REVIEW

Pituitary Ring Sign Plus Sphenoid Sinus Mucosal Thickening: Neuroimaging Signs of Pituitary Apoplexy

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ABSTRACT

Two magnetic resonance imaging (MRI) signs of pituitary apoplexy are the “pituitary ring sign” and “sphenoid sinus mucosal thickening”. The occurrence of both these MRI signs together in patients with ischaemic pituitary apoplexy was investigated. A literature review searching the terms “pituitary ring sign” and “sphenoid sinus mucosal thickening” in the context of pituitary apoplexy from 1990 until present was performed. To be included in the study, each case had to have ischaemic pituitary apoplexy defined as acute expansion of a pituitary adenoma or, less commonly, in a non-adenomatous gland, from infarction without haemorrhage or very little haemorrhage and a T1-weighted MRI of the brain with contrast that displayed both “sphenoid sinus mucosal thickening” and a “pituitary ring sign” either on an actual study (the author’s cases) or in a figure in an article from the literature that could be reviewed and clearly illustrate these two signs. Twelve cases of ischaemic pituitary apoplexy were found, all with MRI images that showed both of these signs. Ten cases from the literature (3 of which were published by this author) plus an additional 2 recently evaluated in our hospital, totalled the 12 cases. Thus, 5 of the total 12 cases were evaluated by this author. Of these 12 patients, both headache and visual loss were present in 5 patients, headache alone was indicated in 5 patients (10 of the 12 presented with headache), and no initial symptoms identified in 2 patients (incidentally found non-functioning pituitary adenomas on MRI). These findings indicate that each sign (“pituitary ring sign” and “sphenoid sinus mucosal thickening”) may exist alone with or without pituitary apoplexy, yet both signs together in the appropriate clinical context is a strong predictor of pituitary apoplexy.

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Introduction

In 2007 in this journal, *Neuro-Ophthalmology*, Vaphiades introduced the term “pituitary ring sign” as a magnetic resonance imaging (MRI) sign of ischaemic pituitary apoplexy.¹ Since then, this author has found the sign to be clinically useful in diagnosing this disorder. Pituitary apoplexy is characterised by sudden onset of headache, visual symptoms, altered mental status, and hormonal dysfunction due to acute haemorrhage or infarction of the pituitary gland. The visual symptoms may include both visual acuity and field loss from involvement of the optic nerve or chiasm and ocular motility dysfunction from involvement of the cavernous sinus.¹ Apoplexy most commonly occurs in the setting of a pituitary adenoma and only rarely in association with a non-adenomatous pituitary gland, Rathke cleft cyst, or craniopharyngioma.² Pituitary apoplexy may be

divided into haemorrhagic or ischaemic types, each with unique neuroimaging findings. Recently, another sign of pituitary apoplexy has been described, “sphenoid sinus mucosal thickening”.³ Thus, there are two MRI signs of pituitary apoplexy, the “pituitary ring sign” (used to describe an enlarged pituitary gland bulging under the optic chiasm with peripheral enhancement surrounding a hypointense gland) and “sphenoid sinus mucosal thickening” (thickening and enhancing of the sphenoid sinus mucosa); the former sign is unique only to ischaemic apoplexy and the latter sign is seen in both ischaemic and haemorrhagic apoplexy types.

Methods

A literature review searching the terms “pituitary ring sign” and “sphenoid sinus mucosal thickening” in the context of pituitary apoplexy from 1990

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Results

Twelve cases of ischaemic pituitary apoplexy were found, all with MRI images that clearly showed both of these signs. Ten cases from the literature (3 of which were published by this author) plus an additional 2 recently evaluated in our hospital (1 of which is the representative case shown in **Figures 1** and **2**), totalled the 12 cases. Thus, 5 of the total 12 cases were evaluated by this author. The mean age of the patients was 49.4 years (range: 30–83 years). Of these 12 patients, both headache and visual loss were present in 5

Figure 1. A 55-year-old man presented with acute onset of severe headache, diplopia, nausea, and vomiting. The neuro-ophthalmologic examination showed a visual acuity with correction at the bedside of 20/50 (right eye), 20/70 (left eye), with normal colour vision and confrontational visual fields. Pupils were normal without a relative afferent pupillary defect. Ocular motility, slit-lamp, and ophthalmoscopic examinations were normal. Post-contrast sagittal T1-weighted scan shows sphenoid sinus roof mucosal thickening. The horizontal arrow shows the “pituitary ring sign”; the vertical arrow shows sphenoid sinus roof mucosal thickening.

Figure 2. Two days after the apoplectic event, post-contrast sagittal MRI reveals further development of a pituitary ring sign and more thickening of the roof of the sphenoid sinus (arrow).

patients, headache alone was indicated in 5 patients (10 of the 12 presented with headache), and no initial symptoms identified in 2 patients (incidentally detected pituitary adenomas on MRI; see Discussion).

Discussion

The term “pituitary ring sign” is used to describe an enlarged pituitary gland bulging under the optic chiasm, with peripheral enhancement surrounding a hypointense gland. This MRI appearance was first noted in 1995 by Lavallée et al. in a patient with Sheehan syndrome on a contrast-enhanced computed tomography (CT) scan and on a T1-weighted contrast-enhanced MRI scan and thought to be unique to ischaemic apoplexy in patients with Sheehan syndrome.⁴

In 1998, Kleinschmidt-Demasters and Lillehei reported the pathological and MRI features of 15 patients with pituitary adenomas presenting with apoplexy.² On T1-weighted contrast-enhanced MRI, they observed a peripheral rim of enhancement with gadolinium in 10 cases; one of the representative MRI images displayed in this paper had sphenoid mucosal thickening in addition to the pituitary ring sign. This is the case that I included among the 12 cases in this current

manuscript. Subsequent reports corroborated this MRI finding in patients with ischaemic pituitary apoplexy and the name was coined “pituitary ring sign” in 2007.^{1,5}

The presumed aetiology of the hypointense centre in the pituitary gland is necrosis, which does not enhance with gadolinium on T1-weighted MRI. The enhancing part of the tumour is the outer most portion of the infarcted pituitary or its “skin”. This was found to correspond to the presence of granulation tissue and lymphocytosis at histological examination.²

The ring sign is not specific for pituitary infarction, because it can be seen in association craniopharyngioma⁶ in addition to lymphocytic hypophysitis, pituitary abscess, and pituitary adenoma that has not undergone apoplexy.⁷ Lymphocytic hypophysitis is a rare inflammatory disorder of the pituitary gland, commonly manifesting late in pregnancy or during the postpartum period. It can mimic pituitary adenoma. In the majority of cases, the diagnosis is made after pituitary surgery for suspected pituitary adenoma.⁸ Symptoms include headache, nausea, and vomiting, fatigue, hypopituitarism, and diabetes insipidus. If there is mass effect on the optic chiasm, vision may be impaired, usually with a typical bitemporal hemianopsia, and if the cavernous sinus is involved, patients may have diplopia and orbital pain.⁹ Pituitary abscess is a rare, life-threatening disease that has a similar presentation to large non-functioning adenomas and if large enough present with visual loss localising to the optic chiasm. Most of the patients present with complaints and symptoms consistent with a sellar mass, generally in the absence of any evidence of infection. Diabetes insipidus, hypopituitarism, and headache are the most common clinical indicators.¹⁰

Sphenoid sinus mucosal thickening, occurring in the setting of pituitary apoplexy, was first described by Arita et al. in 2001.³ They retrospectively evaluated 14 patients with pituitary apoplexy. The mucosa of the sphenoid sinus on MRI had thickened the compartment just beneath the sella turcica in 9 of 11 patients obtained within 7 days after the onset of apoplectic symptoms. Controls consisted of MR images obtained in 100 consecutive patients with pituitary adenomas but without apoplectic symptoms. Included in this

group were 58 functioning and 42 non-functioning pituitary adenomas. Fifteen patients experienced thickening of the sphenoid sinus mucosa, including five with some apparent pansinusitis. The incidence of mucosal thickening of the sphenoid sinus in the patients with apoplexy was significantly greater than that in the patients without apoplexy.³ On histopathological specimens in the apoplexy patients, the thickened sphenoid sinus mucosa demonstrates a swollen sub-epithelial layer presumably responsible for the rim of MRI gadolinium enhancement.³

Not all patients with apoplexy initially present with symptoms. In a separate paper by Arita et al., 42 patients with clinically non-functioning pituitary adenomas who had manifested no neurological or endocrinological disorders were monitored with MRI studies. In the course of 4 years, the size of the incidentalomas increased in 40% of 42 patients and became symptomatic in 20%.⁷ Thus, this accounts for the 2 of patients 12 cases in this current manuscript's Results section with “no initial symptoms”.

In 2006, Liu et al. performed a retrospective review of 28 patients with pituitary apoplexy. Thickening of sphenoid sinus mucosa was present in 22 (79%) of these patients. They also noted that patients with thickened sphenoid sinus mucosa had larger tumours, a higher rate of cranial nerve deficits at presentation than those without mucosal thickening, and a higher rate of hypopituitarism and subsequent long-term hormone replacement therapy compared with those patients without thickened mucosa.¹¹

In 2012, Agrawal et al. concluded that there is a temporal association with the radiographic finding of sphenoid sinus mucosal thickening and pituitary apoplexy and that sphenoid sinus mucosal thickening may precede an apoplectic event.¹² This certainly corresponds to the representative case presented in this article of a patient who suffered ischaemic pituitary apoplexy and whose MRI demonstrated progressive thickening of the sphenoid sinus over 2-day period prior to diagnosis and treatment (Figures 1 and 2).

Each sign (“pituitary ring sign” and “sphenoid sinus mucosal thickening”) alone may exist in patients with or without pituitary apoplexy, yet presence of both signs together in the appropriate clinical context is a strong predictor of pituitary

apoplexy. This is important because timely diagnosis and treatment of pituitary apoplexy may be vision and life-saving in this disorder.

Declaration of interest

The author reports no conflicts of interest. The author alone is responsible for the content and writing of the article.

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References

- [1] Vaphiades MS. The “pituitary ring sign”: an MRI sign of pituitary apoplexy. *Neuro-ophthalmology* 2007;31:111–116.
- [2] Kleinschmidt-Demasters BK, Lillehei KO. Pathological correlates of pituitary adenomas presenting with apoplexy. *Hum Pathol* 1998;29:1255–1265.
- [3] Arita K, Kurisu K, Tominaga A, Sugiyama K, Ikawa F, Yoshioka H, Sumida M, Kanou Y, Yajin K, Ogawa R. Thickening of sphenoid sinus mucosa during the acute stage of pituitary apoplexy. *J Neurosurg* 2001;95:897–901.
- [4] Lavallée G, Morcos R, Palardy J, Aubé M, Gilbert D. MR of nonhemorrhagic post-partum pituitary apoplexy. *AJNR Am J Neuroradiol* 1995;16:1939–1941.
- [5] Vaphiades MS, Simmons D, Archer RL, Stringer W. Sheehan syndrome: a splinter of the mind. *Surv Ophthalmol* 2003;48:230–233.
- [6] Rogg JM, Tung GA, Anderson G, Cortez S. Pituitary apoplexy: early detection with diffusion-weighted MR imaging. *AJNR Am J Neuroradiol* 2002;23:1240–1245.
- [7] Arita K, Tominaga A, Sugiyama K, Eguchi K, Iida K, Sumida M, Migita K, Kurisu K. Natural course of incidentally found nonfunctioning pituitary adenoma, with special reference to pituitary apoplexy during follow-up examination. *J Neurosurg* 2006;104:884–891.
- [8] Flanagan DE, Ibrahim AE, Ellison DW, Armitage M, Gawne-Cain M, Lees PD. Inflammatory hypophysitis—the spectrum of disease. *Acta Neurochir (Wien)* 2002;144:47–56.
- [9] Tubridy N, Saunders D, Thom M, Asa SL, Powell M, Plant GT, Howard R. Infundibulohypophysitis in a man presenting with diabetes insipidus and cavernous sinus involvement. *J Neurol Neurosurg Psychiatry* 2001;71:798–801.
- [10] Liu F, Li G, Yao Y, Yang Y, Ma W, Li Y, Chen G, Wang R. Diagnosis and management of pituitary abscess: experiences from 33 cases. *Clin Endocrinol (Oxf)* 2011;74:79–88.
- [11] Liu JK, Couldwell WT. Pituitary apoplexy in the magnetic resonance imaging era: clinical significance of sphenoid sinus mucosal thickening. *J Neurosurg* 2006;104:892–898.
- [12] Agrawal B, Dziurzynski K, Salamat MS, Baskaya M. The temporal association of sphenoid sinus mucosal thickening on MR imaging with pituitary apoplexy. *Turk Neurosurg* 2012;22:785–790.