Parasellar T2 Dark Sign on MR Imaging in Patients with Lymphocytic Hypophysitis


*AJNR Am J Neuroradiol* 2010, 31 (10) 1944-1950
doi: [https://doi.org/10.3174/ajnr.A2201](https://doi.org/10.3174/ajnr.A2201)
[http://www.ajnr.org/content/31/10/1944](http://www.ajnr.org/content/31/10/1944)
LYH is a rare inflammatory disease of the pituitary gland. This condition is characterized by lymphocytic infiltration and eventual destruction of the pituitary tissue accompanied by various degrees of pituitary dysfunction. This disease is now known to affect both pituitary lobes, at all ages and in both sexes. An autoimmune pathogenesis is suggested by several histopathologic, laboratory, and clinical findings.

LYH is often misdiagnosed because its clinical and radiologic features mimic tumors in the sellar and parasellar region. The main diagnostic issue is that LYH is a relatively rare disease, and its imaging findings are not well-recognized in contrast to those of overwhelmingly more common pituitary tumors, pituitary adenomas. Distinguishing LYH from pituitary adenoma is very important because different therapeutic strategies are used to treat the 2 diseases. The treatment of LYH remains controversial, though conservative management with close clinical observation has been advocated on the basis of its often benign transient course. The correct diagnosis of LYH contributes to avoiding needless surgery, which is invasive and sometimes results in endocrine dysfunction. However, distinguishing LYH from pituitary adenomas can be difficult. Leung et al reported that even with MR imaging studies, approximately 40% of the cases are misdiagnosed preoperatively as pituitary adenomas. MR imaging findings in patients with LYH and pituitary adenoma were reported in some recent articles. However, most previous reports of MR imaging findings of LYH were case reports and/or reviews of the literature.

Recently, we experienced some cases of LYH, which showed dark-signal-intensity areas on T2-weighted images around the pituitary gland and in the cavernous sinus. To the best of our knowledge, no studies have reported such signal-intensity abnormalities. We hypothesized that dark-signal-intensity areas on T2-weighted images around the pituitary gland and in the cavernous sinus were characteristic in patients with LYH and were useful for distinguishing pituitary adenoma from LYH.

The present study was retrospectively performed to review a series of clinical and MR imaging findings in patients with LYH, including signal intensity around the pituitary gland. As
a control study, we also evaluated clinical and MR imaging findings in patients with pituitary adenoma for comparison.

**Materials and Methods**

**Patients**

We retrospectively reviewed the MR imaging findings in 20 patients with LYH who were selected by review of clinical records. Our local ethics committee did not require its approval or informed consent for this retrospective review. A retrospective review of clinical records in 6 hospitals from 1987 to 2009 revealed 24 patients who were clinically diagnosed as LYH. Two patients who had a history of sarcoidosis or pachymeningitis, and 2 patients whose initial MR images had not been available were excluded from the study. As a consequence, 20 patients with LYH were enrolled. Ten were males and 10 were females, from 9 to 72 years of age, with a mean age of 46.0 ± 19.5 years (On-line Table 1). Four of 20 patients had histologically proved disease by transphenoidal biopsy. The remaining 16 patients were diagnosed on the basis of clinical and endocrinologic studies, MR imaging findings, response to steroid therapy, and natural clinical course. Four patients had a history of autoimmune diseases, such as IgG4-related disorders, rheumatoid arthritis, and bullous pemphigoid. One patient was pregnant.

We also reviewed the clinical and MR imaging findings in 22 patients with pituitary adenoma. A retrospective review of clinical records in 1 hospital from 2002 to 2009 revealed 52 patients who were treated with transphenoidal resection and had a proved pathologic diagnosis of pituitary adenoma. Sixteen patients who had recurrent pituitary adenomas and underwent a second operation, 11 patients whose pathologies did not differentiate between functioning and nonfunctioning adenoma because immunostaining was not performed, 2 patients whose initial MR images had not been available, and 1 patient who received irradiation due to malignancy were excluded from the study. As a consequence, 22 patients with pituitary adenoma were enrolled. Ten were men and 12 were women, and they ranged in age from 25 to 73 years, with a mean age of 50.3 ± 15.8 years (On-line Table 2). All patients were treated with transphenoidal resection, and their pathologies were proved.

In all patients with LYH and pituitary adenoma, the plasma concentrations of ACTH, GH, PRL, LH, FSH, TSH, cortisol, free T4, and testosterone were measured. Provocative tests were performed as follows: for TSH and PRL, after a bolus injection of 500 mg of TSH-releasing hormone; for LH and FSH, 100 mg of gonadotropin-releasing hormone; for GH, 100 mg of GH-releasing hormone or 0.1 U of regular insulin per kilogram of body weight; and for cortisol, 0.25 mg of ACTH or 0.1 U of regular insulin per kilogram of body weight. Multiple blood samples were collected to measure plasma hormone concentrations before and for up to 120 minutes after the injections. In patients with LYH except for cases 2, 8, and 13, plasma vasopressin concentrations were determined by radioimmunoassay, and plasma and urinary osmolalities were measured before and after 4–8 hours of water deprivation. In cases 9, 11, 21, and 22 of patients with pituitary adenoma, hormonal examination was done for the posterior lobe by using the same method.

**MR Imaging Acquisition**

All patients with LYH and pituitary adenoma underwent MR imaging of the sella turcica with 1.5T superconductive units. Patients with LYH underwent MR imaging with 6 units in 6 hospitals, and patients with pituitary adenoma underwent 1 MR imaging in 1 hospital. T1-weighted images were acquired in the coronal and sagittal planes with the following parameters: TR/TE/NEX = 300–660/7.9–23 ms/3–4, a 192 × 256 to 512 × 512 matrix, a 14- to 20-cm FOV, a 3-mm section thickness, and a 0.0- to 0.6-mm intersection gap. T2-weighted sagittal or coronal images were obtained with the following parameters: TR/TE/NEX = 2000–3500/80–120 ms/3–4, a 192 × 256 to 512 × 512 matrix, a 14- to 20-cm FOV, a 3-mm section thickness, and a 0.0- to 0.6-mm intersection gap. T1-weighted images after an intravenous injection of contrast medium (0.1 mmol/kg of body weight) were also acquired, except for case 8, in patients with LYH, in the coronal and sagittal planes with the same parameters as those of the T1-weighted images. All patients with LYH had 1–6 follow-up MR imaging studies performed during a period ranging from 1 month to 8 years.

Two neuroradiologists (Y.N., N.S.) who did not know the patients' clinical information evaluated the MR imaging findings of the patients with LYH and pituitary adenoma. In several recent articles, some findings were reported to be useful for distinguishing pituitary adenoma from LYH, such as precontrast homogeneous signal intensity, intact sellar floor, suprasellar extension, loss of PPHI, stalk thickening, mass symmetry, homogeneous enhancement, and adjacent dural enhancement (the so-called dural tail). In this study, evaluation of the precontrast signal intensity was excluded because pituitary adenomas often show complicated signal intensities due to hemorrhagic or cystic changes, and it is a not suitable factor for making a simple assessment. The findings of destruction of the sellar floor and extension to the sphenoid sinus were also excluded because it was obvious that these findings indicate neoplasm. The finding of suprasellar extension was also excluded because it depends on the size of pituitary lesions, and pituitary adenomas vary in size from microadenoma to macroadenoma.

We, therefore, selected the following MR findings as assessment factors: 1) PPHI on T1-weighted images, 2) thickened stalk, 3) pituitary symmetry, 4) pituitary enhancement pattern, 5) the dural tail, and 6) paraspinal signal intensity on T2- and T1-weighted images. PPHI was classified as either "identified" or "not identified." If the diameter of the pituitary stalk exceeded 3.5 mm at the level of the median eminence of the hypothalamus, the stalk was considered "thick." Pituitary symmetry was classified as either "symmetric" or "asymmetric." The enhancement pattern was classified as either "homogeneous" or "heterogeneous." The dural tail was classified as either "identified" or "not identified." Paraspinal signal intensity on T2- and T1-weighted images was classified as either "dark," "low," "iso," or "high" intensity. On T2-weighted images, "dark" was isointense with bone cortex; "low" was isointense with white matter; "iso" was isointense with gray matter, and "high" was hyperintense with gray matter. On T1-weighted images, "dark" was isointense with bone cortex; "low" was isointense with CSF, "iso" was isointense with gray matter, and "high" was hyperintense with gray matter. If different signal intensities were detected in the parasellar areas, the lowest signal intensity was adopted. When the 2 neuroradiologists found different results, they discussed the case and came to a decision by consensus. We also reviewed all images of a series of follow-up MR images in patients who showed parasellar dark-signal-intensity areas on T2-weighted images.

**Statistical Analysis**

Statistical analyses were performed by using StatView 5.0 software (SAS Institute, Cary, North Carolina). Between patients with LYH and pituitary adenoma with LYH.
and those with pituitary adenoma, each imaging finding as described above was compared by using the Fisher exact probability test. \(P\) values \(< .05\) indicated statistical significance. We also calculated sensitivity and specificity for the diagnosis of LYH of each imaging finding as described above.

**Results**

Clinical findings for the 20 patients with LYH are summarized in On-line Table 1. Endocrinologic studies showed that 17 of 20 patients (85%) had some degree of hypopituitarism: panhypopituitarism or partial hypopituitarism with diabetes insipidus in 12 patients, only panhypopituitarism in 2 patients, and only diabetes insipidus in 3 patients.

Clinical findings for the 22 patients with pituitary adenoma are summarized in On-line Table 2. Endocrinologic studies showed partial hyperpituitarism and partial hypopituitarism in 3 patients, only partial hyperpituitarism in 7 patients, and only hypopituitarism in 1 patient. In 4 patients who had hormonal examination of the posterior lobe, none had diabetes insipidus.

MR imaging findings of the patients with LYH and pituitary adenoma are summarized in On-line Table 3. PPHI was absent in 17 patients (85%) with LYH and 3 (14%) with pituitary adenoma. Ectopic PPHI was seen in 1 patient with LYH and 3 with pituitary adenoma. Seventeen patients (85%) with LYH had thickened stalks. On the other hand, no patients (0%) with pituitary adenoma had thickened stalks, though in 2 patients with LYH and 4 with pituitary adenoma, the stalk was unclear due to pituitary tumoral compression. The pituitary gland was symmetric in 17 patients (85%) with LYH and in 2 (9%) with pituitary adenoma. Homogeneous enhancement was seen in 13 patients (65%) with LYH and in only 2 patients (9%) with pituitary adenoma. The dural tail was seen in 13 patients (65%) with LYH and 17 patients (77%) with pituitary adenoma. On T2-weighted images, parasellar dark-signal-intensity areas were seen in 7 patients (35%) with LYH (Figs 1–3); the other 13 patients with LYH showed isointensity. Parasellar low-signal-intensity areas were seen in 2 patients (9%) with pituitary adenoma (Fig 4), but no parasellar dark-signal-intensity areas were seen in any patients with pituitary adenoma.
The other 20 patients with pituitary adenoma showed isointensity. On T1-weighted images, parasellar low-signal-intensity areas were seen in 2 patients (10%) with LYH. The other 18 patients with LYH showed isointensity. On the other hand, all patients with pituitary adenoma showed isointensity. Pituitary adenomas involved the cavernous sinuses in 11 patients; however, the cavernous sinuses were isointense with gray matter on T2- or T1-weighted images, and dark-signal-intensity areas were not seen.

Details of the MR imaging findings in the 7 patients who showed parasellar dark signal intensity on T2-weighted images are summarized in On-line Table 4. Dark-signal-intensity areas in the cavernous sinuses were seen in 6 patients. Cavernous sinuses were swollen in 4 patients (Figs 1 and 2). Enhancement of the cavernous sinuses after an intravenous injection of contrast medium was poor in 3 patients (Figs 1 and 2). ICAs in the cavernous sinuses were narrowed in 3 patients (Figs 1 and 3). In cases 4, 5, and 6, dark-signal-intensity areas in the cavernous sinus were not seen in the first MR imaging study but appeared 2–20 months later. On T2-weighted images, dark-signal-intensity bands around the anterior lobe and/or posterior lobe of the pituitary gland were seen in 4 patients (Fig 3).

In case 5, this band was not seen in the first MR imaging study but appeared 20 months later. In case 4, a very thin dark-signal-intensity band was noted on the upper edge of the posterior gland in the first study and was thickened on follow-up studies 2 and 8 months later (Fig 3).

Between patients with LYH and those with pituitary adenoma, a significant difference was identified by statistical analysis for the number of patients with PPHI on T1-weighted images ($P < .0001$), thickened stalk ($P < .0001$), pituitary symmetry ($P < .0001$), homogeneous enhancement ($P = .0001$; we excluded the cases without contrast enhancement), and dark-signal-intensity areas on T2-weighted images ($P = .0015$). No significant difference was identified for the number of patients with the dural tail ($P = .36$; we excluded the cases without contrast enhancement) and low-signal-intensity areas on T1-weighted images ($P = .11$). Sensitivity and specificity for the diagnosis for LYH were as follows: 0.85 and 0.95 for the loss of PPHI; 0.85 and 0.82 for the thickened stalk; 0.85 and 0.91 for the pituitary symmetry; 0.68 and 0.91 for the homogeneous enhancement (we excluded the cases without contrast enhancement); 0.65 and 0.23 for the dural tail; and 0.35 and 1.00 for the dark-signal-intensity areas on T2-weighted images, and 0.10 and 1.00 for the low-signal-intensity areas on T1-weighted images around the sellar and parasellar areas.
Discussion

The present study reviewed a series of clinical and MR imaging findings in 20 patients with LYH. To the best of our knowledge, this study has reviewed original MR imaging findings in the largest number of patients with LYH. We demonstrated a new characteristic parasellar T2 dark sign (dark-signal-intensity area on T2-weighted images around the pituitary gland and in the cavernous sinus) in patients with LYH for the first time. Although sensitivity for the parasellar T2 dark sign was 0.35, lower than that for loss of PPHI, thickened stalk, pituitary symmetry, homogeneous enhancement, or the dural tail, specificity for the parasellar T2 dark sign was 1.00; and this finding was characteristic enough to distinguish with certainty the more common pituitary adenoma from LYH because false-positive cases were not found. T2-weighted images depicted the parasellar involvement of LYH well. Our results also suggest that there are variations of localization of T2 dark areas in LYH.

Some previous studies reported that loss of PPHI, thickened stalk, pituitary symmetry, homogeneous enhancement, and the dural tail were useful for distinguishing LYH from pituitary adenomas, but only 1 previous study investigated this statistically. Gutenberg et al reported that these findings contributed significantly to classifying the outcome as pituitary adenoma or autoimmune hypophysitis (including lymphocytic and granulomatous hypophysitis), and our results were consistent with their findings.

Although MR imaging findings such as loss of PPHI, thickened stalk, pituitary symmetry, and homogeneous enhancement showed significant difference in the statistical analysis in the present study, these findings were nonspecific and were observed in both diseases. Loss of PPHI was observed in central diabetes insipidus due to idiopathic, inflammatory, or neoplastic processes, including pituitary adenoma. The stalk was sometimes unclear due to pituitary tumoral compression. Pituitary symmetry or asymmetry depends on tumor size, location, or invading areas. Cystic, necrotizing, or hemorrhagic changes also influence the enhancement pattern. Cystic appearance was described in 5% of the patients with LYH. Homogeneous enhancement can also be observed in pituitary adenomas. On the other hand, parasellar T2 dark sign was a characteristic finding in LYH and can contribute to distinguishing pituitary LYH from adenoma with certainty.

Clinical findings revealed that panhypopituitarism or partial hypopituitarism was seen in 17 patients (85%) with LYH. On the other hand, partial hypopituitarism was seen in only 4 patients (18%) with pituitary adenoma. We think that hypopituitarism may be useful clinical information, suggesting LYH rather than pituitary adenoma. The endocrinologic man-
Other anterior pituitary hormones have been described in

Iuchi et al. 40 reported that the signal intensities on T2-

approximately 10% of pituitary adenomas contained fibro-

and did not include fibrous tissue. In the previous reports,

specimens included only a small portion of the anterior lobes

tenuated hyalinized fibrous tissue; however, fibrous tissue was

with lymphoid follicle formation and attached portions of at-

ically by transsphenoidal biopsy. In case 2, biopsy specimens

not seen in the initial MR imaging in patients who were sus-

making an initial diagnosis. If the parasellar T2 dark sign was

time, and thus the parasellar T2 dark sign may not be useful for

and specificity of the parasellar T2 dark sign may vary with

as parasellar T2 dark signs. We also think that the sensitivity

in the diagnosis of LYH.

This study had several limitations. The first is that not all patients with LYH had pathologic confirmation; only 4 of 20 patients with LYH and only 2 of 7 patients with parasellar T2 dark sign had transsphenoidal biopsy. Additionally, there were 5 patients who had a history of autoimmune disease such as IgG4-related disorders, rheumatoid arthritis, and bullous pemphigoid. Other disorders, such as granulomatous hypophysitis or sarcoidosis, could feasibly have similar MR imaging findings. However, the duration of follow-up was relatively long (from 9 months to 9 years) in the 11 patients without pathologic confirmation or a history of autoimmune disease. Sarcoidosis is liable to recur not only in the intracranial area but also in the extracranial portion during longitudinal follow-up, but these 11 patients had no recurrence. In addition, they had no laboratory findings supporting sarcoidosis. Granulomatous hypophysitis is an extremely rare disorder (annual incidence of 1 in 10 million) and is usually diagnosed in postmortem specimens. The other limitation was that the present study was retrospective; most of the patients had only had a routine pituitary MR imaging study. If we had been able to prospectively evaluate these patients by using dynamic contrast-enhanced MR imaging or contrast-enhanced 3D constructive interference in the steady state, more details of the sellar and parasellar structures and signal intensity would have been shown. Further prospective studies that compare the findings obtained from high-field MR imaging systems or long-term follow-up MR imaging with the histopathologic findings should be conducted.

Conclusions

MR imaging findings, such as loss of PPHI, thickened stalk, pituitary symmetry, homogeneous enhancement, and parasellar T2 dark sign, can contribute to distinguishing pituitary adenoma from LYH. The parasellar T2 dark sign in particular was a characteristic finding in patients with LYH, which was not observed in pituitary adenomas.
References

4. Rivera JA. Lymphocytic hypophysitis: disease spectrum and approach to diagnosis and therapy. Pituitary 2006;9:35–45