Skippy John's Topsy Turvy Tale

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Introduction

Meningiomas are the most common brain tumor in cats. They are primary, slow growing tumors that are generally non-invasive[1]. While considered benign histologically, meningiomas can cause considerable clinical signs as the tumor takes up more space in the calvarium. Clinical signs can help localize the cause, and MRI is the gold standard for diagnosis of an intracranial tumor, but histopathologic biopsy is the definitive way to diagnose meningiomas. The treatment of choice is surgical removal, with a median survival time of 38 months post-operatively, as opposed to an 18-day median survival time with medical management alone[6].

History and Presentation

Skippy John, an approximately 11-year-old neutered male Siamese cat, presented to Mississippi State University College of Veterinary Medicine (MSU-CVM) Emergency services the morning of October 7, 2020 after being referred from the Animal Emergency and Referral Center in Flowood, Mississippi for a one-to-two day history of being laterally recumbent and anorexic. His owners reported that Skippy John has had a chronic left-sided head tilt and ear pain that caused him to fall over when attempting to walk. They stated that they had repeatedly taken him to multiple veterinarians with no resolution in symptoms, and he had gained a significant amount of weight in the past year. Since March 2020, Skippy John had intermittent bouts of decreased urination and decreased water consumption. In the past few weeks prior to presentation to MSU-CVM, he began to “not seem himself.” The few days before presentation was the first time he was noted to be so severely affected. He was at the time being given prazosin, buprenorphine, and gabapentin for the ear pain and urinary issues.

On presentation, Skippy John was laterally recumbent and mentally dull. He was obese with a body condition score was 9 out of 9. His body temperature was 102 degrees Fahrenheit, his heart rate at 181 beats per minute with fair pulses, and his respiratory rate was 40 breaths per minute with normal effort. His mucous membranes were pink and tacky, with a capillary refill time of 2 seconds. A painful response was elicited upon palpation of the left side of his head and left ear. A painful response was also elicited upon palpation of his neck. He had a brief incidence of positional nystagmus when rolled from lateral recumbency to dorsal recumbency, which corrected itself shortly thereafter. He pitched to the left and laid in left lateral when possible. Both of his eyes remained closed for the majority of his physical exam. Dental calculus was appreciated on his molars. No crackles, wheezes, murmurs, or arrhythmias were appreciated on cardiothoracic auscultation. Hair loss was present at the region of his caudal abdomen and left side of his head.

On neurologic examination, his cranial nerves appeared intact, with the exception of an inconsistent and incomplete left menace response. Skippy John was reluctantly ambulatory with observed weakness on the left limbs, though he also had an intravenous catheter in his left front limb. When he did walk, he would fall to the left. He had a plantigrade stance, though this was considered to be most likely due to weakness or nervousness in hospital, not due to a neurologic component. Conscious proprioception was absent in the forelimbs bilaterally, more pronounced in the left, and normal in the hindlimbs bilaterally. Hopping was absent in the forelimbs bilaterally and normal in both hindlimbs. Segmental reflexes were normal, though withdrawal was subjectively decreased in the right front limb. Increased extensor tone was appreciated in the right forelimb and less consistently in the left, but present bilaterally.

Triage exam findings included a pulse oximetry of 98 percent, a normal sinus rhythm on electrocardiogram, and an average blood pressure reading of 147/79 with a mean arterial pressure of 102. No free fluid was appreciated on abdominal or thoracic ultrasound.

Diagnostic Approach

After his initial triage and neurologic exam, a complete blood count, chemistry, thyroid panel, and feline leukemia/feline immunodeficiency virus tests were performed. Blood chemistry was unremarkable, as was his complete blood count except for decreased platelets which were revealed to be normal on a manual count. His thyroid panel revealed a mildly low T4 at 1.5 ng/dL, and the FeLV/FIV test was negative for the viruses. Thoracic radiographs were taken, which showed no evidence of any metastatic neoplasia, though there was a bronchial pulmonary pattern which was attributed to feline asthma or chronic bronchitis. Thoracic radiographs also showed an unstructured interstitial pulmonary pattern, decreased basement and apex of the cardiac silhouette and diaphragm, and left mediastinal shift, which were all likely secondary to Skippy John's obtunded status and atelectasis of the "down" lung.

The afternoon of October 7, Skippy John had a computed tomography scan (CT) performed of his skull and cervical spine. The CT revealed an irregularly shaped, smoothly marginated, 30 by 14 by 22 millimeter, heterogeneously mineral and soft tissue attenuating, strongly contrast-enhancing mass adjacent to the right temporal bone within the calvarium, that caused a leftward midline shift and attenuation of the right lateral ventricle. A thickening of the calvarium directly adjacent to the mass was also seen, as well as permeative lysis of the temporal bone dorsal to the right tympanic bulla. The mass was suspected to be a meningioma or, less likely, a primary bone tumor such as osteosarcoma, and Skippy John was scheduled for surgery the following day.

Pathophysiology

Meningiomas are the most common neurologic tumor in cats, accounting for over half – 56 percent – of all brain tumors. As the name suggests, they arise from the meningeal tissue surrounding the brain. Histologically, meningiomas are fibrotic, benign tumors, as they have a low mitotic index, do not regularly invade into adjacent tissue, and rarely metastasize[1]. The most common sites for feline meningiomas are tela choroidea of the third ventricle, the supratentorial meninges, and the cerebellar meninges. Unlike in dogs, it is not uncommon for multiple meningiomas to be present at one time, with 17 percent of patients having two or more tumors[6]. Though usually meningiomas are intracranial, brainstem, spinal, and orbital meningiomas have also been reported[1].

The signalment for cats with meningiomas are geriatric patients with a mean age of 12 years, with no sex or breed predilection[9]. Meningiomas are slow-growing tumors, which leads to a correspondingly slow and insidious onset of clinical signs. Clinical signs and their severity depend on the size and location of the tumor, with the most common signs being associated with forebrain lesions, such as lethargy, altered mental and behavioral status, circling towards the side of the lesion, central blindness, as well as decreased menace response, delayed conscious proprioception, and decreased facial sensation, all on the side opposite the lesion. Seizures are relatively rare in cats with meningiomas compared to dogs, which have seizures as their most common clinical sign[1].

Diagnosis of intracranial tumors should start with a thorough history, and include a minimum database, thoracic radiographs, abdominal ultrasound, and then computed tomography (CT) or magnetic resonance imaging (MRI) if a tumor is suspected. A minimum database of a complete blood count, chemistry, and urinalysis can help rule out any systemic causes for

neurologic signs. Thoracic radiographs and abdominal ultrasound should be included to screen for tumors elsewhere in the body, either primary tumors that may have metastasized to the brain, or metastases from a primary brain tumor[1].

CT and MRI are the major diagnostic tools used to determine the presence of an intracranial meningioma, however definitive diagnosis relies on histopathology either from surgical biopsy or necropsy. There are imaging features of meningiomas that can used with fair reliability to classify the type of intracranial tumor. In one study, CT could be used with approximately 80 percent accuracy to classify a tumor as a meningioma prior to histopathologic confirmation, though this study was in dogs. These features included extra-axial location, a well-demarcated mass with irregular margins, compression of adjacent tissue, enhancement with contrast, and close proximity to the meninges[7]. Other diagnostic features of meningiomas include the “dural tail” sign, which is contrast enhancement of the dura mater which connects to the mass, as well as calvaria hyperostosis, which is bone erosion due to pressure atrophy of the adjacent mass. The tumor then invades the Haversian canals in the bone itself and causes thickening of the calvarium[6]. While these characteristics may highly suggest that a tumor is a meningioma, it cannot definitively diagnose the tumor type as these features can be shared with other neoplasms. CT and MRI are also useful tools in surgical planning, if that route is taken[6].

Treatment and Management Options

Surgical excision is the treatment of choice for cats with meningiomas. It drastically increases a patient’s long-term survival; conservative medical management of cats with meningiomas yields a median survival time of 18 days, while surgical debulking has a median survival time of 37 months and a perioperative mortality rate of 6 percent[3]. The majority of cats who survived surgery showed significant neurologic improvement within the two weeks

following surgical debulking[5]. Recurrence can happen, with approximately one-fifth of feline patients having the meningioma return within an average of 9.5 months[6].

Glucocorticoids are used both as a palliative therapy and a pre-operative management. The steroid shrinks the tumor by decreasing capillary permeability and therefore decreasing the blood volume in the tumor itself over 24 hours after administration, which in turn improves clinical signs by lowering intracranial pressure and cerebral edema. Though useful for shrinking the tumor prior to surgical removal, it does not significantly increase survival times when used as a standalone therapy[1].

Radiation therapy is much more common in the treatment of canine meningiomas than feline and is often used as an adjuvant post-surgical excision or on inoperable tumors. In studies on dogs, radiation alone improved survival times over palliative therapy, and radiation plus surgery had better long-term survival over surgery alone[6]. Cats, however, have much longer overall median survival times with surgery alone compared to dogs – 37 months versus 7 months – and currently surgery combined with radiation does not appear to significantly improve survival time in cats[1].

Chemotherapy in treatment of meningiomas has been historically lackluster, with survival times not significantly longer than palliative care[1]. However, hydroxyurea is being investigated as an adjunctive therapy post-surgery and shows potential in both dogs and cats. In cats it is still in vitro research, but hydroxyurea has shown to decrease cell multiplication of feline meningioma cells[6].

Case Outcome

On October 7, Skippy John was hospitalized in the intensive care unit and started on intravenous Plasmalyte (15 mL/hr), dexamethasone-SP (0.1 mg/kg) intramuscularly once, and mannitol (0.5 g/kg) intravenously once to decrease intracranial pressure. His neurologic status remained unchanged overnight, and food was withheld in the morning in preparation for surgery.

On October 8, Skippy John underwent a right-sided rostrotentorial craniectomy to remove the intracranial tumor identified on CT. Approximately 90 percent of the tumor was removed, with the remaining tumor ventrally adhered to the skull and so could not be excised without potential damage to vital structures. No complications occurred during his surgery. Due to the possibility of Skippy John developing hepatic lipidosis from his weight combined with a history of two-day inappetence, an esophageal tube was placed immediately after surgery with no complications, and proper placement was confirmed with radiographs. He was maintained on flow-by oxygen until he recovered from anesthesia, which occurred uneventfully.

Around midnight on October 9, 2020, Skippy John was found unresponsive and coded after being evaluated by ICU approximately ten minutes prior. Cardiopulmonary resuscitation was initiated and performed for 15 minutes with no evidence of spontaneous return to function. CPR was ceased with consent from his owners, and necropsy was declined.

Conclusion

Skippy John was unfortunately in the six percent of patients that succumb to post-surgical complications. A full necropsy would have given a better understanding as to why he died so acutely, but there are a few possibilities as to the cause of his decline.

One likelihood is that there were complications due to the craniectomy itself. Surgical trauma from removing the mass can lead to cerebral edema or hemorrhage into the calvarium,

leading to an increased intracranial pressure and associated morbidities[4]. As stated in the Monroe-Kellie doctrine, the skull has a fixed volume with three internal components – brain, blood, and cerebrospinal fluid (CSF). If one of these three components increases, such as with cerebral edema, hemorrhage, or obstructed outflow of the CSF, the other components must decrease as a result, or the intracranial pressure will increase. The compensation can only account for so much change before the ICP increases despite physiologic compensatory mechanisms and lead to compromised neurologic function and ischemic events[8]. It is possible Skippy John's decline in the post-operative period was due to the surgery itself, and hemorrhage or edema caused an increased intracranial pressure and a subsequent disruption of his vital neurologic functions.

Another possibility is what is called Pickwickian syndrome, or obesity hypoventilation syndrome (OHS). OHS is defined as the presence of obesity combined with a hypercapnia that cannot be attributed to another cause of hypoventilation. This syndrome, if untreated, has an increased risk of morbidity and mortality in patients compared to those without it[2]. This syndrome is best described in human patients. These patients are more likely to have cardiovascular comorbidities and have an increased risk of dying in hospital compared to patients that are obese without the associated hypoventilation. Due to decreased functional lung capacity, poor ventilation/perfusion ratio, and increased pulmonary resistance associated with this syndrome, OHS patients make for complicated anesthetic candidates and have a higher risk of post-operative mortality[2]. OHS is a diagnosis of exclusion, however, so in Skippy John's case neurologic impairments would have had to be ruled out first, and post-operative CO_2 readings were not taken to confirm hypercapnia, so this cause of his mortality is speculative.

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