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Source: Journal of Feline Medicine and Surgery Open Reports, 6(2)

Published By: SAGE Publishing

URL: <https://doi.org/10.1177/2055116920935017>

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# A case of central diabetes insipidus associated with a congenital cyst of the sella turcica in a young cat

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*Journal of Feline Medicine and Surgery Open Reports*  
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DOI: 10.1177/2055116920935017  
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This paper was handled and processed by the European Editorial Office (ISFM) for publication in *JFMS Open Reports*



## Abstract

**Case summary** A 1-year-old neutered male domestic shorthair cat was presented for polyuria and polydipsia which had progressed since adoption, 7 months previously. On admission, clinical examination did not reveal any remarkable features. Urinalysis showed marked hyposthenuria and calculated plasma osmolality was high, suggesting diabetes insipidus. A positive response to desmopressin administration appeared to confirm pituitary dysfunction. Brain MRI revealed a lesion compatible with a cyst or a neoplasm compressing the pituitary gland. A follow-up MRI performed 9 months later showed that the lesion was stable, which at first argued in favour of a congenital pituitary cyst. Intranasal administration of desmopressin was then used to achieve a long-term clinical response.

**Relevance and novel information** Central diabetes insipidus (CDI) is a rare cause of polyuria and polydipsia in cats, resulting from inadequate or impaired secretion of antidiuretic hormone from the posterior pituitary gland. Recognised causes include head trauma, central nervous system (CNS) neoplasia, idiopathic CDI and congenital pituitary cysts. Apart from one cat with CNS lymphoma, the few previously reported feline cases have described CDI in young cats with a previous history of trauma, but brain imaging has rarely been performed to look for underlying anatomical abnormalities. This report describes the first case of CDI in a cat with a confirmed congenital pituitary cyst and, as in previous cases, demonstrates successful treatment with desmopressin.

**Keywords:** Polyuria; polydipsia; central diabetes insipidus; plasma osmolality; Rathke's cleft cyst; pituitary congenital cyst; sellar cyst

**Accepted:** 26 May 2020

## Introduction

Diabetes insipidus (DI) is an uncommon cause of polyuria and polydipsia in cats. The disease is caused by decreased production of arginine vasopressin (AVP) by the pituitary gland (central DI [CDI]) or renal insensitivity to this hormone (nephrogenic DI; NDI). Idiopathic CDI can occur in young cats, but post-traumatic and congenital causes have also been described.<sup>1–11</sup> Here, a case of CDI associated with a presumptive congenital pituitary cyst is reported.

## Case description

A 1-year-old neutered male domestic shorthair cat presented with polyuria and polydipsia (PU/PD). Water intake was estimated at 170 ml/kg/day since its adoption 7 months before presentation. The previous

owners reported that the cat had fallen from a high window at 2 months of age but that it had recovered uneventfully. The cat had received vaccinations for feline viral rhinotracheitis, calicivirus and panleukopenia, and had received praziquantel and milbemycin for

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**Table 1** Plasma biochemistry and urinalysis

| Parameters  | Before treatment  |   | After treatment   |   | RI         |
|---|---|---|---|---|------------|
|   | Day -15   | Day 0   | Day 15  | Day 365   |            |
| BUN (mmol/l)  | 13.3<br>(37.3 mg/dl)  | 11.6<br>(32.54 mg/dl)   | NA  | NA  | 3.3–9.9    |
| Creatinine (µmol/l)   | 114   | 114   | NA  | NA  | 109        |
| SDMA (µmol/l)   | 0.11  | NA  | NA  | NA  | <0.12      |
| Total protein (g/l)   | 85  | 82  | NA  | NA  | 60–80      |
| PCV (%)   | 50  | 47  | NA  | NA  | 25–45      |
| Sodium (mmol/l)   | 162<br>(162 mEq/l)  | 163<br>(163 mEq/l)  | NA  | NA  | 145–160    |
| Potassium (mmol/l)  | 3.3   | 3.4   | NA  | NA  | 3.8–5.2    |
| Glucose (mmol/l)  | 7.15<br>(128.8 mg/dl)   | 6.05<br>(109 mg/dl)   | NA  | NA  | 3.3–6.1    |
| Total calcium (g/l)   | 1.25  | NA  | NA  | NA  | 1.15–1.37  |
| Calculated serum osmolality<br>= 2 × (natraemia [mEq/l]) +<br>(glycaemia [mg/dl]/18) +<br>(BUN [mg/dl]/2.8) (mOsm/kg) | 344.4   | 343.6   | NA  | NA  | 280–300    |
| USG   | 1.004   | 1.005   | 1.018   | 1.020   | >1.035     |
| Urinalysis<br>(pH, dipstick and sediment<br>analysis)   | pH 7,<br>dipstick and<br>sediment<br>analysis<br>unremarkable | pH 7,<br>dipstick and<br>sediment<br>analysis<br>unremarkable | pH 7,<br>dipstick and<br>sediment<br>analysis<br>unremarkable | pH 7,<br>dipstick and<br>sediment<br>analysis<br>unremarkable | pH 5.5–7.5 |
| Urine culture   | Negative  | NA  | NA  | NA  | –          |

RI = reference interval; BUN = blood urea nitrogen; NA = not available; SDMA = symmetric dimethyl arginine; PCV = packed cell volume; USG = urine specific gravity

endoparasite infection prophylaxis. The physical examination revealed no abnormalities; body condition and hydration status were normal.

Urinalysis and plasma biochemical findings are detailed in Table 1. Urinalysis showed hyposthenuria (urine specific gravity [USG] between 1.004 and 1.005 on two separate days) without any other abnormalities. Mild increases in urea and total protein concentration were present and compatible with slight dehydration. The symmetric dimethyl arginine measurement was within the normal range. The serum electrolyte panel revealed mild hypernatraemia and hypokalaemia. Calculated plasma osmolality was high on day 1 (344.4 mOsm/kg; reference interval [RI] 280–300 mOsm/kg) and on day 15 (343.4 mOsm/kg). When combined with the concomitant hyposthenuria, these findings were suggestive of DI.

An abdominal ultrasound showed mild bilateral pyelectasia (right kidney pelvis 2.2 mm, left kidney pelvis 5 mm) without signs of ureteral obstruction, and was compatible with severe polyuria.

A therapeutic trial with intranasal drops of desmopressin (Minirin; Ferring) was prescribed (one drop in one eye q12h). After administration of desmopressin, water intake reduced significantly to 120 ml/kg/day,

and repeated USG measurements showed an increase in the isosthenuric range (USG 1.015). The response to desmopressin treatment was consistent with CDI.

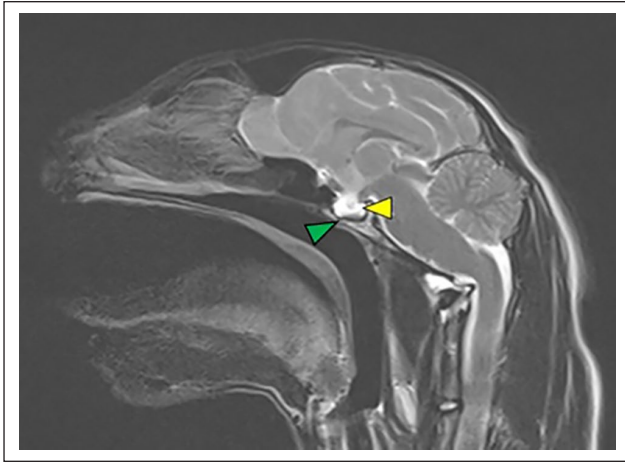
To investigate the aetiology, a brain MRI scan was performed (Figures 1 and 2). Examination of the images revealed fluid collection in the sella turcica, compressing the pituitary gland. These features suggested a congenital pituitary cyst or craniopharyngioma. The lesion location made the possibility of congenital epidermoid, dermoid and arachnoid cysts less likely. Cystic pituitary adenoma was not included in the differential diagnosis, given the age of the cat.

A follow-up brain MRI was performed 9 months later and the lesion was found to be stable. Because it is a rapidly growing tumour, craniopharyngioma was ruled out. The final diagnosis was a congenital pituitary cyst.

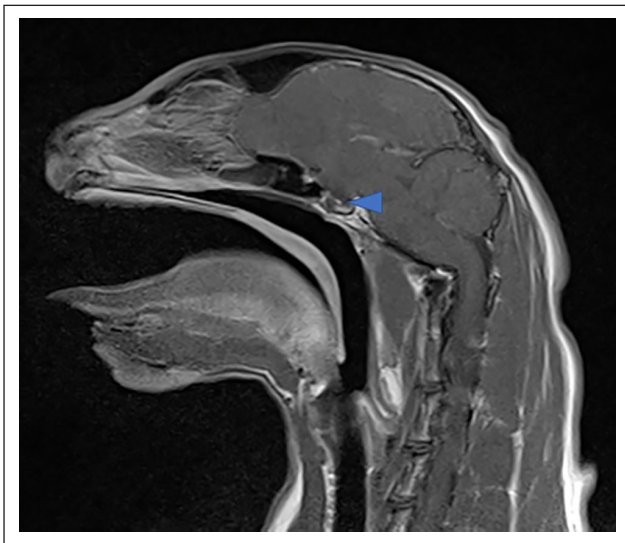
Desmopressin treatment was maintained over the long term. One year after diagnosis, water intake was found to be about 125 ml/kg/day and the USG increased to 1.018.

## Discussion

CDI is a condition that is rarely reported in cats. Thus far, there have been 12 single case reports and one case



**Figure 1** Brain MRI (T2-weighted sagittal plane MRI scan). An abnormal spontaneous hyperintense signal is observed in the hypophyseal area (yellow arrowhead). Deformation of the sella turcica is present and the sphenoid bone is thin (green arrowhead). The appearance is compatible with a fluid-filled lesion deforming the sella turcica and compressing the pituitary gland



**Figure 2** Brain MRI (T1-weighted sagittal post-contrast plane MRI scan). The hypophyseal area presents a heterogeneous signal (blue arrowhead). A fluid-filled lesion is suggested by a focal area of hypointensity, which is compressing the hyperintense pituitary tissue against the ventral sella turcica. The pituitary stalk also shows a hyperintense signal

series involving five cats.<sup>1–13</sup> CDI is the result of a complete or partial lack of AVP secretion by the hypophysis. No gender or breed predispositions have been reported. Pituitary congenital anomalies are more prevalent in young animals, while pituitary neoplasia is more frequent in older cats.<sup>2,3,11</sup> Post-traumatic, iatrogenic (surgery) and idiopathic CDI have been reported in cats of all ages.<sup>1,5,6,8</sup> In these cases, the main clinical

signs were PU/PD. Physical examination is often unremarkable on admission, but clinical signs indicating the cause (amaurosis, circling) or intracellular dehydration (decreased consciousness, coma) may be present. In dogs, transient PU/PD has commonly been described after traumatic head injury and may be explained by neuronal regeneration in the infundibular stalk.<sup>14</sup> In the cat studied here, a history of a fall from a high window was reported at 2 months of age. The relationship between the traumatic event and DI cannot be ruled out, but it seems unlikely when faced with the sellar cystic lesion observed during MRI.

An exhaustive work-up to rule out pyelonephritis, hypercalcaemia, congenital hepatic disease (storage or vascular disorder), electrolyte disorder (hyponatraemia and hypokalaemia) and/or erythrocytosis is mandatory before diagnosing CDI in a young animal. According to the published literature,<sup>14</sup> a modified water deprivation test is the gold standard for differentiating psychogenic polydipsia, central DI and nephrogenic DI. An unfortunate fallout of this test is that it may lead to hypertonic dehydration, making it particularly hazardous. A water deprivation test was therefore not performed in this patient. Instead, repeated calculations of plasma osmolality followed by evaluation of the response to trial therapy with desmopressin were used to guide our diagnosis. Measurements of random plasma osmolality could help to differentiate between DI and psychogenic polydipsia. DI is a primary polyuric disorder leading to decreased blood volume and increased serum osmolality, while psychogenic polydipsia results in increased blood volume, in turn leading to compensatory polyuria. In the latter scenario, serum osmolality is theoretically decreased.

Because desmopressin is a specific treatment for CDI, trial therapy is an interesting approach to investigate such a disease. Ideally, in cats with CDI, a decrease in water intake should occur after 5–7 days of therapy. This is followed by an increase in USG by 50% or more as measured on the last couple of days of trial therapy. In contrast, there would be minimal improvement in cats with NDI or psychogenic polydipsia.<sup>14</sup> In the cat studied here, the high plasma osmolality observed without water deprivation favoured a DI diagnosis. Following this observation, a 15-day therapeutic trial with desmopressin was performed, leading to a decrease in water intake and an increase in USG from 1.005 to 1.018, thus supporting the CDI hypothesis.

The identification of CDI in a young animal raised questions about the presence of a visible congenital pituitary anomaly and congenital nearby compressing structure. A brain MRI showed a large fluid lesion localised in the sella turcica.

Differential diagnoses include congenital pituitary cysts, dermoid and epidermoid cysts, subarachnoid diverticulum and craniopharyngioma.<sup>15–17</sup>

Pituitary cysts are caused by differentiation or obliteration failures of the neural tube during fetal development. The hypophysis derives from a dorsal evagination of the oropharyngeal ectoderm named Rathke's pouch and the diverticula of a second neural tube, the infundibulum. Rathke's pouch increases the craniopharyngeal duct, followed by the pars tuberalis, pars distalis and the posterior wall of the pars intermedia. A failure of the ectoderm of Rathke's pouch to differentiate into secreting cells of the pars distalis results in persistence of the residual lumen of the pouch, thus becoming a cyst in the sella turcica. The cyst is lined by pseudostratified epithelium composed of mucin-secreting goblet cells, and ciliated and columnar cells. Another type of pituitary cyst is derived from remnants of the distal craniopharyngeal duct, which normally disappears by the time of birth in most species. This type of cyst is encountered in many species, especially in canine brachycephalic breeds. These lesions are often found at the periphery of the pars tuberalis and pars distalis.<sup>15,18</sup>

The location of the lesion in the present case points to a cyst resulting from failure of differentiation of Rathke's pouch ectoderm (Rathke's cleft cyst). This congenital abnormality is well described and quite frequent in dogs and people; a necropsy series reported its presence in 13–22% of humans without related clinical signs.<sup>15,19</sup> In humans, Rathke's cleft cysts are mainly asymptomatic, although they are occasionally responsible for headaches, vision disorders or pituitary dysfunction.<sup>20,21</sup> In dogs, it might be associated with pituitary dwarfism, especially in German Shepherds.<sup>14</sup> There has been one reported case of clinical manifestation of a Rathke's cleft cyst in a feline patient, which was in an 11-year-old spayed cat and was associated with a syndrome of inappropriate antidiuretic hormone secretion.<sup>22</sup>

The long-term outcomes of pituitary cysts are unknown. Cases of enlarging Rathke's cleft cysts have been reported in children,<sup>23</sup> but a reduction in size has also been described in the context of suspected rupture of the cyst.<sup>24</sup>

Dermoid and epidermoid cysts are rare and probably result from inclusions of epithelial elements within the neural groove at the period of its closure.<sup>15</sup> In humans, epidermoid and dermoid cysts can occur in the suprasellar and the parapituitary region.<sup>25</sup> In dogs and cats, epidermoid cysts in the brain are located in the fourth ventricle, and dermoid cysts have mostly been described in the lumbosacral area.<sup>26</sup> Subarachnoid diverticula have also been described in small and brachycephalic breeds of dogs and young Persian cats. Intracranial diverticula have been predominantly described in the quadrigeminal cistern and cerebromedullary angle.<sup>15,27</sup> Growing arachnoid cysts have also been described in dogs.<sup>17</sup> A dermoid cyst, epidermoid cyst and subarachnoid diverticula were therefore ruled out because the lesion location/MRI appearance was not consistent with these diagnoses.

Craniopharyngioma is a neoplastic process present in either a suprasellar or infrasellar location. It is thought to arise either from Rathke's pouch or Rathke's cleft cyst. As it is usually reported in adult cats<sup>28</sup> and is expected to be progressive, this diagnosis was excluded.

In the present case, the lesion location as revealed by MRI examination is strongly indicative of a pituitary cleft cyst, and specifically of a Rathke's cleft cyst. However, image findings are extremely variable, depending heavily on the cyst content. All fluid lesions and some neoplasms could exhibit similar MRI appearances and the only way to determine the nature of the abnormality is through histology. In humans, the diagnosis of Rathke's cleft cysts is challenging. Nevertheless, MRI diagnostic tree models have been determined and relatively specific imaging criteria have been identified.<sup>29</sup>

Desmopressin is the standard therapy for CDI. This synthetic analogue is three times as potent as AVP, with fewer side effects. The ocular route is effective for the treatment of CDI in cats. One or two drops administered once or twice daily controls the clinical signs of CDI in most cats.<sup>30</sup> Nasal administration is also possible but is not recommended. In France, there is currently no once-a-day intranasal formulation of this drug available. An oral route of administration is also available, but its bioavailability is very low. The frequency of administration should be adjusted according to clinical signs. Using injectable solution or previously sterilised nasal form, subcutaneous injection is also described.<sup>31</sup> Other agents, such as chlorpropamide or thiazide diuretics used in humans and dogs, have shown no established effects in cats.<sup>31</sup>

If owners elect not to treat their pets, they should ensure that their animals have continuous access to water to avoid the severe consequences of hypertonic dehydration described above. Restricting salt intake as the sole therapy of DI reduces urine output by increasing the volume of filtrate absorbed isosmotically in the proximal nephron. This singular method of therapy may be helpful in the treatment of both CDI and NDI.

## Conclusions

This is the first report of a congenital pituitary cyst associated with CDI in cats. Although rare in occurrence, these cysts should be included as a differential diagnosis in young cats with signs of pituitary dysfunction. Given a lack of specific criteria to differentiate cystic lesions and neoplasms, follow-up imaging is recommended to rule out neoplasms.

**Acknowledgements** The authors wish to thank the owner, staff and students involved in the care of this patient.

**Conflict of interest** The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

**Funding** The authors received no financial support for the research, authorship, and/or publication of this article.

**Ethical approval** This work involved the use of non-experimental animals only (including owned or unowned animals and data from prospective or retrospective studies). Established internationally recognised high standards ('best practice') of individual veterinary clinical patient care were followed. Ethical approval from a committee was therefore not necessarily required.

**Informed consent** Informed consent (either verbal or written) was obtained from the owner or legal custodian of all animal(s) described in this work (either experimental or non-experimental animals) for the procedure(s) undertaken (either prospective or retrospective studies). For any animals or humans individually identifiable within this publication, informed consent (either verbal or written) for their use in the publication was obtained from the people involved.

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