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Idiopathic granulomatous hypophysitis: clinical and imaging features

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Abstract Idiopathic pituitary granuloma is a rare disorder similar to lymphocytic adenohypophysitis. Few cases have been reported. We report a new histologically case proven with MRI. The patterns of clinical and radiological presentation and the management of this disorder are discussed. MRI findings suggestive of this condition include an intensely enhancing pituitary mass, associated with dural enhancement. Steroid therapy may be suggested avoiding unnecessary surgery.

Key words Granuloma · Pituitary · Computed tomography · Magnetic resonance imaging

Introduction

Idiopathic pituitary granuloma is a rare chronic inflammatory process. Most pituitary granulomas represent a specific lesion such as syphilis, sarcoidosis, histiocytosis X, or tuberculosis [1–6]. After excluding such aetiologies, very few patients remain with granulomatous hypophysitis of unknown origin [7–19]. The purpose of this paper is to present a case of granulomatous hypophysitis mimicking a pituitary adenoma and to discuss the clinical and radiological presentation.

Case report

A 40-year-old woman was admitted for recurrent headaches and fever. Examination was normal except for a minimal notching of the superior part of the right temporal field of vision. Mild anterior pituitary insufficiency, with diabetes insipidus, was found. The white cell count was 10000/mm^3 and the erythrocyte sedimentation rate was raised to 80/1st h. Lumbar puncture showed a white cell count of 2000/mm^3 (98 % neutrophils), protein 1.54 g/l and normal sugar. No organism was demonstrated on microscopy or culture.

CT demonstrated a low density intra- and suprasellar lesion with marked contrast enhancement (Fig. 1 a). T1-weighted MRI demonstrated an oblong suprasellar mass isointense with grey mater reaching up to the optic chiasm, 30 mm in height (Fig. 1 b). The lesion had a central nonenhancing zone and very intense marginal enhancement similar to that of the cavernous sinus. The adjacent

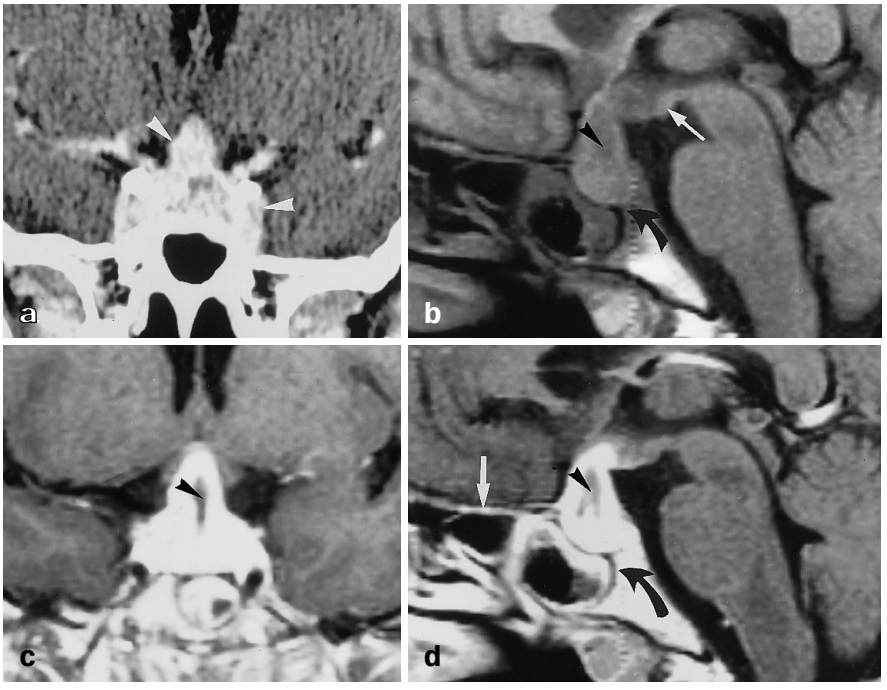

Fig. 1 a–d **a** Contrast-enhanced CT shows an intra- and suprasellar lesion with marked enhancement similar to that of cavernous sinus *(white arrowheads)*. **b** T1-weighted sagittal MRI (450/15) shows an oblong mass, isointense with grey matter, between the optic chiasm and pituitary stalk, abutting the mamillary body *(white arrow)*. Central low-to-intermediate signal *(black arrowhead)*. Absence of normal high signal of pituitary posterior lobe. Note mucosal thickening in the sphenoid sinus and the low signal from sphenoid bone marrow *(curved black arrow)*. **c** Contrast-enhanced image demonstrates intense but heterogeneous *(black arrowhead)* enhancement, stronger than that of the cavernous sinuses. **d** Sagittal contrast-enhanced image shows intense enhancement extending along the infundibulum. Note enhancement of the adjacent dura mater *(white arrow)* and sphenoid bone marrow *(curved black arrow)*, with cystic hypertrophy of the nasopharynx and sphenoid mucosal thickening

dura mater enhanced. Sphenoid mucosal thickening and abnormal sphenoid bone marrow were present.

The patient underwent a trans-sphenoidal procedure. The whole pituitary fossa was occupied by a very firm, whitish mass adherent to the adjacent dura mater. Two fragments were obtained, measuring 1×1 cm and 0.5×0.7 cm. Histopathological examination showed altered pituitary tissue. The normal columnar pattern was disrupted by a major inflammatory infiltrate which also invaded the interstitium. The mononuclear cells were mainly lymphocytes and plasmacytes, mingled with some granulocytes (Fig. 2). In some places there was very marked collagenous fibrillogenesis. There was no vessel-wall damage or necrosis and no foreign-body giant cells were demonstrated. The histological features suggested granulomatous hypophysitis.

The patient was tested for systemic granulomatous disease including tuberculosis, syphilis, histiocytosis X and sarcoidosis, but none of these could be demonstrated. No local infection, osteomeningeal tear, or prior trauma to the skull base was identified from the history. The final diagnosis was idiopathic granulomatous hypophysitis. Rapid complete remission of the visual disturbance occurred. Endocrine follow-up demonstrated worse pituitary function, with hypopituitarism and persistence of polyuria and polydipsia. MRI 1 year later showed no recurrence of the mass.

Discussion

Granulomatous hypophysitis, a chronic inflammatory disease, is rare representing about 1 % of sellar pathology approached via the trans-sphenoidal route. There is no predilection for either sex. The agent responsible for the granulomatous inflammation is unknown [15].

It is thought to be a granulomatous foreign-body reaction to conditions including infection, systemic inflammatory processes and even an adenoma. Rathke's cleft cyst or mucocele [18]. It has been suggested that immunological or mechanical factors play a key role [15]. Some cases show foreign-body giant cells; such cells are demonstrated in some specific inflammatory reactions. Some lesions were considered primary granulomas [13]. In other patients surgical removal of the lesion disclosed isolated histiocytosis X [4] or sarcoidosis [2].

Until recently, granulomatous hypophysitis has been diagnosed on autopsy [15]. During the last 10 years there have been a few reports dealing with one to six patients [8, 9, 13–15, 19]. Cases have been increasingly reported because of neuroradiological advances.

This lesion generally exerts mass effect, causing visual disturbance or headaches and hypopituitarism [20, 21]. Hyperprolactinaemia is an extremely rare manifestation [14, 15, 22]. Granulomatous hypophysitis is sometimes associated with meningitis, as in our case [21]. Although a causal relationship with meningitis was not ascertained, possible exposure of the cerebrospinal fluid to the inflammatory process in the pituitary gland was likely because of the positive pituitary reaction.

Few data on imaging of pituitary granuloma are in the literature (Table 1). It is characterised by sellar mass, mimicking an adenoma and showing variable contrast enhancement. The striking CT features are an intrasellar mass (17 of 19 cases) with cystic areas and ring enhancement (7/19). On MRI (7/19), the lesion is usually isointense with brain on T1-weighted images

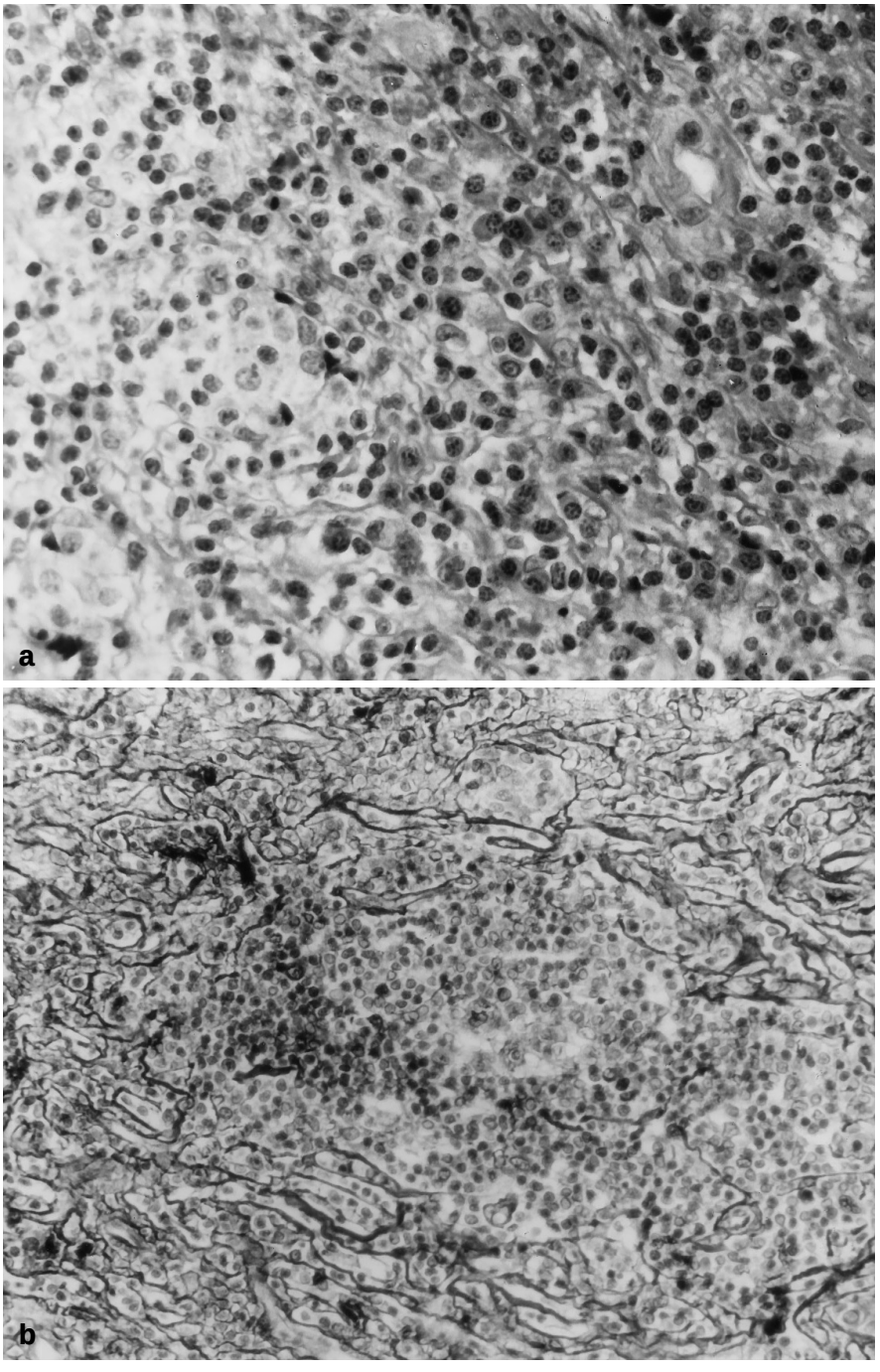

Fig. 2a,b Photomicrograph of the surgical specimen. **a** PAS-orange G stain, original magnification × 250. A mononuclear cell infiltrate, mainly lymphocytes and plasmocytes. **b** Wilder's stain original magnification × 250. Silver impregnation shows the cordonal basal lamina cell around a mononuclear cell granuloma

(4/7), heterogeneous on T2 weighting (2/2). Abnormal thickening of the pituitary stalk and infundibulum were described in 3 of 7 cases. Contrast enhancement is frequently homogeneous (3/7), but cystic areas with ring enhancement may be seen (3/7). Findings suggesting inflammation, such as linear enhancement of the dura mater [23], sphenoid mucosal thickening and adjacent bone marrow abnormality can be observed. However, these findings are nonspecific and quite indistinguishable from other neoplastic or inflammatory hypophysed processes on imaging [24].

The diagnosis can be suggested when a history of sarcoidosis, histiocytosis X, tuberculosis or a meningeal tear is obtained and when hypopituitarism is present.

Lymphocytic adenohypophysis may have similar MRI features. Only the presence or absence of nodular

Table 1 Imaging features of granulomatous hypophysitis

Reference (and number of cases)	Case	Contrast enhancement on CT	MRI
Scanarini et al. [15] (4)	1	Low-density intrasellar lesion with marked ring enhancement	
	2	Low-density lesion with slight ring enhancement	
	3	Slightly enhancing isodense intrasellar mass	
	4	Uniformly enhancing isodense mass	
Oeckler et al. [13] (6)	1–6	Cystic lesions with minor enhancement of the wall	"Semiliquid consistency" on T2 weighting
Pamir et al. [14] (2)	1	Enlarged pituitary gland, with calcification laterally, poorly enhancing	Isointense hypertrophy on T1 weighting; heterogeneous with irregular high signal on T2 weighting
	2	Isodense mass, slight enhancement	
Higuchi et al. [9] (5)	1	Intra- and suprasellar enhancing mass	
	2	Slight enlargement of the sella turcica	Isointense sellar mass on T1-weighted images
	3	Normal	Ring enhancing intrasellar mass
	4	Normal	Contrast-enhanced mass, thickened pituitary stalk and infundibulum
	5	Enlargement of the sella turcica	Isodense mass with thickened pituitary stalk and infundibulum, homogeneously enhancing. Low-intensity area on T2 weighting
This report (1)		Intra- and suprasellar mass with intense enhancement; central low-density area	Isointense mass, low-to-intermediate signal centrally; thickened pituitary stalk and infundibulum; intense, heterogeneous enhancement; dural enhancement

aggregates of epithelioid histiocytes and multinucleate giant cells may distinguish these two rare lesions [24].

In fact, their management is the same.

Biopsy may avoid major resection. A therapeutic trial of corticosteroids can be useful when a pituitary mass suggests the diagnosis. This course of action was successfully followed in a subsequent patient. Regression of the mass may avoid unnecessary surgery. Clinical follow-up, particularly concerning visual disorders, is essential. Biopsy is necessary if a trial of steroid therapy fails. The presence of visual disturbance remains an indication for surgery.

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BOOK REVIEW

Pang, D.: Neurosurgery Clinics of North America: Spinal Dysraphism. Vol. 6, No. 2. Saunders 1995.

This issue of *Neurosurgery Clinics* aims, in the words of guest editor Dachling Pang, to "cover aspects of spinal dysraphism not often discussed". The opening articles provide an up-to-date overview of the epidemiology, aetiology and embryonogenesis of spinal dysraphism, followed by an excellent account of the use of ultrasound in the pre- and postnatal assessment of spina bifida. Following an article defining open myelomeningocoele and its associated anomalies, assessment and treatment from neurophysiological, urological, orthopaedic, and plastic surgical standpoints are described. Then follows a series of comprehensive accounts of other aspects of spinal dysraphism ranging from the relatively common Chiari malformation to rare cervical dysraphic lesions and caudal agenesis. I particularly enjoyed Dias and Pang's paper on split cord malformations which contains a clear explanation of the nomenclature associated with these lesions, and suggests an alternative classification. The authors remind us that CT myelography is the method of choice for complete evaluation of these cases – perhaps our rapidly atrophying myelographic skills can still be put to occasional use! Finally, an article on rehabilitation emphasises the need for a team approach to the management of patients with spinal dysraphism, and provides a reminder of the lifetime of care required by these children and their families.

Overall, the style of the text is clear and concise. The illustrations are of uniformly high standard, but I was a little disappointed in the quality of a few of the MRI reproductions, and found the use of "metrizamide-enhanced CT scans" somewhat dated. Despite these minor criticisms, the issue achieves the editor's stated aims and I would commend it to anyone involved in neuroimaging who wishes for more insight into the clinical problems encountered with spinal dysraphism.

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