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Neuroradiology

Rathke's cleft cyst associated with pituitary granulomatosis with polyangiitis: An unusual combination of hypothalamus-pituitary region pathologies

Riccardo Draghi MD^{a,*}, Giovanna Mantovani MD, PhD^{b,c}, Letterio Runza MD^d,
Giorgio Carrabba MD^e, Nicola Fusco MD^d, Paolo Rampini MD^e, Antonella Costa MD^f,
Marco Locatelli MD, PhD^e

^a Neurosurgery Unit, Department of Medical and Surgical Pathophysiology of Organs and Transplantation, Università degli Studi di Milano, Milan, Italy

^b Endocrinology Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy

^c Department of Clinical Sciences and Community Health, University of Milan, Milan, Italy

^d Division of Pathology, Fondazione IRCCS "Ca' Granda" Ospedale Maggiore Policlinico, Milan, Italy

^e Department of Neurosurgery, Fondazione IRCCS "Ca' Granda" Ospedale Maggiore Policlinico, Milan, Italy

^f Neuroradiology, Fondazione IRCCS "Ca' Granda" Ospedale Maggiore Policlinico, Milan, Italy

ARTICLE INFO

Article history:

Received 22 January 2017

Received in revised form 12

September 2017

Accepted 25 September 2017

Available online 31 October 2017

Keywords:

Rathke's cleft cyst

Granulomatosis with polyangiitis

Pituitary gland

ABSTRACT

The authors present an unusual case of a patient suffering from visual deficit due to pituitary granulomatosis with polyangiitis (GPA) associated with Rathke's cleft cyst (RCC). The patient was referred to our Neurosurgery Department presenting right eye amaurosis, third cranial nerve palsy, and left temporal hemianopsia. Magnetic resonance imaging documented a sellar or suprasellar lesion with solid and cystic components. The dura mater of the skull base was also strongly enhanced. The patient underwent surgery. Histologic examination revealed RCC associated with pituitary GPA. To our knowledge, this is the first reported case of concomitant pituitary GPA and RCC. Pituitary involvement in GPA is rare, usually diagnosed in hormonal dysfunctions. The patient in case first presented optic chiasm compression, probably due to inflammation of both the pituitary gland and the previously asymptomatic RCC. We focus on the symptoms that led us to diagnose GPA pituitary involvement and on the peculiar and unusual Magnetic resonance imaging of the case presented.

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* Corresponding author.

E-mail address: riccardo.draghi@gmail.com (R. Draghi).

<https://doi.org/10.1016/j.radcr.2017.09.018>

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Case report

In September 2012, a 48-year-old woman started complaining of headache associated with central scotoma in her right eye. Ophthalmological assessment documented right papilloedema. Her general physician ordered a magnetic resonance imaging (MRI) of brain and corticosteroid therapy. Her vision recovered after a few days.

Brain MRI documented a sellar or suprasellar lesion causing compression of the optic chiasm. The lesion was round and showed solid and cystic components. Its solid part (inferior and anterior sellar contents) was enhanced after gadolinium injection, whereas its posterior part contained fluid (isointense). The medial dura lining of the right cavernous sinus was thick-

ened and clearly enhanced. The pituitary stalk was swollen and enhanced, whereas gadolinium staining of the gland was irregular and faint (Fig. 2A, arrow). The sphenoid sinus showed no pneumatization (conchal variant according to Hamberger's classification [1]). The dura mater of the sphenoid-ethmoidal plate, diaphragma sellae, clivus, and mesial part of both middle cranial fossas was strongly enhanced after gadolinium injection. Bilateral upper pharynx mucosa was also enhanced (Figs. 1 and 2). Panhypopituitarism was established after basal hormonal evaluation.

A few weeks later, the patient developed right eye amaurosis, diplopia, right eyelid ptosis, and visual field loss, and was admitted to the Neurosurgical Unit. Neurologic examination revealed right third nerve palsy, right eye amaurosis, and left temporal hemianopia. The patient underwent surgery using an

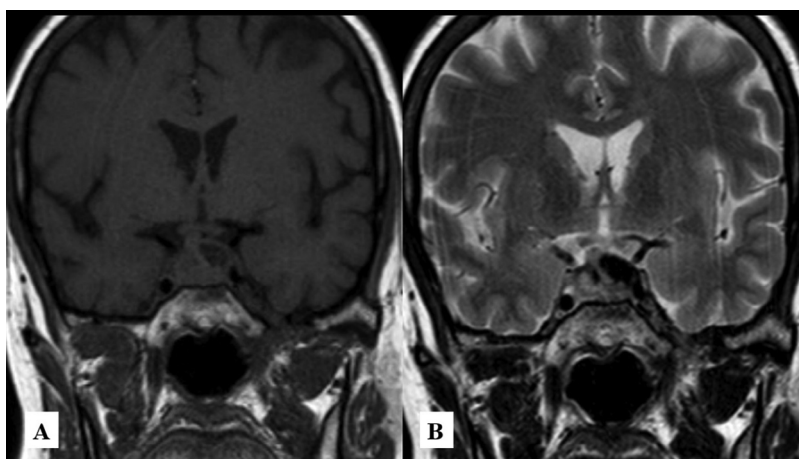


Fig. 1 – (A) Magnetic resonance imaging (MRI) T1 coronal section documenting the sellar or suprasellar lesion. The cystic fluid component was hypointense, whereas the solid part, the pituitary stalk, and gland were isointense to gray matter. (B) MRI T2 coronal section revealing the strongly hypointense fluid contents of the lesion.

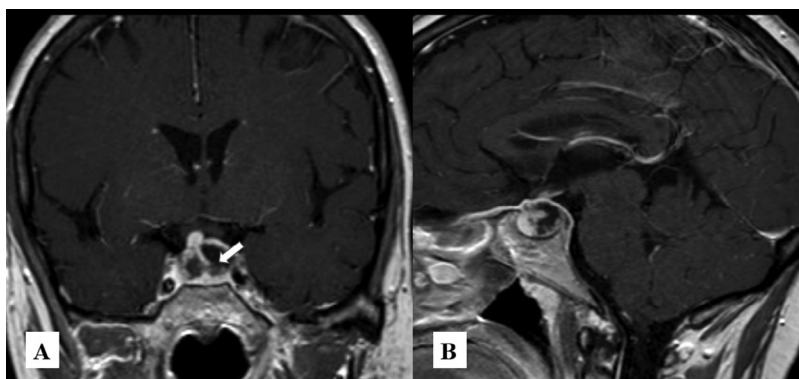


Fig. 2 – (A) Magnetic resonance imaging (MRI) T1 coronal section after gadolinium injection showing a sellar or suprasellar lesion with solid and cystic components. The pituitary stalk was swollen and enhanced, whereas the gland was not enlarged; gland staining after gadolinium injection was faint and inhomogeneous (arrow), both atypical features of hypophysitis. (B) MRI T1 sagittal section after gadolinium injection. The sphenoid sinus showed no pneumatization (conchal variant). The solid part of the lesion was clearly enhanced (inferior and anterior sellar contents) whereas its posterior part confirmed its fluid content (isointense). Intense enhancement involved the dura mater of planum sphenoidale, diaphragma sellae, clivus and the mucosa of upper pharynx too. The lesion did not present typical MRI features of RCC (hyperintensity in T2 sequences, intracystic enhanced nodule and “claw-sign”) or of hypophysitis—except for enhancement of the stalk—since the gland was not enlarged and its contrast enhancement was slight/faint.

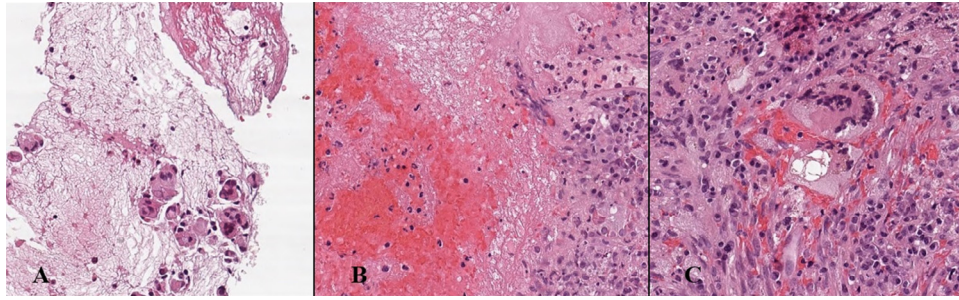


Fig. 3 – Rathke's cleft cyst with associated pituitary granulomatosis with polyangiitis (GPA). Cystic amorphous and corneum-like material with multiple thin fragments of cystic wall with pseudo-stratified columnar ciliated epithelial cells (A, original magnification 5×) in the proximity of lymphocyte and monocyte infiltration involving the pituitary gland with associated hemorrhagic necrosis (B, original magnification 5×). (C) On close examination, chronic-aspecific granulomatous flogosis is evident (various poorly formed granulomas with minimal lymphocytes, multinucleated giant cells, with no significant lymphoid infiltrates) with amorphous whitish oil-like material, consistent with chronic xanthogranulomatous inflammation which almost invariably accompanies GPA (original magnification 20×).

endoscopic trans-sphenoidal approach to reduce the mass effect on the optic chiasm and obtain a histologic diagnosis. After surgery, the patient's left eye vision improved. The third nerve did not recover. Histologic findings confirmed Rathke's cleft cyst (RCC) associated with acute and chronic (xanthogranulomatous) inflammation, consistent with pituitary and sellar granulomatosis with polyangiitis (GPA) (Fig. 3). Postoperative endocrinological evaluations confirmed panhypopituitarism; thus, the patient was transferred to the Department of Internal Medicine. GPA was found to involve the lungs, the patient's right eye, and nasal sinuses. Rituximab was administered, which reduced the intracranial lesion and dural inflammation. The patient's visual field and oculomotor nerve palsy showed no further improvement. Pituitary function had not recovered at 2-year follow-up.

Discussion

RCC is an epithelium-lined cyst developing from the remnant cells of the Rathke's cleft, the pouch resulting from the embryological union of the anterior and posterior parts of the pituitary gland. RCCs are relatively common (13%-33% prevalence at autopsy) and are often detected on imaging as incidental findings, causing no clinical disturbance. In some cases, the cyst grows, creating a mass effect on the surrounding pituitary and neurovascular structures, requiring neurosurgical treatment. RCC accounts for less than 1% of all primary intracranial space-occupying lesions [2–4].

GPA is a systemic disease characterized by necrotizing small-vessel vasculitis of unknown etiology, often associated with antineutrophil cytoplasmic antibodies. It is a rare disease whose incidence is 10 cases per million inhabitants per year [5,6]. Although the disease can potentially involve any organ or tissue, it mostly targets the respiratory tract, kidney, and ear, nose, and throat (ENT). The nervous system is involved in 22%-54% of cases [7], but GPA is far more likely to affect peripheral and cranial nerves. Central nervous system involvement occurs in less than 10% of patients [8,9]. To date, 51 cases of pituitary involvement in GPA have been reported in the literature.

The estimated incidence of pituitary gland involvement in GPA patients is 1.1% [9]. GPA hypophysitis is usually associated with pituitary secretion deficit (PD), which can affect both anterior and posterior hormones. Hormonal deficits can be transient or permanent, according to the degree of injury of the pituitary gland parenchyma.

Therefore, the clinical presentation of pituitary GPA is usually a deficiency in the secretion of pituitary hormones. The French Vasculitis Study Group documented that only 9 of the 51 cases (17.6%) with pituitary GPA reported in the literature experienced vision loss due to compression of the optic chiasm [9]. Hence, visual deficits related to GPA pituitary involvement are quite uncommon. The small incidence of this neurologic deficit in these patients may be due to the following hypothesis. The pituitary inflammatory process needs to be associated with marked swelling of the gland; otherwise, direct compression of the optic pathways would not occur.

Visual field deficit in GPA is usually associated with a secretory disorder of the gland, which remains the main clinical abnormality and presenting symptom of this condition. In the case described, the first symptom was a visual deficit due to optic chiasm compression, not pituitary hormone deficiency. The patient also had a histologically demonstrated RCC, leading us to hypothesize that this unusual and significant mass effect resulted from an inflammatory process involving not only the hypophysis but also the Rathke cyst, thus increasing the mass effect on the optic chiasm.

Right third nerve palsy was probably due to the extension of the inflammatory process into the cavernous sinus. Indeed, in some cases, GPA can be seen to extend into this venous structure, leading to cranial nerve dysfunction or inflammation of the internal carotid artery (ICA) [10]. ICA wall inflammation can lead to vessel occlusion and ischemic stroke. In our case study, the right cavernous sinus was clearly involved, as confirmed by gadolinium staining of its medial wall (Fig. 2A). Although this process was not so widespread as to affect the ICA, cavernous dural inflammation most likely determined oculomotor nerve palsy. This finding is extremely rare in pituitary GPA and has been reported in just one case to date [9].

The other distinctive feature of this case is the widely diffuse skull base dura mater enhancement, which is rarely reported in the literature describing pituitary GPA [9,11,12]. The nearly continuous enhancement from the upper pharyngeal mucosa to the olfactory groove dura involving also the middle skull base could suggest the primary source of pituitary GPA (Fig. 2B). Several mechanisms have been suggested that may explain pituitary involvement in GPA, such as vasculitis, granuloma formation in the hypophysis, and the spreading of the granulomatous process from contiguous sites (eye, ENT). The latter mechanism appears to be the most frequent in the findings of the French Vasculitis Study Group [9]. In our case, pituitary GPA involvement seems to be related to diffusion from a contiguous site (in this particular case from the ENT), given the nearly continuous enhancement from the upper pharyngeal mucosa to the olfactory groove dura mater including the middle skull base. This particular MRI feature of intracranial GPA has been reported in only 3 cases to date [9,11,12].

From a review of the literature, pituitary GPA MRI features seem to be extremely variable. In fact, the gland can display characteristic features of hypophysitis (diffuse gland enlargement exhibiting homogeneous enhancement) or inhomogeneous enhancement, with an iso- or hyperintense solid mass with hypointense cystic components associated with hyperintense peripheral ring enhancement after gadolinium injection. The inconsistency of the MRI findings may be accounted for by the different stages of inflammatory processes occurring in the pituitary gland. The only consistent feature would appear to be the marked thickening of the stalk, clearly enhanced after contrast medium infusion.

Despite radiological improvement after rituximab therapy, the patient did not recover pituitary function, probably due to gland tissue destruction. In fact, according to De Parisot's review of the literature, PD occurs in 80% of GPA patients (88% in their study population) and resolution of hormonal deficits does not correlate directly with imaging findings. A review of the literature carried out by the French Vasculitis Study Group [9] demonstrated that the majority of patients with persistent pituitary dysfunction showed a partial or total resolution of intracranial abnormalities in MRI studies.

In summary, the authors wish to present a case of concomitant GPA and RCC and its atypical clinical presentation. The distinctive imaging feature in this case was the widely diffused enhancement of the skull base dura mater (rarely reported in the literature in pituitary GPA [9,11,12]), which points the primary source of GPA dissemination to the pituitary (Fig. 2). Even though it is a rare entity, pituitary GPA should be con-

sidered in differential diagnosis in patients with sellar lesions associated with PD and strong diffuse skull base dura enhancement, especially with concomitant signs of ENT inflammation.

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