected on the pre- and postgadolinium images, respectively. The RAH was accepted as visible only in the presence of a clear delineation in the form of a stronger enhancement pattern than the lesion after the contrast injection. Respective topography and the shifts of the BS and the RAH were evaluated according to the presence of extrasellar and lateral displacement. Pathologies were grouped as adenomas and nonadenomas. Modified Vezina-Hardy classification was used for the staging of the size of the adenomas.[6] Patients with a deficiency in one or more hormonal axis of the adenohypophysis in the pre-operative endocrinological work-up were accepted as hypopituitary. Preoperative diabetes inspidus was evaluated separately.

Magnetic resonance imaging of 102 patients without any intra- or suprasellar lesions were reviewed to assess the presence and the signal intensity of the BS according to age and gender. Only T1-weighted sagittal images were used in this group. The signal intensity was classified as "very bright" or "moderately bright".

All cases were evaluated by each of the authors and BS and RAH were referred to as "positive" only when confirmed by all authors.

Chi-square and Fisher Exact tests were used for the comparison of the groups.

Results

The group of patients who did not have any intra- or suprasellar pathology consisted of 51 males and 51 females with an average age of 50±17 (range 20-85). The BS was present in 91.2% of the patients with midline location in all cases. Its frequency was 98% in females as compared to 82.4% in males. The presence of the BS fell to 82.4% from 94.1% after the age of 60. In terms of signal intensity, a "very bright" BS was observed in 68.8% of the patients below age 60, as compared to 39.3% of patients above.

In the group of 100 patients who had an intra- or suprasellar pathology, 54 were males and 46 were females with an average age of 49±17 (range 18-90). There were 73 pituitary adenomas (27 nonfunctioning, 26 prolactinomas, eight growth hormone secreting, six adrenocorticotropic hormone secreting, six mammosomatotrophic), 11 Rathke's cleft cysts (RCC), five craniopharyngiomas, four meningiomas and seven miscellaneous lesions (two suspected choristomas, one granulomatous infiltrative lesion, one multiple myeloma, one metastasis, one intrasellar arachnoidocele and one postpartum pituitary enlargement).

The BS was visible in 75% and the RAH in 58% of the cases. In all cases where the RAH was identified, it enhanced more than the associated lesion (Figures 1, 2 and 3). In 74.1% of the 58 cases with a positive RAH, "The Sign of Stalk" also helped in localizing the RAH (Figure 3). The pre-operative identification of the BS and the RAH according to lesion type and size (adenomas) was demonstrated in Table 1.

In addition the BS was visible in 77.2% of the 79 eupituitary

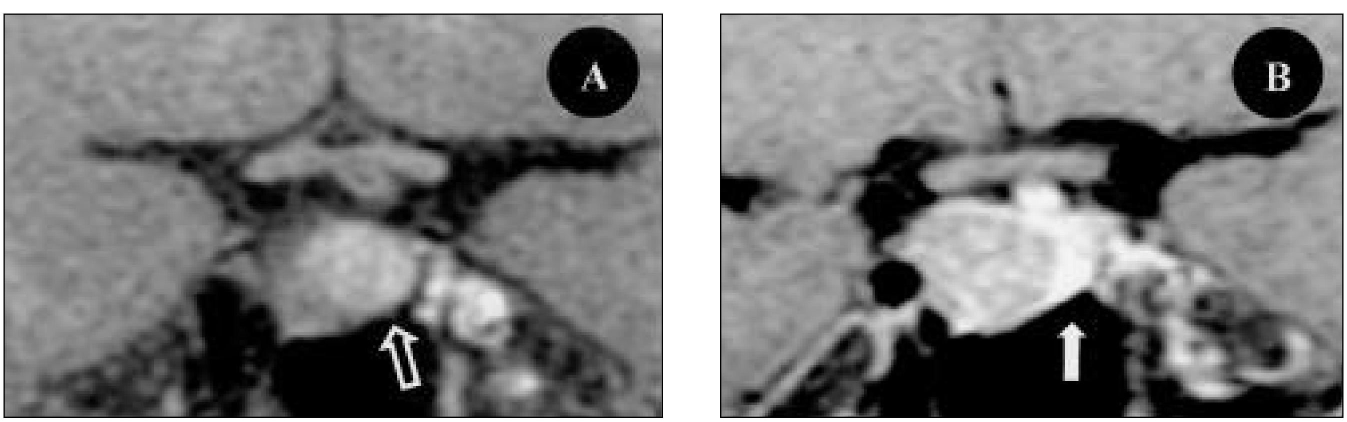

Figure 1: Coronal pre- (A) and postgadolinium (B) T1-weighted images of a right sided prolactinoma with stage A suprasellar extension. The bright spot (empty arrow) and the residual adenohypophysis (solid arrow) are both displaced to the left, remaining intrasellar.

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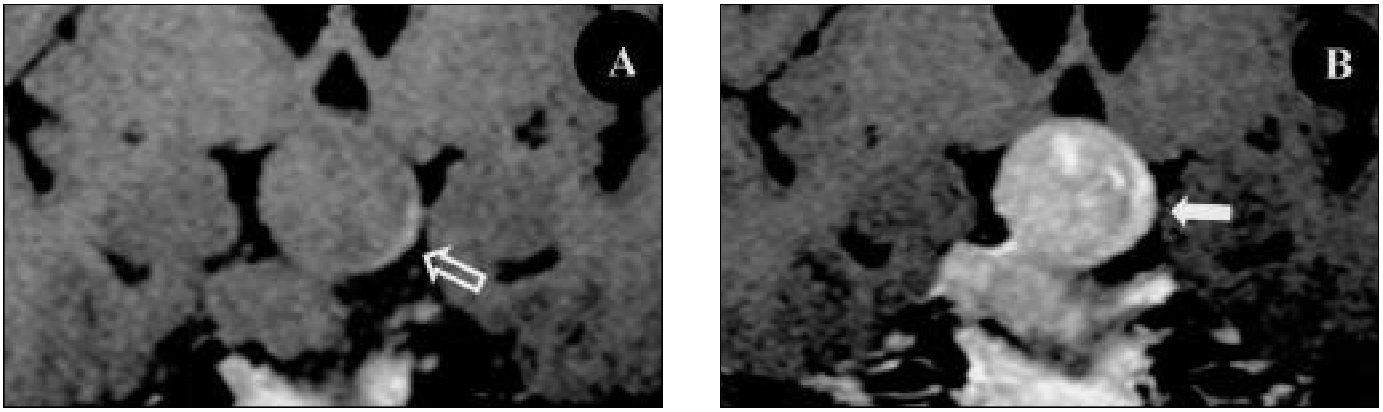

Figure 2: *Coronal pre- (A) and postgadolinium (B) T1-weighted images of a nonfunctioning adenoma with stage B suprasellar extension. The bright spot (empty arrow) and the enhancing residual adenohypophysis (solid arrow) are both displaced to left and extrasellar location.*

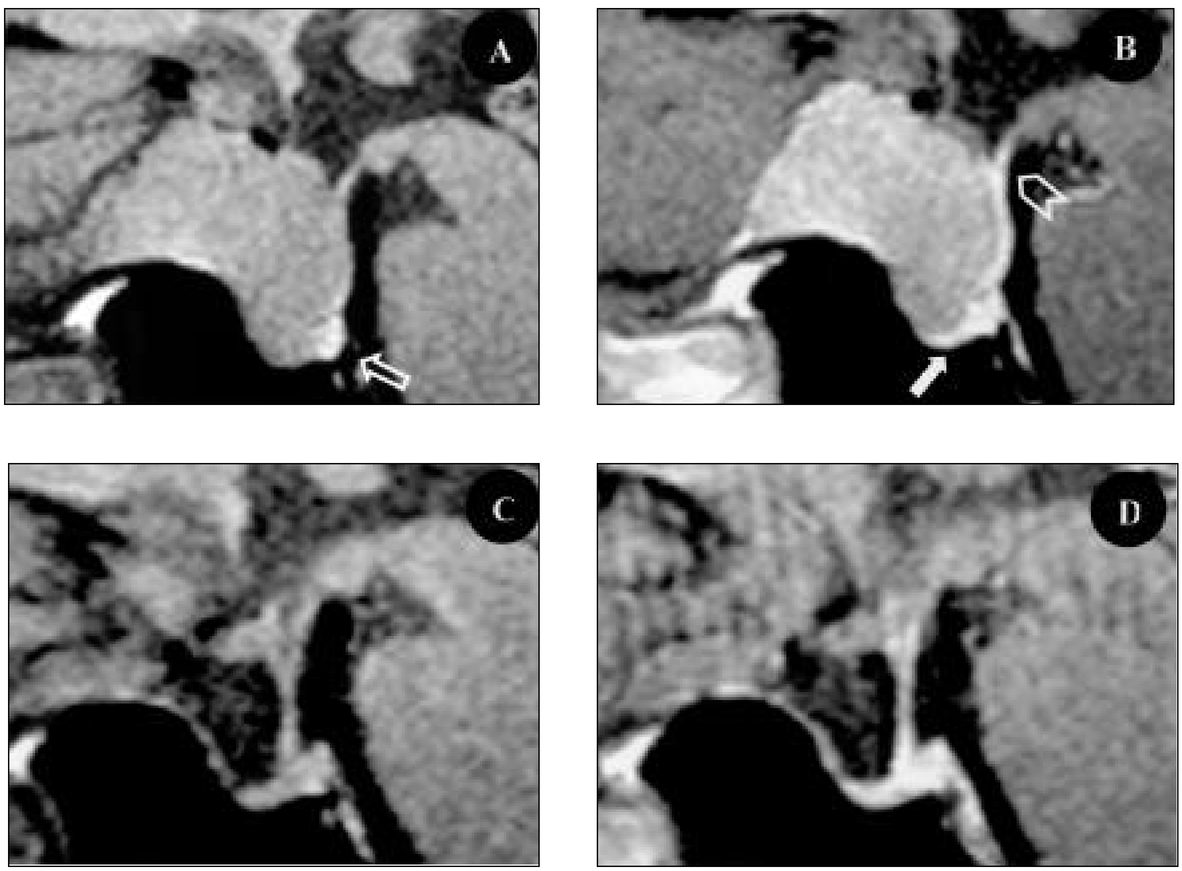

Figure 3: *Preoperative sagittal pre- (A) and postgadolinium (B) and postoperative sagittal pre- (C) and postgadolinium (D) T1-weighted images of a diaphragma sellae meningioma. Both the bright spot (empty arrow) and the residual adenohypophysis (solid arrow) remain in intrasellar location. Note the "Sign of the Stalk" with enhancement of the pituitary stalk up to the premamillary region (empty chevron). Resection of the lesion confirms the location of the pituitary gland.*

patients, and in 66.7% of 21 with hypopituitarism. The RAH was identified in 63.1% of eupituitary, as compared to 23.8% of hypopituitary patients (p=0.003). Four patients had diabetes insipidus at their initial presentation. Two of them were RCCs, one craniopharyngioma and one pituitary metastasis from small cell carcinoma of the lung. Of these four, one patient with a RCC had a BS on the initial MRI, whereas, the RAH was identified in all but one patient with RCC.

Table 1: MRI identification of bright spot and residual adenohypophysis according to lesion type and size (adenomas) in 100 patients with intra-or suprasellar lesions.

	Bright spot positive	Residual Adenohypophysis positive
Total (n=100)	75 (75%)	58 (58%)
Adenoma-All Sizes (n=73)	**59 (80.8%)**	**39 (53.4%)**
No SSE (n=19)	17 (89.4%)	15 (78.7%)
With SSE Stage (n=54)	42 (77.8%)	24 (44.4%)
Non-adenoma * (n=27)	**16 (59.3%)**	**19 (70.4%)**

SSE: suprasellar extension
* Including 11 Rathke's cleft cysts and 5 craniopharyngiomas

Table 2: Spatial displacement patterns of the bright spot (BS) and the residual adenohypophysis (RAH) in various lesion type and sizes.

	BS Displacement (BS positive: 75)	RAH Displacement (RAH positive: 58)
ADENOMA(n=73)		
No SSE (n=19)	(BS positive: 17)	(RAH positive: 15)
Lateral displacement	BS: 11 (64.7%)	RAH: 12 (80%)
Extrasellar displacement	BS: 0	RAH: 0
With SSE (n=54)	(BS positive: 42)	(RAH positive: 24)
Lateral displacement	BS: 32 (76.2%)	RAH: 22 (91.7%)
Extrasellar displacement	BS: 26 (61.9%)	RAH: 18 (75 %)
NON-ADENOMA(n=27)	(BS positive:16)	(RAH positive 19)
Lateral displacement	BS: 2 (12.5%)	RAH: 3 (15.8%)
Extrasellar displacement	BS: 2 (12.5%)	RAH: 0

SSE: suprasellar extension

The RAH was identified in only 36% of the 25 BS negative patients, as compared to 65.3% of the 75 BS positive (p=0.02). The respective topography and displacement of the BS and the RAH is shown in Table 2.

In the group with nonadenomatous pathologies, three of the seven RCC with visible BS and RAH, showed anterior displacement of the RAH while the BS remained in the intrasellar medial posterior location (Figure 4). In all of the four meningiomas, both the BS and the RAH remained in their normal intrasellar locations without any displacement (Figure 3).

Transnasal transsphenoidal microsurgery was performed in 52 of the patients and the normal residual gland was visible in 33 (63.5%). In patients having both positive BS and RAH the chance of intraoperative visibility of the gland was 91.3% as compared to 10% in patients in whom neither of these structures were visible on the pre-operative MRI (Table 3).

Table 3: Intraoperative visibility of the normal residual gland according to preoperative MRI-identification of bright spot (BS) and residual adenohypophysis (RAH) in 52 transsphenoidally operated patients.

	Intraoperative Visibility of Normal Residual Gland	p
Total operated (n=52)	33 (63.5%)	
BS positive (n=37)	30 (81.1%)	<0.001
BS negative (n=15)	3 (20%)	
RAH positive (n=28)	23 (82.1%)	=0.006
RAH negative (n=24)	10 (41.2%)	
Both BS & RAH positive (n=23)	21 (91.3%)	<0.001
Both BS & RAH negative (n=10)	1 (10%)	

Discussion

The spontaneous hyperintense appearance of the BS has drawn attention and different theories have been postulated about its chemical nature: Kucharczyk et al[2,7] proposed that the hyperintense appearance was due to phospholipid vesicles that are responsible for the release of vasopressin, whereas, Holder and Elster[8] suggested that it could be due to the interaction of water with a low molecular weight molecule such as vasopressin or neurophysins.

The overall visibility of the BS in the population without any sellar or suprasellar pathology ranges between 52-100 %.[1,9] Its visibility decreases in the elderly population, in males[9] and in patients with macroadenomas.[1] Bonneville et al[10] reported that this decrease becomes more pronounced in macroadenomas larger than 20mm. This is in parallel with our findings. In our series, one of the four patients with initial diabetes insipidus (DI) was "BS positive". In other publications, none of the patients with DI had a visible BS on the MRI.[11-13] Therefore, although the BS is usually absent on MRI in patients presenting with central DI, a visible BS does not exclude it. This finding may necessitate further studies on the biochemical composition of the BS.

The RAH was identified in 58% of the patients in our series and it was identified almost two-fold more on pre-operative MRI, when the BS was visible. In all of these cases, it showed stronger enhancement than the associated lesion. "The Sign of Stalk" was also used to locate normal pituitary gland: the pituitary stalk has a dense vasculature starting from the median eminence[14] and, therefore, shows strong contrast enhancement which helps locating the pituitary gland when followed distally both in the antero-posterior and lateral projections.

The significance of the BS in locating the normal residual gland may appear relatively less in cases where the delineation

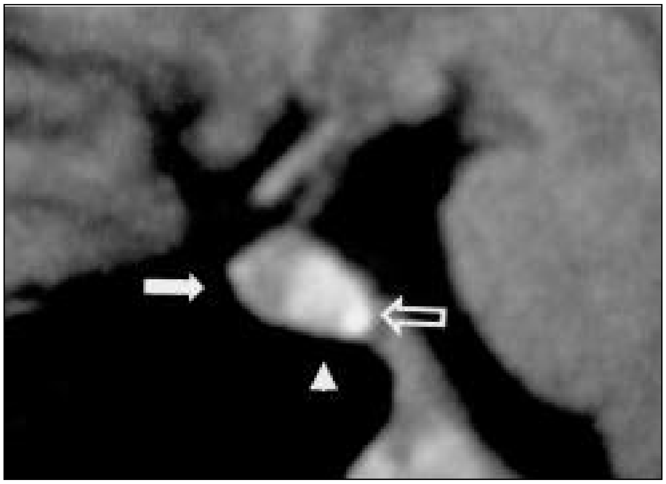

Figure 4: *Sagittal T1-weighted image in a Rathke's cleft cyst. The residual adenohypophysis (solid arrow) is displaced anteriorly and the bright spot (empty arrow) is located posteriorly. The hyperintense cyst is seen in between (arrow-head). This pattern appears to be typical for these lesions*.

between the RAH and the lesion is clear. However, the BS is identified more frequently (75%) as compared to the RAH (58%). Therefore, it may have a more practical and important role in locating the normal residual gland in patients who do not have a clear delineation of the RAH. In nonadenomas, identification of BS decreased and RAH increased as compared to adenomas, due to the relatively more frequent involvement of the neurohypophysis in pathologies like the Rathke's cleft cysts and craniopharyngiomas.

In our study, with an increase in the size of the adenomas, the pre-operative identification of the RAH decreased. This was significantly more pronounced than that of the BS. This effect of the size can be observed even between pre-operative and post-operative MRI of the same patient who has undergone partial resection of an adenoma (Figure 5). Magnetic resonance imaging identification of the RAH in larger macroadenomas is often difficult, since both structures are subject to contrast enhancement: Gorczyca and Hardy[15] have shown in their anatomical study that 66% of microadenomas receive direct arterial supply. This concept was also supported radiologically by dynamic CTand MRI studies.[16,17] With an increase in the size of the adenoma, this supply is likely to increase, explaining the

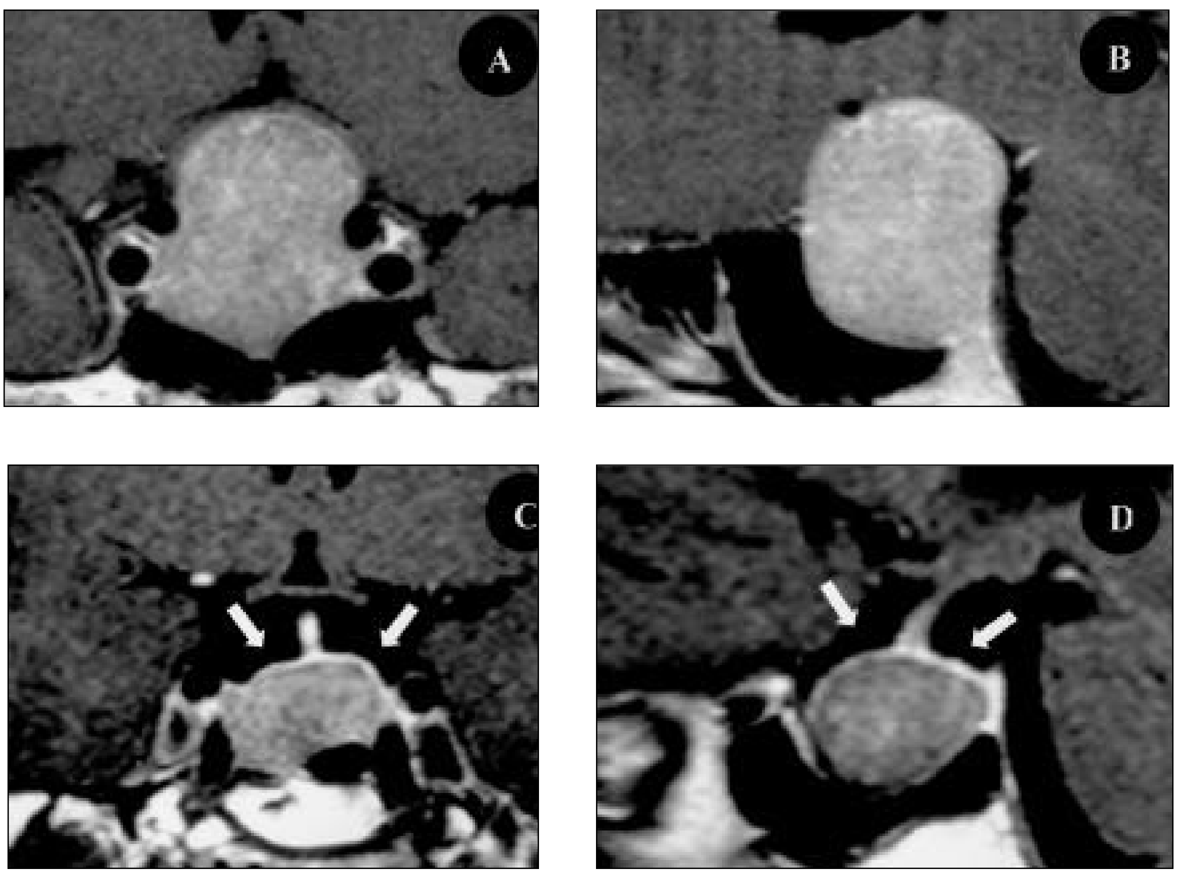

Figure 5: *Preoperative coronal (A), sagittal (B) and postoperative coronal (C), sagittal (D) T1-weighted postgadolinium images of a nonfunctioning adenoma. The adenoma was resected partially in a first sitting due to adherence of the dome. The residual adenohypophysis can be clearly identified three months later, enhancing more than the adenoma (Arrows) after a reduction in the adenoma size, while it was not visible at all preoperatively.* .

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increased enhancement of the adenoma, while the RAH receives its supply from the portal system via the superior hypophyseal artery. A dominant arterial blood supply to macroadenomas has been suggested by Finelli.[18] As the normal residual gland undergoes progressive compression by the tumor simultaneously, the delineation between the RAH and the adenoma becomes less clear, despite gadolinium administration. Dynamic MRI has been described as a useful tool in identifying the RAH in such cases.[19]

The majority of the patients with suprasellar extension had their BS and RAH located outside the sella. Bonneville et al[10] also described an increase in the extrasellar displacement of the BS with an increase of the adenoma size. Extrasellar location of BS has been described in other conditions as well, such as congenital pituitary dwarfism[20-22] or after hypophysectomy.[23] In this study, lateral displacement of the RAH was seen slightly more than that of the BS in adenomas either with or without suprasellar extension. These findings may suggest different patterns of displacement for the normal pituitary structures in different adenoma sizes: during growth of the adenoma, the RAH is initially pushed laterally. Meanwhile, the neurohypophysis remains in its normal posterior location. With further increase of the size, the neurohypophysis is also displaced laterally while remaining intrasellar. As the adenoma continues to grow, both the RAH and the neurohypophysis are displaced outside the sella, paramedially. The initial lack of displacement of the neurohypophysis may be due to its increased adherence to dura of the sellar wall, as compared to the RAH.[24]

In all of the patients with nonadenomas, the RAH was identified within the sella. Both extrasellar and lateral displacements of the BS were less frequent in this group as compared to the adenomas. The anterior displacement of the RAH and posterior intrasellar location of the BS appears to be a typical feature of the RCC. Kleinschmidt-DeMasters et al[25] and Sumida et al[26] also described the same pattern in the majority of the patients in their series.

In meningiomas, neither the BS nor the RAH showed any displacement, because of the extrinsic nature of the pathology. De Monte et al[27] described a group of patients with sphenocavernous meningiomas, in which the pituitary gland was totally displaced towards the suprasellar cistern. However, these patients had extensive invasion of the sphenoid sinus by the meningioma. It is important to differentiate pituitary adenomas from tuberculum sellae meningiomas preoperatively for the surgical planning. Enhancement pattern, tumor epicenter and dural base are described to be useful in making this differentiation.[28] The patterns of distortion of the BS and the RAH we are proposing, may be helpful from this point of view as well.

Identification of these patients is also important from the radiosurgical point of view. In the series of Vladyka et al[29] the residual gland was identified in 82% of the patients with stable eupituitary status as compared to 37% of the group who had worsening of their pituitary function during the follow-up period after gamma-knife radiosurgery. The importance of clear visibility of the target for gamma knife is also emphasized by Wowra and Stummer.[30]

After the first description of selective adenoma removal in transsphenoidal surgery by Jules Hardy,[31] identification and preservation of the normal residual gland has gained major attention.[6,32] Our data showed that the chance of intra-operative visibility of the residual normal gland increased significantly when either the BS or the RAH were identified on the preoperative MRI. This chance increased even up to 91.3%, when both of these structures where identified simultaneously. However, this study's purpose was more of a descriptive one rather than assessment of postoperative outcomes. Consequently, the data regarding the postoperative hormonal outcomes were not included, the numbers being too limited. The formal comparison between radiological and functional outcomes will be subject to a further study.

Our results indicate that the posterior pituitary BS can be identified in the majority and the RAH in more than half of the cases with sellar and suprasellar lesions.

The RAH is more difficult to identify in patients with larger adenomas, whereas size does not seem to have a significant impact on BS visibility. This increases the importance of the BS in predicting the location of the RAH, particularly in macroadenomas.

The visibility of either the BS or the RAH on the preoperative MRI, is a favorable sign for intraoperative identification and, therefore, preservation of the normal residual gland. It will also gain increasing signification in dosimetry and planification for stereotactic radiosurgery of pituitary adenomas.

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