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Outcome of diabetes insipidus in patients with Rathke's cleft cysts

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ABSTRACT

Objectives: It is well-known that Rathke's cleft cysts (RCCs) infrequently cause headache, endocrinological dysfunction, and visual disturbance, and in rare cases, cause diabetes insipidus (DI). Although surgical evacuation of the cyst content can result in high rates of symptomatic improvement, not only the treatment efficacy but also the pathophysiology of DI with RCC are undetermined. The aim of this study is to elucidate the underlying mechanisms and outcomes of DI associated with RCCs.

Patients and Methods: We retrospectively studied 109 patients with RCCs treated at Kanazawa University Hospital between 2000 and 2016. Their age, sex, symptoms, endocrinological status, DI, visual disturbance, neuroradiological findings, pathological appearances, and pre-/post-operative hormone levels and status of antidiuretic hormone replacements were assessed.

Results: Among 109 cases of RCCs, five cases (4.6%, 2 males and 3 females) manifested with DI as initial presentation were included. These five cases could be divided into two types: the acute type and the chronic type, based on the onset and duration of symptoms. Three acute onset cases presented with not only strong thirst but also sudden headaches without pituitary dysfunction, whereas the two chronic onset cases presented with chronic headaches and hypopituitarism. Pathological examination in the acute type revealed inflammatory cell infiltration into only the posterior lobe of the pituitary and disruption of the cyst wall adjacent to the posterior lobe, which might suggest RCC rupture. In contrast, the chronic type showed inflammatory cell infiltration into both the anterior and posterior lobes of the pituitary and thickened fibrosis beneath the cyst wall. Postoperatively, two cases of the acute type could be controlled with a smaller amount of 1-deamino-8-D-arginine vasopressin (DDAVP) than that required preoperatively, whereas no change was observed in the cases of the chronic type.

Conclusion: The cases of DI onset caused by RCCs could be divided into the acute type and the chronic type. In the chronic type, surgical treatment could not affect the status of DI. However, in acute type, urgent surgical intervention partially relieved DI.

1. Introduction

Rathke's cleft cysts (RCCs) are benign cystic lesions of the sellar and suprasellar regions and originate from the remnants of the embryonic Rathke's pouch. In routine autopsies, they are encountered in 3.7–22% of normal pituitary glands [1–4]. RCCs are usually asymptomatic, but they can be infrequently symptomatic [5–10]. The typical symptoms include headache, visual disturbance, and hypopituitarism, and less commonly, diabetes insipidus (DI) that is observed in up to 21% of patients with RCCs [5,9,11–16]. Since symptoms of RCCs are reported to be caused by the effect of their mass, rupture of the cyst, or inflammation spreading to the surrounding pituitary gland, they are managed by surgical evacuation of cyst contents, which can eliminate the effect of the mass or prevent the spread of inflammation. Surgical treatment can resolve headache, visual disturbances, and sometimes endocrine dysfunction, but DI generally persists postoperatively [2,8,10,11,15,17–21]. The underlying mechanism and outcome of DI in patients with RCCs remain unclear. The purpose of this study was to elucidate the clinical and pathological characteristics of RCCs accompanied by DI.

Abbreviations: ACTH, adrenocorticotropic hormone; DDAVP, 1-deamino-8-D-arginine vasopressin; DI, diabetes insipidus; FSH, follicle stimulating hormone; GH, growth hormone; GnRH, gonadotropin-releasing hormone; IGF-1, insulin-like growth factor-1; LH, luteinizing hormone; MR, magnetic resonance; PRL, prolactin; RCCs, Rathke's cleft cysts; TRH, thyrotropin-releasing hormone; TSH, thyroid-stimulating hormone; TSS, transsphenoidal surgery

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Table 1
Summary of the five cases of Rathke's cleft cysts with diabetes insipidus.

Case number	Age (years)/ Sex	Type of DI at onset	Duration of DI	Associated symptom	Pituitary dysfunction	Visual disturbance	T1WI hyperintensity area of posterior lobe	Location	Cyst intensity on T1WI	Cyst intensity on T2WI	Operation	Histopathology	Endocrinological outcome
1	67/F	acute	2 months	sudden headache	–	–	–	sellar	hyper	hyper	+	RCC lined by a single columnar ciliated epithelium, lymphocytic infundibulo-neurohypophysitis	DDAVP
2	55/M	acute	1.5 months	sudden headache	–	–	–	sellar	iso	hyper	+	RCC lined by a single columnar ciliated epithelium, lymphocytic infundibulo-neurohypophysitis	DDAVP
3	47/F	acute	30 years	sudden headache	–	–	–	sellar	hyper	hyper	–	–	DDAVP
4	63/F	chronic	2 years	fatigue	hypopituitarism	+	–	sellar~supra-sellar	iso	hyper	+	RCC lined by a thickened columnar epithelium, squamous metaplasia, lymphocytic infundibulo-panhypophysitis, thickened fibrosis	DDAVP, hydrocortisone, levothyroxine
5	8/M	chronic	4 months	–	hypopituitarism	–	–	sellar~supra-sellar	hyper	iso	+	RCC lined by a thickened columnar epithelium, squamous metaplasia, lymphocytic infundibulo-panhypophysitis, thickened fibrosis	DDAVP, hydrocortisone, levothyroxine

DI: diabetes insipidus, WI: weighted image, DDAVP: 1-deamino-8-D-arginine vasopressin.

2. Patients and methods

2.1. Characteristics of patients

This study was approved by the Kanazawa University Institutional Review Board. We retrospectively studied 109 patients who were diagnosed with RCCs based on magnetic resonance (MR) images, or intraoperative and pathological findings, between 2000 and 2016 in our institute. Among them, 60 patients were diagnosed using surgical specimens and the other 49 patients were diagnosed using MR imaging findings alone. Among the 109 patients, this study included five patients who manifested with DI at onset. Four patients, who underwent transsphenoidal surgery (TSS), were diagnosed using histological findings. Patient demographics, including age, sex, symptoms, endocrinological abnormalities, DI, visual disturbance, MR imaging findings, pathological remarks, pre- and post-operative hormone and anti-diuretic hormone replacements were obtained from their clinical records.

2.2. Endocrinological evaluation

An endocrinological study was performed pre- and post-operatively. This included tests for levels of plasma growth hormone (GH), insulin-like growth factor-1 (IGF-1), prolactin (PRL), adrenocorticotropic hormone (ACTH), cortisol, thyroid-stimulating hormone (TSH), triiodothyronine, thyroxin, luteinizing hormone (LH), and follicle stimulating hormone (FSH). Postoperatively, a combined test for anterior pituitary function [insulin, thyrotropin-releasing hormone (TRH) and gonadotropin-releasing hormone (GnRH) loading test] was performed.

2.3. Diabetes insipidus

If patients' complaints concerning polydipsia and polyuria were confirmed, and the excretion of over 2500 ml of urine within 24 h having a specific gravity of less than 1.005 g/l was observed, a diagnosis of central-type DI was made [22]. For determining the final diagnosis of DI, endocrinologists confirmed low levels of urine osmolality that did not increase with hypertonic saline loading. 1-deamino-8-D-arginine vasopressin (DDAVP) was used for the control of DI in the hospital and after discharge.

2.4. Radiological evaluation

RCCs were confirmed with MR images by at least two neurosurgeons (M.O., Y.H.). MR images were obtained using a Signa HDx 3T (GE Medical Systems, Milwaukee, WI). Radiologic evaluation involved location, signal intensities of cyst contents in both T1WI and T2WI, and areas of hyperintensity in the pituitary stalk and posterior lobe on T1WI. Contrast enhancement with gadolinium administration in T1WI was used for evaluating the cyst wall of the RCCs and the normal pituitary gland.

2.5. Surgical procedures

TSS for RCCs was performed in appropriate patients who had visual field abnormality, pituitary dysfunction, severe headaches that were not controlled with painkillers, and daily-life disruption owing to these symptoms. Patients without any symptoms and those who only developed DI did not require surgical management. Our surgical strategy was to remove the cyst wall partially and evacuate the cyst content completely with an endoscope, as described previously [23]. In brief, our aim during surgical procedures was to make minimal and accurate incisions of both the inferior aspect, and the thinnest part of the cyst wall detected on the sagittal section on T1WI with contrast enhancement. After incision of the cyst wall, the cyst content was drained out sufficiently and the cyst wall was resected partially for pathological