CASE REPORT

Multiple metastases of thyroid cancer in the cranium and pituitary gland in two dogs

Two dogs, a 14-year-old, female American Eskimo dog and a 14-year-old, male Maltese dog, were presented with thalamic syndromes, including lowered levels of consciousness, poor postural responses and presence of masses in the neck region. In both dogs, magnetic resonance imaging revealed multiple masses inside the cranium, including the pituitary gland. One dog died from status epilepticus two days after magnetic resonance imaging and the other died two months after magnetic resonance imaging from respiratory failure. These dogs were histopathologically diagnosed with multiple metastases of thyroid cancer occurring inside the cranium, including the pituitary gland. To the authors’ knowledge, this is the first time this tumour pattern has been reported in dogs, but it is possible that it is not uncommon.

S. TAMURA, Y. TAMURA, N. SUZUOKA*, A. OHOKA*, T. HASEGAWA* AND K. UCHIDA†


INTRODUCTION

In human beings, intracranial metastasis of thyroid cancer is a rare condition representing only one per cent of thyroid cancer cases (McWilliams and others 2003). To the authors’ knowledge, no canine cases have previously been reported. Metastatic tumours in the pituitary area are also uncommon in human beings, accounting for one to 26 per cent of pituitary tumours (Bell and others 2001, Simon and others 2004), and in dogs, there is only one previous report of metastatic tumours in the pituitary (a transmissible venereal tumour [Spence and others 1978]). This report describes two canine cases of multiple metastases of thyroid cancer in the cranium, including the pituitary gland.

CASE HISTORIES

Case 1

A 14-year-old, female American Eskimo dog was presented with reduced appetite and energy of three-weeks duration and cluster seizures that had been occurring since the day before presentation. During a physical examination, masses in the neck and mammary glands, as well as swelling of the mandibular lymph nodes, were found. Neurological examination revealed a lowered level of consciousness and a poor postural response in both hindlimbs and the left forelimb. Serum chemistry findings were normal. Chest radiographs showed a round mass in the cranial lobe of the left lung.

On magnetic resonance imaging (MRI), on both T1- and T2-weighted images, an extraparenchymal mass with the same signal intensity as the surrounding brain parenchyma was seen in the area extending from inside the sella turcica towards the upper part. The image of the mass was enhanced by intravenous administration of 0.3 ml/kg meglumine gadopentetate (Magnevist; Schering-Plough). Oedema was noted in the thalamus along the edge of the mass. Another mass was found on the border between the grey and white matter in the left temporal lobe, which was thought to be a metastatic tumour on the basis of its location, its roughly round shape and the severe oedema in the surrounding white matter (Fig 1).

On the basis of these findings, tumours in the pituitary, thyroid and mammary glands and metastatic tumours in the temporal lobe and lung were suspected. The cluster seizures were treated with phenobarbital and dexamethasone, but the dog died from status epilepticus two days after MRI examination.

On postmortem examination, a red mass in the temporal lobe and a milky-white mass in the pituitary area were found. Swollen mandibular lymph nodes and many nodules in the lung and spleen were also observed. Histopathologically, the neck mass comprised solid growths of tumour cells with round nuclei varying in size, undergoing active mitosis. The tumours were positive for thyroglobulin and negative for calcitonin and adrenocorticotropic hormone (ACTH) on immunostaining (Fig 2). Similar cells were observed in the other masses. On the basis
of these results, the dog was diagnosed with follicular thyroid cancer and systemic metastasis. The difference in the colours of the temporal lobe and pituitary masses was attributed to the differences in blood vessel distribution in the surrounding tissue. The mass in the mammary gland was diagnosed as a benign mixed tumour.

**Case 2**

A 14-year-old, male Maltese dog was presented with claudication of the left hindlimb and anisocoria. It had had reduced appetite and energy for the past three months and had been diagnosed with a thyroid tumour and hypothyroidism two months previously, after which the dog had been treated with thyroid hormone.

On physical examination, masses in the neck and swelling of the mandibular lymph nodes were found. Neurologically, lowered levels of consciousness and postural responses in all limbs, as well as anisocoria, were observed. In serum chemistry, an elevated cholesterol level ($390.7 \text{ mg/dl}$; reference range: $70$ to $303 \text{ mg/dl}$) and lowered values of $T4$ and $FT4$ ($6.05 \text{ nmol/l}$ and $0.08 \text{ pmol/l}$, respectively; lower limit of reference ranges, $T4$: $2.25 \text{ nmol/l}$ and $FT4$: $0.5 \text{ pmol/l}$) were found two months before presentation, but after one month of drug therapy, the levels mostly returned to normal.

There were no abnormal findings during chest radiography. Masses with similar MRI characteristics as those of the masses in case 1 were detected in the pituitary area and in the extraparenchymal area in the posterior cranial fossa (Fig 3). MRI findings suggested that the mass in the neck was located in the left thyroid. On fine-needle aspiration biopsy, scattered masses of cells arranged in a palisading pattern, with ill-defined cell boundaries and nuclei of varying sizes, and a large number of blood components were found.

On the basis of these results, multiple intracranial tumours and thyroid cancer were considered as differential diagnoses. Although the symptoms were treated (including administration of dexamethasone), the dog developed anastasia one month later and died two months later.

On postmortem examination, other than the masses observed during MRI, a small extraparenchymal tumour was noted in the left pyriform lobe. Histopathological examinations were carried out on the masses in the cranial and neck. In the thyroid mass, tumour cells with clear nucleoli, oval to polygonal-shaped nuclei and weakly acidophilic cytoplasm proliferated densely. Mitosis was found sporadically. The other intracranial masses were comprised of similar tumour cells (Fig 4). These tumour cells were clearly positive for calcitonin. On the basis of these findings, the dog was diagnosed with thyroid C-cell carcinoma and metastases.

**DISCUSSION**

It is likely that the number of reported cases of intracranial metastasis in cats and dogs is less than those in human beings because, in many cases, animals with tumours die or are euthanased before metastasis occurs. The incidence of intracranial metastatic tumours might also have been underestimated because craniotomy is not routinely carried out at postmortem examination in cats and dogs (Bagley 2005). However, the structure of the aortic arch branch in cats and dogs, which is different from that in human beings, may prevent intracranial metastasis from occurring readily (Summers and others 1995). Although metastases of thyroid
cancer into the cranium or pituitary gland have not been previously reported in dogs, the two cases reported here were encountered within a short period of time. So such metastases might not necessarily be rare conditions.

In case 1, intracranial lesions were strongly indicated by the epileptic seizures caused by the temporal lobe lesion. The lowered levels of consciousness and poor postural responses observed in both cases are symptoms of thalamic syndromes caused by pituitary metastasis and are characteristic of such disorders. However, if a thorough examination is not carried out at the initial presentation, these symptoms may not be linked to intracranial diseases and may be attributed to debility instead. Furthermore, in neither case did any clinical finding suggest an abnormal secretory function of the pituitary gland.

Metastatic tumours in the pituitary area rarely produce clinical symptoms in human beings (Ruelle and others 1992). Therefore, it is likely that metastatic tumours in the pituitary area in dogs have been under-reported because these tumours produce no clear clinical symptoms and tend to be overlooked. In fact, it could be difficult to detect primary pituitary tumours other than those producing ACTH. If lowered levels of consciousness and poor postural response are erroneously interpreted as lethargy and peripheral neuropathy, respectively, they could be confused with the clinical symptoms of hypothyroidism. Therefore, in cases with hypothyroidism caused by thyroid cancer, thyroid preparations alone could be administered without intracranial diseases ever being suspected.

In human beings, it is difficult to diagnose metastatic tumours in the pituitary area before surgery (Komninos and others 2004). Endocrine function tests (for example, ACTH-stimulation tests) are useful for differential diagnosis, especially for ACTH-producing tumours. The presence of central diabetes insipidus is the most crucial criterion for the differential diagnosis of pituitary metastatic tumours in human beings if it is found in one per cent of cases of pituitary adenoma and in 45-2 per cent of cases of metastatic tumour (Schubiger and Haller 1992). In dogs, however, 10 to 20 per cent of pituitary macroadenomas develop pituitary macroadenoma syndrome at, or immediately after, diagnosis (Nelson 1998). As central diabetes insipidus is a component of pituitary macroadenoma syndrome, it is unlikely to be a useful criterion for differential diagnosis in dogs. Dumbbell-shaped tumours extending from the intrasellar to the suprasellar area are likely to be metastatic tumours (Komninos and others 2004). Moreover, the presence of multiple tumours suggests that they are metastatic.

It will be a challenge in the future to develop an approach for the differential diagnosis of canine metastatic tumours in the pituitary area.

References


