

NOTE *Internal Medicine***Pituitary Chromophobe Carcinoma with a Low Level of Serum Gonadotropin and an Aspermatogenesis in a Dog**Jun SATO¹⁾, Reeko SATO¹⁾, Mitsuru KINAI²⁾, Nobuyuki TOMIZAWA¹⁾, Takeshi OSAWA¹⁾, Ken NAKADA³⁾, Atsushi YANO⁴⁾, Masanobu GORYO⁴⁾ and Yoshihisa NAITO¹⁾¹⁾Departments of Clinical Veterinary Medicine and ⁴⁾Veterinary Pathology, Faculty of Agriculture, Iwate University, Ueda, Morioka, Iwate 020-8550, ²⁾L Animal Clinic, 1-5-12 Tokiwadai, Kitakami, Iwate 024-0012 and ³⁾Department of Veterinary Obstetrics and Gynecology, School of Veterinary Medicine, Rakuno Gakuen University, Bunkyodai, Ebetsu, Hokkaido 069-8501, Japan

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ABSTRACT. A 5-year-old male Shiba dog with progressive neurologic signs was examined by computed tomography (CT). A CT image of the brain disclosed a large, spherical high-density lesion in the thalamus and diencephalon. Serum LH, FSH and testosterone levels were all low. Macroscopically the large mass was connected with the sella turcica, and it was histopathologically diagnosed as a pituitary chromophobe carcinoma. An aspermatogenesis was observed in the testes. Therefore, it was suggested that the low levels of gonadotropin secretion from the pituitary gland due to the pituitary tumor resulted in the failure of maturation of spermatozoa and spermatids.

KEY WORDS: aspermatogenesis, canine, pituitary chromophobe carcinoma.

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There have been many reports on pituitary "macrotumors" (tumor size ≥ 1 cm in diameter) in canine pituitary-dependent hyperadrenocorticism (PDH) cases [2, 6, 8, 11-13]. The clinical signs exhibited by dogs with "macrotumors" often reflect both the endocrine and space-occupying effects of the tumor [6, 8, 12, 13]. Besides PDH, canine pituitary tumors can lead to various endocrine disorders: e.g., acromegaly or hypopituitarism [12]. Hypopituitarism includes hypothyroidism, hypoadrenocorticism, hypogonadism and growth hormone failure in the case of a pituitary tumor [1, 12]. Common endocrine disorders, including an insufficiency of growth hormone and gonadotropin secretion were reported in human cases [12]. However, there are few reports on endocrine disorders resulting from pituitary tumors in dogs, except for PDH cases. This report aims to describe a canine case of a large pituitary tumor accompanied by a failure of gonadotropin secretion and an aspermatogenesis.

A 5-year-old male Shiba dog weighing 4.7 kg had shown clinical signs of anorexia, inactivity, stupor, aimless barking and irritability to sounds and touches for 2 months. These signs once subsided upon symptomatic treatment by administration of steroids and vitamins for 5 days in a private animal hospital. After discontinuation of the treatment, the dog showed the same severe neurologic symptoms again and was admitted to Iwate University Veterinary Hospital.

On the first day of hospitalization, the dog was thin and dehydrated, and showed depression, intermittent coma, irritability, blepharoptosis of the left side, occasional circling to the left, and head pressing to a corner of the cage. Anorexia and adipsia were also observed. The body temperature was 38.3°C. The testes were apparently normal. Exaggerated patellar tendon reflex on both sides and hypoactive pupillary

reaction to the light on the left side were observed at neurologic examination. The case was diagnosed as a disorder of the thalamus and the oculomotor nerve, judging from irritability and hypoactive reaction to the light. Hematological and biochemical examinations were performed on the first day and the 10th and 20th days (day 10 and day 20) of hospitalization (Table 1). Hematological examination revealed anemia on the first day, day 10 and day 20, and hypoproteinemia and hypoalbuminemia on day 10 and day 20. The serum creatine kinase level rose from 136 to 535 U/l, and its isoenzymes comprised 95% MM fraction on day 20. White blood cell count, concentrations of glucose, blood urea nitrogen, total cholesterol, total bilirubin, sodium and potassium, and levels of alanin aminotransferase, γ -glutamyl transpeptidase and lactate dehydrogenase were within normal ranges, respectively. The dog was examined by computed tomography (CT)^{a)} to confirm brain lesions on day 20. A CT image of the brain at 3 cm anterior to the occipital bone revealed a spherical high-density lesion in the thalamus and diencephalon (Fig. 1). The lesion extended from the base to

Table 1. Hematological, biochemical and endocrinological findings of the case

	The first day	Day 10	Day 20
Red blood cell ($10^4/\mu\text{l}$)	555	537	438
Hematocrit (%)	35	34	23
Hemoglobin (g/dl)	12.2	11.9	9.7
Serum total protein (g/dl)	6.0	4.6	4.3
Serum albumin (g/dl)	3.1	2.2	2.2
Creatine kinase (mg/dl)	N.D.	136	535
Cortisol ($\mu\text{g/dl}$)	N.D.	N.D.	1.5
T4 ($\mu\text{g/dl}$)	N.D.	N.D.	3.3
Thyroid stimulating hormone (ng/ml)	N.D.	N.D.	0.2
Luteinizing hormone (ng/ml)	N.D.	N.D.	0.3
Follicle stimulating hormone (ng/ml)	N.D.	N.D.	< 2.0
Testosterone (ng/ml)	N.D.	N.D.	< 0.2

N.D.: Not determined.

Footnote

^{a)} μE , Yokogawa Medical Systems, Ltd.

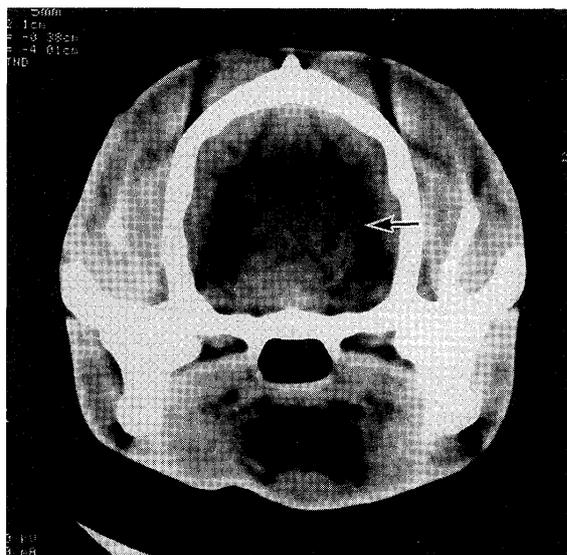


Fig. 1. Frontal CT image of the brain at 3 cm anterior to the occipital bone, showing a large high density lesion (arrow) in the thalamus and diencephalon.

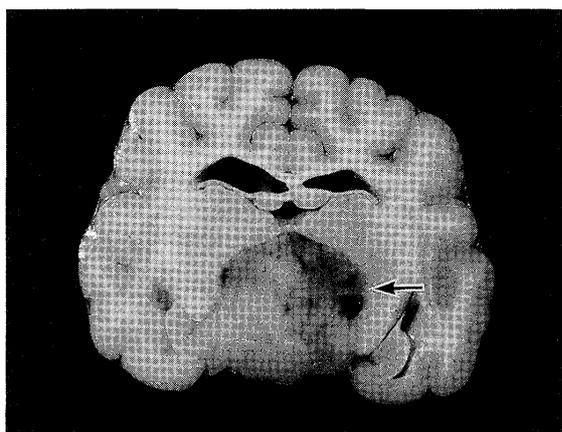


Fig. 2. Frontal plane of the brain. A large mass (arrow) located in the thalamus and diencephalon, is connected to the sella turcica and compresses the surrounding cerebral parenchyma.

the center of the brain, and was distinguished from the surrounding cerebral parenchyma.

Because the CT image was suggestive of the pituitary tumor, endocrine examinations were performed on day 20 (Table 1). Serum concentrations of T4 and cortisol were determined by fluorescence polarization immunoassays, and were 1.5 $\mu\text{g}/\text{dl}$ and 3.3 $\mu\text{g}/\text{dl}$, respectively. The serum concentration of thyroid stimulating hormone was determined by immunoradiometric assay, and was 0.15 ng/ml . These results were all within normal ranges. Serum concentrations of luteinizing hormone (LH) and follicle stimulating hormone (FSH) were determined by radioimmunoassays [7]. The serum testosterone concentration was also determined by radioimmunoassay. The serum LH concentration was 0.28 ng/ml , while FSH and testosterone levels were

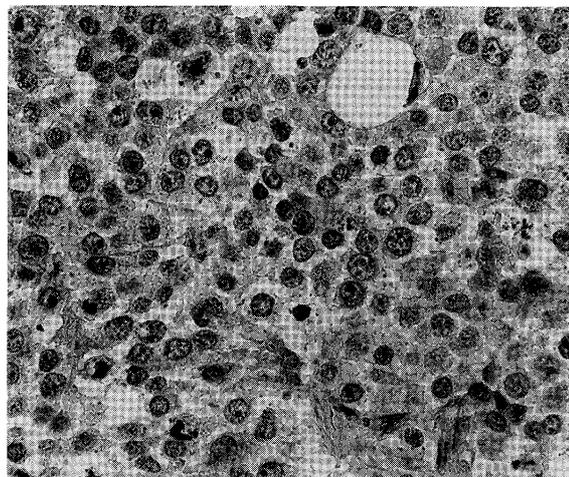


Fig. 3. Pituitary chromophobe carcinoma. The cytoplasm of the tumor cells is abundant and lightly eosinophilic with sparse granules. HE stain. $\times 330$.

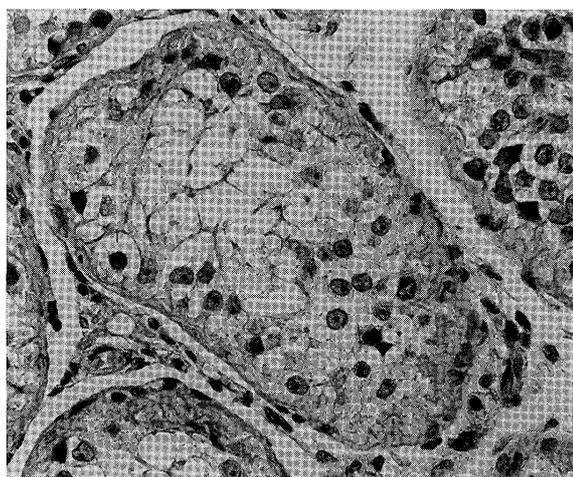


Fig. 4. Failure of maturation of spermatozoa and spermatids in the testis. The tubules are denuded of Sertoli cells. HE stain. $\times 330$.

undetectable, i.e., $<2.0 \text{ ng}/\text{ml}$ and $<0.2 \text{ ng}/\text{ml}$, respectively.

The dog was euthanized because of continuous coma and deterioration of the clinical symptoms. At autopsy, the mass was found to be connected with the sella turcica, to compress the surrounding cerebral parenchyma and to be in accord with the lesion detected by CT (Fig. 2). Histopathologically, the mass was a well-circumscribed tumor, which was composed of sparsely granulated chromophobe cells, and therefore it was diagnosed as a pituitary chromophobe carcinoma (Fig. 3). No spermatozoa and spermatids at all were observed in the seminiferous tubules of the testes (Fig. 4). The tubules were denuded of Sertoli cells. The Leydig cells were normally observed in the testes. No lesion was observed in either the adrenal glands or the thyroid gland by macroscopic and microscopic examinations.

The causes of anemia, hypoproteinemia and hypoalbuminemia were obscure by macroscopic and microscopic

examinations. Long-term anorexia may have resulted in those symptoms in the case.

It has been reported that clinical signs in dogs with large pituitary tumors were dullness, anorexia, disorientation, aimless wandering, difficulty laying down, ataxia, head pressing, circling, incontinence, seizures and upper motor neuron signs [6, 11]. These were also reported to be subsequent to polyuria, polydipsia, generalized truncal alopecia and abdominal enlargement in cases of PDH with a large pituitary tumor [6]. Clinical signs in this case were in accord with some of the signs having been reported in canine PDH cases with large pituitary tumors. However, no clinical signs of PDH occurred before signs of the tumor in this case. Moreover, the original tissue of the lesion was not distinguishable on the CT image, because the lesion's size was too large. For these reasons, even though this case was suspected of having a large pituitary tumor, but could not be certainly diagnosed as that based on the clinical examination and the CT image.

Hypopituitarism due to pituitary tumors can lead to endocrine disorders [12]. However, no abnormality of the thyroid gland or adrenal cortex was observed in the clinical findings or any other kind of examination in this case. In cases of pituitary tumors, failure of gonadotropin secretion can lead to azoospermia [4, 10]. Olson *et al.* [10] reported that the histopathological findings of testes revealed normal Leydig cells and inactive seminiferous tubules in dogs with hypogonadism. Although the testes, the seminiferous tubules and the Leydig cells were normal in our case, spermatogenesis was not observed at all. Measurement of blood testosterone and gonadotropin concentrations provides information on the functional status of the hypothalamic-pituitary-gonadal axis [4]. Concentrations of serum LH, FSH and testosterone were 0.28 ng/ml, less than 2.0 ng/ml and less than 0.2 ng/ml, whereas those in normal male dogs are reported to be 6.0–7.6 ng/ml [5, 9], 89 ± 28 ng/ml [9] and 1–5 ng/ml [4], respectively. The peripheral testosterone level may not reflect alterations in testicular testosterone nor be a useful diagnostic aid for spermatogenesis [4]. However, it is thought that the low level of testosterone in this case was caused by a failure of LH secretion from the pituitary. Production of mature spermatozoa requires the pre-

sence of both FSH and androgens, primarily testosterone, within the testes [4]. Judging from these findings, it is suggested that pituitary dysfunction due to the tumor caused inhibition of gonadotropic production, and secondarily the level of serum testosterone decreased due to low LH secretion, and consequently no spermatogenesis occurred in normally developed seminiferous tubules.

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