

Original Article

MR imaging analysis of posterior pituitary in patients with pituitary adenoma

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Abstract: Objective: This study is to investigate posterior pituitary bright spot (PPBS) occurrence, distribution and its influencing factors by analyzing MRI-T1WI images in patients with pituitary adenoma (PA). Methods: A total of 123 cases of PA patients were enrolled in this study. PPBS occurrence, distribution and MR signal characteristics were studied. The relationship of PPBS with PA morphology, tumor size, tumor height and immunohistochemical types were explored. Results: Among the 123 case of PA patients enrolled in the study, 98 cases were PPBS (+) and 25 cases were PPBS (-). According to tumor morphology, PA was divided into hourglass type (43 cases), barrel type (63 cases) and wedge type (17 cases). Occurrence rate of PPBS (+) in barrel type was less than those in hourglass and wedge types ($P < 0.05$). Tumor volume and height in PPBS (+) group were less than these in PPBS (-) group ($P < 0.05$). PPBS signal size in wedge and barrel types were larger than that of hourglass type ($P < 0.05$). Conclusions: Sagittal MRI-T1WI images could well show posterior pituitary and PPBS (+) was related to tumor morphology, volume and height but had nothing to do with immunohistochemical types.

Keywords: Pituitary adenoma, pituitary, MRI, posterior pituitary bright spot

Introduction

Posterior pituitary locates in the rearmost section of pituitary gland and is involved in the regulation of water and electrolyte. In MRI-T1WI, it usually shows high signal in rear sella turcica [1, 2]. The signal intensity is known as posterior pituitary bright spot (PPBS) in iconography and often suggests complete neural pituitary function [3-5].

In the past 20 years, scholars have tried to elucidate the origin of PPBS and have proposed several different hypotheses. At earliest time, some scholars consider that PPBS is caused by the fat pad that located in deep lateral sellar region [6], however, this view is denied by MRI imaging with fat suppression [7]. Fujisawa et al. [8] found that PPBS was lacked in central diabetes insipidus patients, and then they inferred that this characteristic could be used for pituitary functional assessment. Meanwhile, they argue that the neuro-secretory granules of antidiuretic hormone (ADH) that inside posteri-

or pituitary is the cause of PPBS in T1WI. At present, researchers agree that PPBS reflects the ADH storage capacity of neurohypophysis [9-11]. A latest study [12] has found that the longest diameter and shortest diameter of PPBS was around 1.2 mm-8.5 mm and 0.4 mm-4.4 mm respectively, otherwise, indicating the existence of pituitary lesions. It is reported that in adult patients without pituitary disease, about 52%-100% are with PPBS [12], meanwhile, individual difference also exists. PPBS tends to lack in older people while PPBS enlarge is often visible in children, pregnant women and breast-feeding women [10].

Scholars have focused on normal human pituitary. However, reports on posterior pituitary in patients with pituitary adenoma (PA) are rare. Saeki et al. [5] have investigated posterior pituitary by combining PA morphology with posterior pituitary position. However, they did not study the size of PPBS nor did they analyze the signals. In the present study, 3.0T magnetic resonance machine scanning was used for observ-

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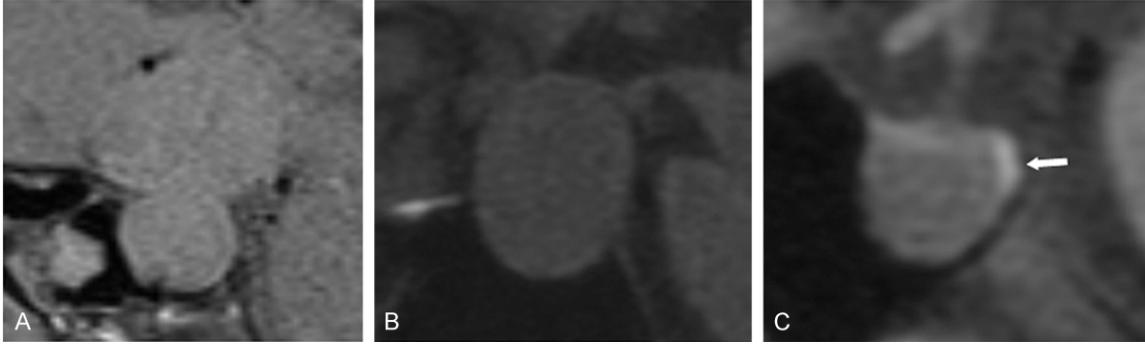


Figure 1. The morphological classification of pituitary adenoma at sagittal MRI-T1WI. A. Hourglass type: the tumor had broken through sellar diaphragm, compressing optic chiasm and forming a dent in the sella turcica. B. Barrel type: the tumor had broken through sellar diaphragm, compressing optic chiasm but without forming a dent in the sella turcica. C. Wedge type: the tumor did not compress optic chiasm and the pituitary stalk was visible. The white arrow indicated PPBS.

ing posterior pituitary in patients with PA so as to investigate the changed imaging characteristics and clinical significance of PPBS.

Materials and methods

Patient' data

A total of 152 candidates of patients who were diagnosed as PA and were admitted to our hospital from September 2012 to September 2014 and 123 cases were enrolled in this study finally. Among the 123 cases, 70 were male and 53 were female. They aged from (17-76) years old, with an average of 47.2 years old. The main clinical manifestations were headache, blurred vision, menstrual disorders, lactation, acromegaly, ect. According to similar prismatic table volume calculation method [13], the tumor volumes were (0.4-27.5) cm³ with a mean volume of 8.5 cm³, and the tumor heights was (0.9-5.4) cm with an average of 2.7 cm. Postoperative immunohistochemistry confirmed that there were 24 cases of null cell adenoma, 30 cases of prolactin type, 23 cases of multiple hormone type, 3 cases of adrenocorticotrophic hormone type, 31 cases of gonadotropin type and 12 cases of growth hormone type. The inclusion criteria were defined as follows: patients those took preoperative MRI examination in our hospital and were with complete clinical data; patients those took operation for the first time; patients those were confirmed as PA by postoperative pathology. The exclusion criteria were described as follows: patients those took sec-

ond surgery or had preoperative radiotherapy history; patients those were with incomplete image data; patients those were combined with other types of lesions in sellar region.

Prior written and informed consent were obtained from every patient and the study was approved by the ethics review board of Fuzhou General Hospital, Fujian Medical University, China.

MRI scanning

MRI scanning was performed with 3.0T magnetic resonance scanner (Tim Trio; Siemens Medical Solutions, Erlangen, Germany). All patients had taken preoperative MRI including at least plain scan and enhanced scan of SE sequential T1WI and T2WI in sagittal, coronal and axial views. The parameters used were as follows: scanning field, 180 mm × 180 mm; matrix, 320 × 240; layer thickness, 2.5 mm; interlaced scan. GD-DTPA was used as contrast agent with the dose of 0.1 mmol/kg and with a velocity of 2 ml/s.

MRI signal data processing

Tumor morphology was observed in the sagittal MR-T1WI. Saeki et al. [5] have classified tumor into hourglass type and barrel type according to whether the tumor that compressing optic chiasm has a dent in the sella turcica. In this study, on the basis of their classification method, non-optic chiasma oppression type was added and

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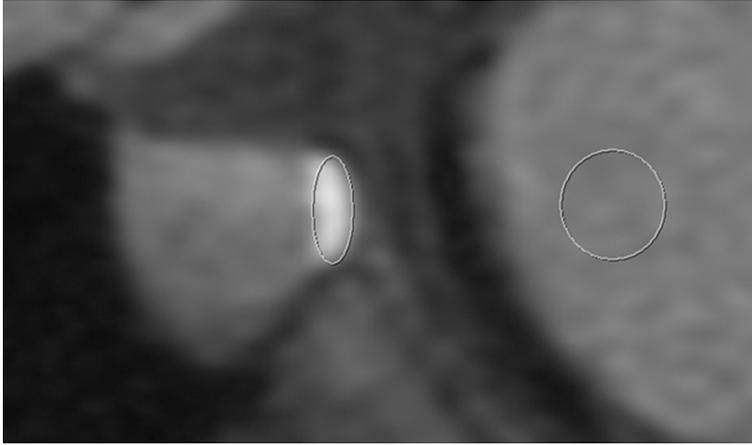


Figure 2. PPBS size and the ratio of signal intensity of PPBS to pons measured at sagittal MRI-T1WI.

Table 1. Comparison of preoperative PPBS size and signal intensity ratio of the PPBS to pons between hyponatremia group and normal serum sodium group (Mean \pm SD)

	Hyponatremia group (n = 9)	normal serum sodium group (n = 114)	P value
PPBS size (mm ²)	8.47 \pm 4.53	6.95 \pm 4.40	0.27
Signal intensity ratio	1.58 \pm 0.46	1.58 \pm 0.31	0.57

Note: the signal intensity ratio refers to the ratio of signal intensity of PPBS to pons.

hence tumors were divided into three types. Hourglass type: the tumor invaded sellar diaphragm, compressed optic chiasm and formed a dent in the sella turcica. Barrel type: the tumor invaded sellar diaphragm, compressed optic chiasm but did not form a dent in the sella turcica. Wedge type: the tumor did not compress optic chiasm and the pituitary stalk was visible. The detailed schematic diagram was shown in **Figure 1**.

PPBS distribution and signal intensity were observed in sagittal MR-T1WI. PPBS distribution was studied with INFINITT PACS medical imaging system (Infinit HealthCare Co., Ltd, Seoul, Korea). PPBS size and signal intensity were automatically generated after PPBS outline was depicted. In the meantime, circular regions within the pontine region with the diameter of about 5.0 mm were selected as the region of interest and the signal intensity was measured. The two signal intensity ratio was considered as the ratio of PPBS to pons [2] (**Figure 2**).

Similar prismatic table volume formula was used to calculate tumor volume in coronal enhanced T1WI [13].

Statistical analysis

All the statistical analyses were performed using SPSS version 18.0 (SPSS Inc, Chicago, IL, USA) for Windows and P value less than 0.05 was considered as statistically significant. Measurement data were expressed as mean \pm standard deviation (SD) and the t test or variance analysis were performed. Enumeration data were expressed by percentage and chi-square test or Fisher's exact test was adopted.

Results

PPBS occurrence and distribution

To distinguish the relationship of PPBS occurrence and distribution with PA, PPBS occurrence and distribution were calculated and identified. Among the 123 cases of PA patients, PPBS (+) was found in 98 cases (79.7%) and PPBS (-) was found in 25 cases (20.3%). In sagittal MRI-T1WI, PPBS size was (1.76-24.06) mm², with an average of (7.08 \pm 4.36) mm², and the ratio of PPBS signal to the pons was (1.11-2.55), with a mean of (1.59 \pm 0.32). There were 10 types of PPBS distribution, namely A-J in sagittal MRI-T1WI (**Figure 3**). There were 9 cases of hyponatremia and 1 case of diabetes insipidus preoperatively. Among the 9 cases of hyponatremia patients, PPBS was seen in 8 cases with the size of (8.47 \pm 4.53) mm² and signal intensity ratio of (1.58 \pm 0.46). PPBS was not seen in the diabetes insipidus case and the other hyperlipidemia case. There was no significant difference in size or signal intensity ratio of PPBS between patients with or without hyponatremia (**Table 1**). It is possible that the morphology and position of PPBS in PA patients are diversity, PPBS cannot be seen in sagittal MRI-T1WI in part of PA patients, and that PPBS is prone to be lost in central diabetes insipidus and hyponatremia patients.

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Table 2. Comparison of PPBS size and signal intensity ratio of the PPBS to pons in patients with different morphological classification of adenoma (Mean \pm SD)

	Hourglass type (n = 43)	Barrel type (n = 63)	Wedge type (n = 17)	P value
PPBS size (mm ²)	7.1 \pm 4.2	6.9 \pm 4.4	7.6 \pm 4.9	0.829
Signal intensity ratio	1.45 \pm 0.29	1.63 \pm 0.31	1.74 \pm 0.37	0.01

Table 3. Comparison between PPBS (+) group and PPBS (-) group (Mean \pm SD)

	PPBS (+) (n = 98)	PPBS (-) (n = 25)	P value
Age (years)	47.2 \pm 13.0	47.3 \pm 15.0	0.97
Gender (cases)			0.37
Male	57	17	
Female	41	8	
Tumor height (cm)	2.6 \pm 1.1	3.1 \pm 1.0	0.039
Tumor volume (cm ³)	7.8 \pm 6.9	11.3 \pm 6.8	0.007
Tumor morphology			0.006
Hourglass type	39	4	
Barrel type	43	20	
Wedge type	16	1	
Tumor type			0.414
Prolactin type	26	4	
Null cell type	19	5	
Multi hormone type	18	6	
Growth hormone type	11	1	
Gonadotropic hormone type	21	9	
Adrenocorticotrophic hormone type	3	0	

The relationship between PA morphology and PPBS

To identify the relationship between PA morphology and PPBS, a series of comparisons were performed. The cases of hourglass type, barrel type and wedge type were 43, 63 and 17, respectively. The occurrence of the three types were 90.1%, 68.2% and 94.1%, respectively, and the difference was statistically significant ($P = 0.006$). By mutual comparison, it was shown that PPBS was prone to appear in hourglass and wedge types. For the hourglass type group, PPBS located mainly in A (21 cases) and B (10 cases) while for the barrel type, PPBS located mainly in G (14 cases), H (17 cases). The ratio of signal intensity of PPBS to pons in the three types were (1.45 \pm 0.29), (1.63 \pm 0.31) and (1.74 \pm 0.37), with statistically significant ($P = 0.01$). However, there was no significant difference in PPBS largest size among the three groups ($P = 0.829$) (Table 2). To sum up,

the results indicated that there are differences in PA patients with different PPBS appearance rate, signal intensity, morphology and location, whereas there is no obvious difference in patients with different PPBS size.

The correlation of PPBS with gender, age, tumor size and tumor height in PA patients

To further investigate the relationship of PPBS and PA, a series of other indexes were measured and compared. The male to female ratio in PPBS (+) group was 57:41, in PPBS (-) group was 17:8, and there was no statistical difference ($P = 0.37$). The average age of PPBS (+) and PPBS (-) groups were (47.2 \pm 13.0) years old and (47.3 \pm 15.0) years old, with no

statistical difference ($P = 0.97$). The average tumor volume of PPBS (+) group and PPBS (-) group were (7.8 \pm 6.9) cm³ and (11.3 \pm 6.8) cm³, and there was significant difference between them ($P = 0.01$). Tumor height of PPBS (+) group and PPBS (-) group were (2.6 \pm 1.1) cm and (3.1 \pm 1) cm, PPBS (+) group was lower than PPBS (-) group ($P = 0.039$) (Table 3). There was no significant difference between PPBS (+) and PA immunohistochemistry types ($P = 0.414$). In summary, these results indicate that PPBS appearance rate is related to tumor volume and height, but is not related to gender, age or immunohistochemical type.

Discussion

In this study, PA morphology was classified into hourglass type, barrel type and wedge type, containing all the adenomas morphology, which, was more comprehensive than the classification method of Saeki et al. [5]. Similar pris-

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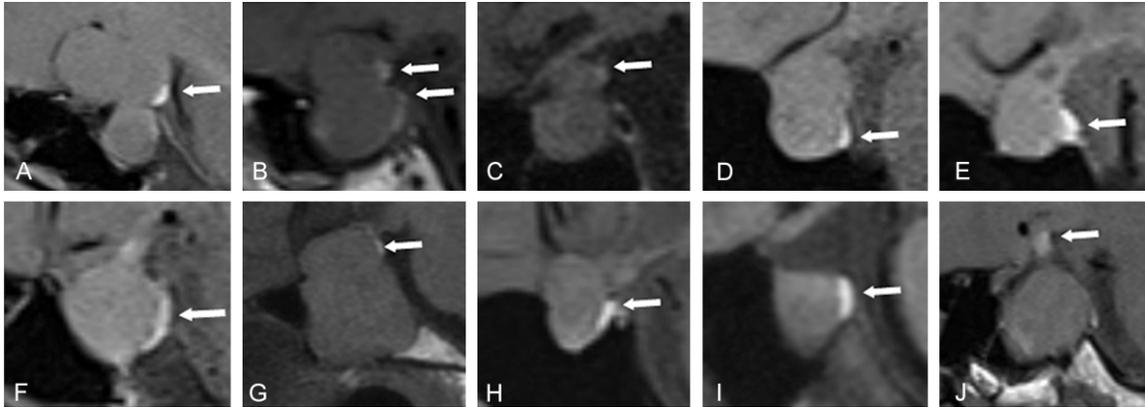


Figure 3. Sagittal MRI-T1WI of 10 cases of pituitary adenoma with different distributions in sellar region displaying morphological classification of adenoma and location of PPBS. A. PPBS located above the sellar diaphragm in hourglass type tumor patient. B. PPBS located above and under the diaphragma sellae in hourglass type tumor patient. C. PPBS located in the sella turcica, on the back side of the tumor and at the distal end of pituitary stalk. D. PPBS located under the sellar diaphragm in hourglass type tumor patient. E. PPBS located above the sellar diaphragm in barrel type tumor patient. F. PPBS located above and under the diaphragma sellae in barrel type tumor patient. G. PPBS located in the sella turcica, far away from sellar diaphragm, near optic chiasma. H. PPBS located under the sellar diaphragm in barrel type tumor patient. I. PPBS located under the sellar diaphragm in wedge type tumor patient, i.e. in the sella turcica. J. PPBS located at the lower portion of pituitary stalk and above the adenoma. The white arrow indicated PPBS.

matic table volume formula was adopted so as to lower the error as far as possible. Sagittal maximum PPBS size and signal intensity ratios to the pons were firstly measured. The results showed no difference in PPBS size in hourglass type, barrel type and wedge type and the signal intensity of wedge type and barrel type was larger than that of hourglass type. In this study, the correlation of PPBS distribution with PA morphology was investigated. It was found that in hourglass type PA, PPBS located mainly behind the tumor, was divided into supero-inferior parts by sellar diaphragm, and the more obvious the tumor was compressed, the more significant the separation degree of PPBS. In some cases those with tumors seriously stuck, PPBS was only found above the sellar diaphragm (**Figure 3A** and **3C**). However, in barrel type PA, PPBS was found mostly along the posterior surface of the adenoma, in tumor trailing edge below sellar diaphragm or crossing sellar diaphragm, additionally, it was continuous with no signs of compression.

Previous studies on PPBS in patients with PA are rare. According to Bonneville et al. [14], PPBS occurrence is rather high in patients with tumor height less than 20 mm. They also found that PPBS mainly appeared in rear sellar region in the tumor height less than 20 mm group while did not have well-established location in

the tumor height more than 20 mm group. Saeki et al. [5] have divided adenoma into hourglass and barrel types according to tumor morphology. PPBS was seen in 80% the cases of patients and more were found in hourglass type than in barrel type. They also found that there was no correlation between PPBS occurrence with tumor volume and tumor height. Not all adenoma forms were enrolled in the study of Saeki et al. and only a small number of cases were included. In the present study, adenoma type was re-classified on the basis of the previous classification method. It was found that PPBS occurrence was similar to the result of Saeki et al., however, PPBS ratio lowered as tumor volume and height became larger, which, was on the contrary. Our results was consistent with Liu et al. [15]. In addition, INFINITT PACS medical image system was used for PPBS size and signal intensity measurement in PA patients, which, had not been reported to date.

In wedge type group, as the tumor did not invade sellar diaphragm, PPBS located in rear sella turcica. For tumors those invaded sellar diaphragm, they were further divided into hourglass type and barrel type and the former was characterized by a dent. The reason for the dent formation was that the tuberculum sellae and dorsum sellae encircled a 10.5 mm × 14 mm bone window, the diameter of sellar dia-

phragm opening was 3-9 mm, which, was narrower than the bone window. As a result a dent formed in PA surface at the edge of sellar diaphragm [5]. This dent was affected by sellar diaphragm development and soundness, it was also affected by internal carotid artery, optic chiasma, tumor growth direction, etc. This dent had a blocking function for antidiuretic hormone transport channel, leading to accumulation of antidiuretic hormone above diaphragma sellae, thus forming ectopic PPBS. Bonneville et al. firstly reported that two patients with large pituitary macroadenoma had a PPBS inside and outside the sella at the same time [14] in 2002. They consider that it is the result of ADH particles filling the hypothalamo-neurohypophyseal channel. Due to the lack of specific site blocking ADH particle transport, PPBS appears widely in the hypothalamo-neurohypophyseal axis position, such as sellar diaphragm, pituitary stalk above sellar, the whole pituitary stalk or the junction region of the above regions [5].

It is reported that ectopic PPBS can be formed after pituitary stalk end breaking or pituitary stalk oppression so as to replace the function of the true posterior pituitary [14]. Our study showed that PPBS occurrence was related to tumor size, and the larger the tumor volume, the lower ratio the PPBS occurrence. This was because that ADH transmit was decreased by the direct oppression of tumor, which leading to ADH accumulation decrease or disappear in neurohypophysis, thus, no high signal was shown in posterior pituitary gland [15]. In this study, in some cases those with tumors seriously stuck, PPBS was only found above the sellar diaphragm, it is reasonable to assume that this is a pathological upward moving result caused by sellar diaphragm compression.

Preoperative understanding of PPBS location in patients with PA can help the protection in operation. It is less susceptible to be interfered by operation and the postoperative risk of diabetes insipidus is lower if PPBS was farther away from the sphenoid sinus and more close to the hypothalamus [14]. No PPBS was found preoperatively in 1 case of hyponatremia and 1 case of multiple urinary patients, this might be caused by ADH excessive release or deficiency. PPBS was found in 8 cases of hyponatremia patients preoperative, there were no significant differences in PPBS size and signal intensity while compared with normal serum sodium

patients. Because pituitary hormone secretion can also affect the level of serum sodium, cortisol and thyroid hormone levels should be assessed at the same time [16]. No polydipsia, polyuria or electrolyte disturbance performance cases were found in other patients, this prompting that the neurohypophysis was still playing an important function.

No high signal intensity was seen on MRI, this might be due to the dynamic balance of ADH release and synthesis, known as the "exhaustion of posterior pituitary" [17].

In conclusion, in this study, the imaging change characteristics and clinical significance of PPBS in PA patients were studied. The results showed that sagittal MRI-T1WI images could well display the posterior pituitary gland and PPBS (+) was related to tumor morphology, volume and height but had no relationship to immunohistochemical types. As the volume of posterior pituitary is quite small and posterior pituitary is prone to be pressed by tumor, thus, there might exist some measurement error. With the development of MRI imaging technology and improvement of accuracy, PPBS assessment would be more accurate in the future.

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Disclosure of conflict of interest

None.

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