Case Report

JVC Journal of Veterinary Clinics

pISSN 1598-298X • eISSN 2384-0749
J Vet Clin 2023;40:341-348
https://doi.org/10.17555/jvc.2023.40.5.341

Neoadjuvant Chemotherapy and Subsequent Adjuvant Chemotherapy with Hydroxyurea after Craniotomy in a Cat with a Meningioma

Chae-Yeon Kim[1]
Jin-Young Kim[1]
Yoon-Ho Roh[2]
Kun-Ho Song[1]
Joong-Hyun Song[1,*]

[1]Department of Veterinary Internal Medicine, College of Veterinary Medicine, Chungnam National University, Daejeon 34134, South Korea
[2]Institute of Animal Medicine, College of Veterinary Medicine, Gyeongsang National University, Jinju 52828, South Korea

*Correspondence: jh.song@cnu.ac.kr

ORCID
Chae-Yeon Kim:
https://orcid.org/0009-0003-6333-2002
Jin-Young Kim:
https://orcid.org/0000-0001-7610-3442
Yoon-Ho Roh:
https://orcid.org/0000-0002-3097-838X
Kun-Ho Song:
https://orcid.org/0000-0001-8478-2035
Joong-Hyun Song:
https://orcid.org/0000-0001-9961-6451

Abstract An 11-year-old neutered male domestic short-haired cat presented with neurological symptoms that developed over a three-month period. These included mental dullness, vocalization, ataxia, and visual impairment. The patient was diagnosed with a primary intracranial tumor at a local animal hospital. After the first diagnosis, the cat was administered hydroxyurea, prednisolone, omeprazole, and gabapentin for 3 months. After the initiation of medical treatment, the patient's clinical symptoms did not improve and the size of the tumor was static on the second magnetic resonance imaging (MRI). The dosage of hydroxyurea and prednisolone was increased for two weeks. The patient's clinical signs improved, and subsequently, a craniotomy was performed. The clinical signs completely resolved six days after surgery. Adjuvant chemotherapy with hydroxyurea was continuously administered after the craniotomy. The patient demonstrated a good clinical status during the nine-month follow-up period. Neoadjuvant chemotherapy has not yet been reported for meningiomas in cats. Further clinical trials with longer follow-up periods and larger patient cohorts will be required to confirm the effectiveness of neoadjuvant chemotherapy with hydroxyurea in feline meningioma.

Key words cat, corticosteroid, hydroxyurea, meningioma, neoadjuvant chemotherapy.

Received July 7, 2023 / Revised August 3, 2023 / Accepted September 19, 2023

Introduction

Meningioma is the most common feline intracranial tumor, accounting for 56-58% of all primary brain tumors in cats (35,37,43). Meningiomas are usually diagnosed in older cats; no significant sex predisposition has been observed (37). In previous studies, mixed-breed cats, American short-hair cats, and Norwegian forest cats were observed to be predisposed to developing meningiomas (30,32,35,37). Very few reports have described the etiology of feline meningiomas. Clinical signs of meningiomas vary according to the tumor location; the most common signs are behavioral changes and ataxia (4). Advanced imaging modalities for the diagnosis of intracranial meningiomas include computed tomography (CT) and magnetic resonance imaging (MRI) (3). On MRI, a meningioma usually presents as an extra-axial, strongly contrast-enhancing, space-occupying mass (9,15). Some specific characteristics, such as the dural tail sign have also been identified (9). A definitive diagnosis of meningioma is established on the basis of histopathology (9). Most intracranial meningiomas in cats are benign and slow growing (37). Therefore, surgical excision is the primary treatment option for these tumors (8,33). The long-term outcomes of surgical excision alone are good, with a median survival of 23-37 months (4,8,12,37). However, in cases where complete surgical removal of the tumor is not possible, adjuvant chemotherapy and radiation therapy could be considered (18,28,42). There is limited information about adjuvant chemotherapy for feline meningiomas (8,9,21). Currently, hydroxyurea is the only well-known chemotherapeutic drug for feline meningiomas (8,9,42). Neoadjuvant chemotherapy involves the administration of chemotherapeutic drugs before the surgical removal of the cancer (41).

Neoadjuvant chemotherapy is a well-accepted treatment option for various tumor types in human medicine (31,38). However, the use of neoadjuvant medicine has not been extensively explored in veterinary medicine (41). Neoadjuvant chemotherapy has been reported for specific types of cancer in cats (3,34,41), but not for meningiomas. In this case report, we describe the use of hydroxyurea as a neoadjuvant and adjuvant chemotherapeutic agent in a cat with a meningioma. To the best of our knowledge, this is the first case report of a feline meningioma treated with neoadjuvant chemotherapy.

Case Report

An 11-year-old neutered male domestic short-haired cat presented with neurological signs, including mental dullness, wandering, vocalization, ataxia, and visual impairment.

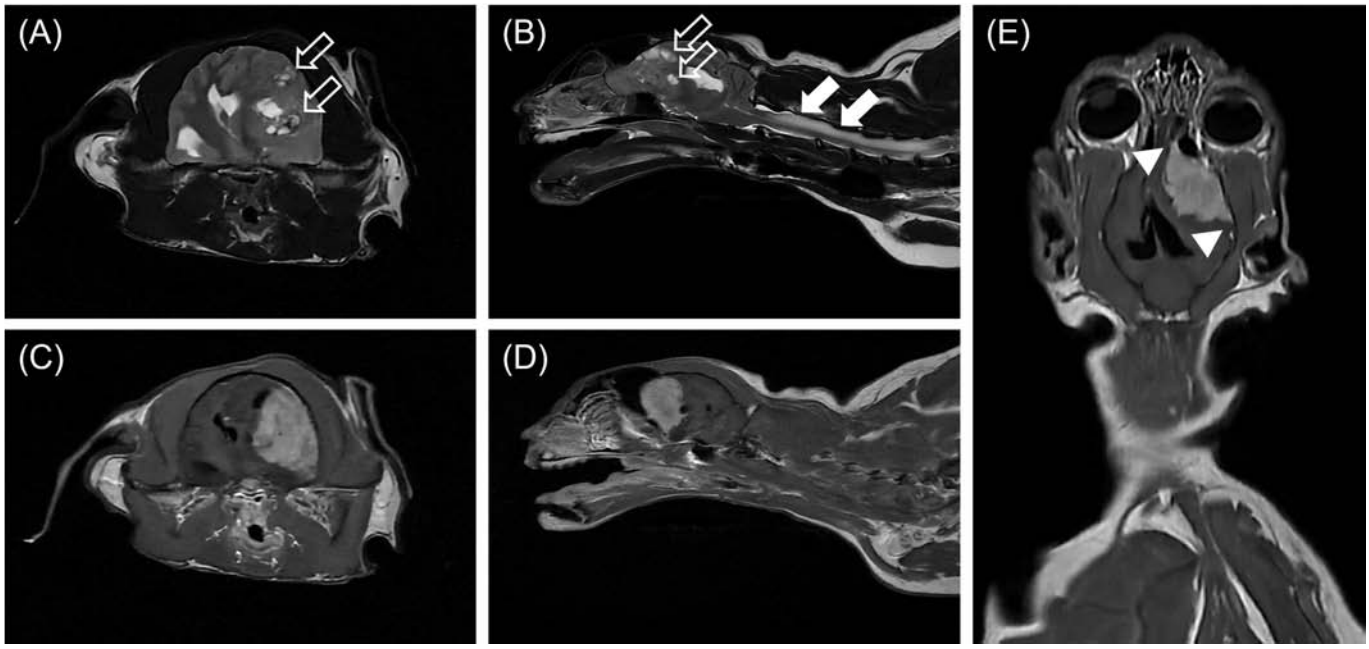

Fig. 1. Brain MRI scans obtained at a local animal hospital; T2-weighted sequences: transverse (A) and sagittal plane (B); T1-weighted post-contrast sequences: transverse (C), sagittal (D), and dorsal plane (E). (A, B) Multiple cystic lesions can be observed in the peritumoral and intratumoral regions (empty arrows) with cervical syringomyelia (arrows). (C, D) An extra-axial, broad-based enhanced mass is identified. (E) A solitary large extra-axial mass in the left frontal lobe is observed, with a dural tail sign (arrowheads).

These signs had developed over a three-month period. The patient was diagnosed with a primary intracranial tumor based on an MRI scan performed at a local animal hospital (Fig. 1). MRI results demonstrated an extra-axial mass that was slightly hyperintense on T2-weighted images. Diffuse peritumoral and intratumoral cyst-like lesions and cervical syringomyelia were also observed. The cerebellum was herniated. After the initial diagnosis, this patient was prescribed hydroxyurea (25 mg/kg per os [PO] once every alternate day; Hydrin®, Korea United Pharm, Seoul, South Korea), prednisolone (0.5 mg/kg PO once daily; Solondo®, Yuhan, Seoul, South Korea), omeprazole (0.7 mg/kg PO once daily; OMP® tab, CKD Pharm, Seoul, Korea), and gabapentin (10 mg/kg PO once daily; gabapentin cap.; Donga Pharm, Seoul, Korea). After the initiation of medical treatment, the patient did not exhibit any significant improvement in the neurological signs. The patient was referred to our hospital 3 months after the first diagnosis. The physical examination at that time revealed no remarkable findings. Complete blood count (ProCyte Dx®, IDEXX, Portland, ME, USA) and serum biochemistry profile (Catalyst One, IDEXX, Westbrook, USA) results were within normal reference ranges. Neurological examination revealed mental dullness and lack of bilateral menace reactions. On the repeat MRI, the size of the mass was static (2.4 × 1.7 × 2.1 cm, L × W × H) as compared with the previous MRI results (2.7 × 1.7 × 2.4 cm, L × W × H) (Fig. 2). However, the number and size of cyst-like lesions within or around the tumor had decreased compared to previous results. The size of the largest cyst had decreased from 5.5 × 4.0 (W × H) to 4.3 × 3.2 mm (W × H). Cervical syringomyelia was not observed in this scan. Cerebrospinal fluid (CSF) tapping was not performed because of cerebellar herniation and suspicion of raised intracranial pressure. After repeat MRI scans, omeprazole was discontinued, and the dose of prednisolone was increased from 0.5 mg/kg once daily to 1 mg/kg twice daily. The dose of hydroxyurea was also increased from 25 mg/kg once every alternate day to 25 mg/kg once daily. Gabapentin was continued at the same dose. We observed the complete resolution of the patient's blindness and significant improvement in the severity of their mental dullness after dose adjustment for prednisolone and hydroxyurea. Oral prednisolone was discontinued seven days before the surgery, while oral hydroxyurea was stopped one day before the surgery. The patient underwent a craniotomy two weeks after the second MRI scan for the removal of the intracranial tumor (Fig. 3). After left-sided transfrontal craniotomy, the dura mater was opened to expose the tumor. An ultrasonic aspirator (Sonopet, Stryker, Tokyo, Japan) was placed in the

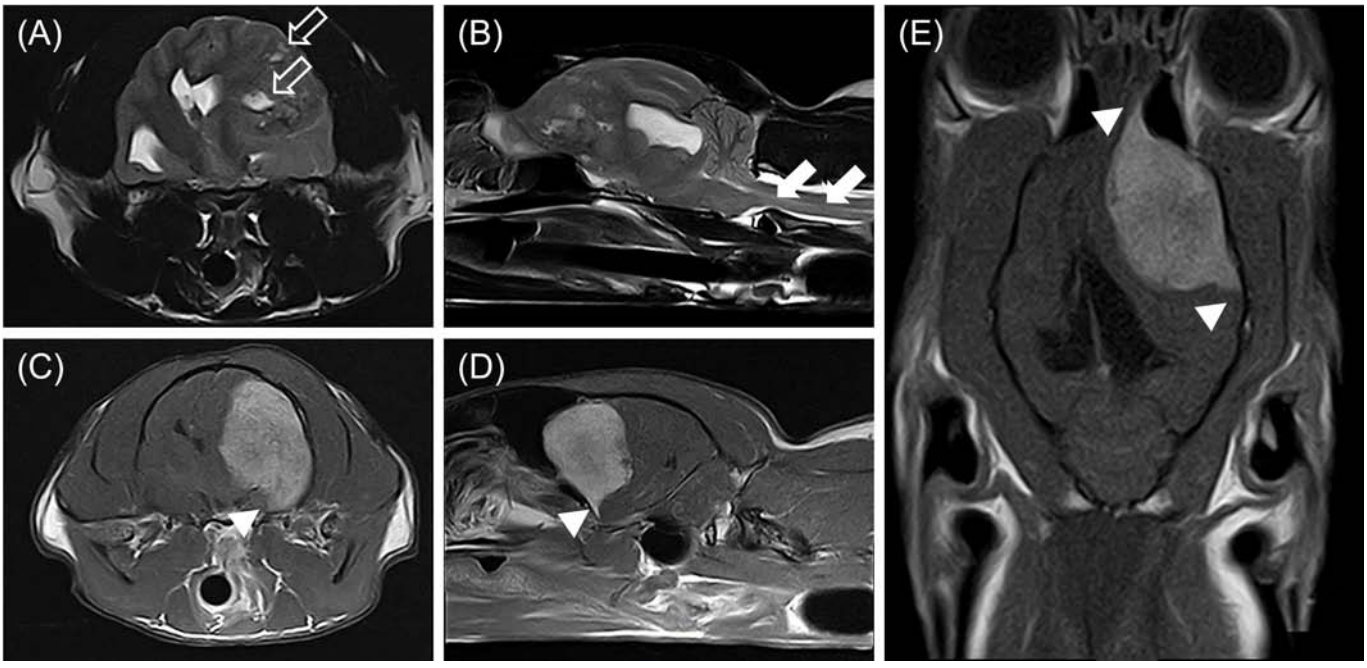

Fig. 2. Repeat MRI images 3 months after the initiation of medical treatment; T2-weighted sequences: transverse (A) and sagittal plane (B); T1-weighted post-contrast sequences: transverse (C), sagittal (D), and dorsal plane (E). (A, B) The number and size of the cystic lesions have decreased compared to 3 months before (empty arrows). The cervical syringomyelia can no longer be observed (arrows). (C, D) An extra-axial, broad-based enhanced mass is observed with severe midline right shifting and dural tail sign (arrowhead). (E) A solitary large extra-axial mass is observed with a dural tail sign (arrowheads).

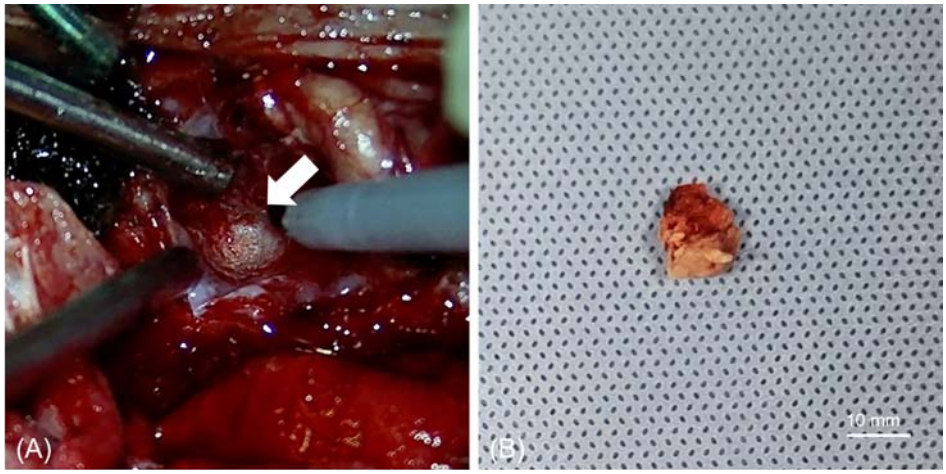

Fig. 3. Intraoperative appearance of the craniotomy site and the gross findings of the mass; (A) the dura mater is opened and an ultrasonic aspirator machine is used to remove the mass (arrow). (B) Aspirated meningioma. Bar = 10 mm.

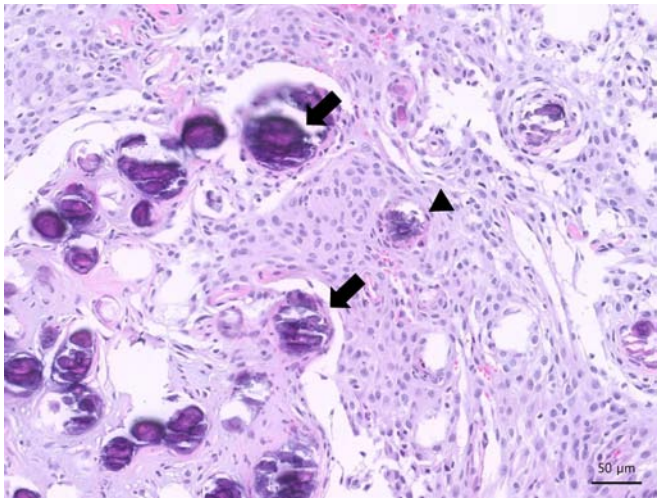

Fig. 4. Histopathology image of the resected mass; a mass comprised of densely packed streams, whorls (arrowhead), and solid sheets of a monomorphic population of neoplastic cells is observed. Psammoma bodies are also identified (arrows). There are numerous deposits of hyalinized collagen and mineral throughout the mass. This is consistent with the psammomatous subtype meningioma. Hematoxylin and eosin stain. Original magnification ×200. Bar = 50 μm.

middle of the tumor. After aspirating the inner part of the tumor, the cutaneous muscle was transplanted to suture the dura mater and suture glue was applied. The surgical margin was incomplete due to methodological limitations of the ultrasonic aspirator machine. The tumor tissue was sent to a commercial laboratory (IDEXX Laboratories, Inc., USA); histopathological evaluation confirmed the psammomatous meningioma subtype (Fig. 4) of the tumor. Neurological signs, including mental abnormalities, ataxia, and visual impairment were observed to completely resolve six days after the surgery. The patient was discharged eight days after the surgery with the prescription of hydroxyurea (25 mg/kg orally once daily) as adjuvant chemotherapy. A complete blood cell count was obtained every two weeks during the first one month and every four weeks thereafter. Renal toxicity was monitored by evaluating blood urea nitrogen and creatinine levels every four weeks. The patient tolerated chemotherapy well. After 74 days of adjuvant chemotherapy, complete blood cell count revealed mild neutropenia (1,560 cells/μL; reference range, 5,050-16,760 cells/μL). Hence, the dose of hydroxyurea was decreased to 20 mg/kg once daily. After four weeks, neutropenia (1,390 cells/μL) still persisted; thus, the dose was further decreased to 25 mg/kg once every alternate day. Subsequently, the patient demonstrated a good clinical status without any hematological abnormalities or other adverse effects. No neurological abnormalities were observed during the nine-month follow-up period.

Discussion

This case report describes neoadjuvant and adjuvant chemotherapy for a feline meningioma. In dogs, the complete excision of meningiomas is difficult because of their highly infiltrative characteristics (13). Therefore, the prognosis is usually poor after surgical treatment of canine meningiomas (16). Unlike in dogs, most feline meningiomas do not commonly infiltrate the brain tissue (37). Thus, long-term remission of clinical signs associated with intracranial meningiomas can be achieved by surgical excision followed by adjuvant chemotherapy with hydroxyurea in cats (27). In an in vitro study, multiplication of feline meningioma cells was inhibited by the administration of hydroxyurea (8). In another study, four cats treated with hydroxyurea after surgery were still alive with no neurological sequelae at 12-24 months postoperatively (9).

Neoadjuvant chemotherapy involves the administration of chemotherapeutic drugs before the surgical removal of

cancer (41). The aim of neoadjuvant chemotherapy is to reduce tumor size, decrease mass density, and alter the tumor microenvironment prior to surgery (41). In veterinary and human medicine, neoadjuvant chemotherapy for meningiomas has not yet been reported, except in one human experimental study (2). This experimental study demonstrated that the growth of meningiomas in tissue culture media was markedly inhibited after the preoperative administration of methotrexate. A human case report demonstrated a marked reduction in preoperative tumor size of an intracranial glioma after temozolomide-based neoadjuvant chemotherapy (1). In veterinary medicine, neoadjuvant chemotherapy has been well described for other tumor types such as mast cell and mammary tumors (41). According to previous studies, the tumor response to neoadjuvant chemotherapy is correlated with both disease-free survival and overall survival (6,38,42).

Several human studies have described the process of clinical and pathological evaluation for neoadjuvant chemotherapy; changes in tumor size are often used for evaluation (6,38). However, the goal of neoadjuvant chemotherapy is not only to reduce tumor size but also to alter the tumor microenvironment (31,39). In addition, various pathological changes that occur after the administration of neoadjuvant chemotherapy can influence tumor size (31,39). Thus, the tumor can be overestimated clinically or macroscopically due to various pathological changes (7). In conclusion, the effects of neoadjuvant chemotherapy should not be evaluated based on tumor size alone because tumor cellularity can decrease without significant changes in tumor size; pathological changes can also influence tumor size (7,31,39). In the present case, the patient was treated with hydroxyurea for three months prior to the surgery. Sequential MRI scans demonstrated no significant difference in tumor size compared with that in the previous 3 months. However, the peritumoral edema, cyst-like lesions, and cervical syringomyelia improved. In addition, the clinical signs improved after increasing the doses of hydroxyurea and corticosteroids. Corticosteroids decrease the permeability of tumor capillaries, tumor-associated inflammation, and blood supply to the tumor (24). Corticosteroids also reduce inflammation and CSF production (11,14,40). Therefore, most cats with meningiomas receive corticosteroids preoperatively (4,12). When combined with neoadjuvant chemotherapy, the corticosteroid dose is usually described as anti-inflammatory (30). Thus, for feline meningiomas, the addition of corticosteroids can be recommended at an anti-inflammatory dose with neoadjuvant chemotherapy before surgery. In the present case, it could not be definitively defined whether the corticosteroids or hydroxyurea contributed to the improvement of lesions, such as the improvement in peritumoral edema. However, it seems that corticosteroid has contributed to these changes due to their anti-inflammatory properties. In conclusion, our experience suggests that a combination of hydroxyurea and corticosteroids can be helpful in the management of feline meningiomas. Further studies are required to determine the exact effects of hydroxyurea and corticosteroids on feline meningiomas.

In human and veterinary medicine, there is no consensus regarding when hydroxyurea chemotherapy should be discontinued and resumed before and after the surgery. In one human study, hydroxyurea chemotherapy for a meningioma was administered immediately after the surgery (19). However, the exact interval between surgery and chemotherapy has not yet been determined. Another human medicine study described a patient treated for polycythemia vera who underwent gastrectomy for gastric cancer (26). In that study, hydroxyurea was administered before and after the surgery to manage the polycythemia vera. Hydroxyurea was discontinued three days before the surgery and resumed seven days postoperatively. Administration of hydroxyurea during the perioperative period led to good clinical results. In the present study, hydroxyurea was discontinued one day before the surgery and re-administered eight days after the surgery with the patient discharged home. No significant adverse effects were associated with hydroxyurea during the perioperative period. Thus, this regimen can be considered for feline meningiomas. Further studies with a larger cohort of patients and extended follow-up periods are required to establish the protocol.

Adjuvant chemotherapy involves treatment with chemotherapeutic drugs after surgery or radiotherapy. The goal of this treatment is to delay the recurrence or distant metastasis and improve survival. The patient receive adjuvant chemotherapy after surgery because of incomplete surgical margins. The postoperative MRI scan was refused by the owner for financial issues and concerns about the patient. In cats, most cases managed with neoadjuvant chemotherapy, included feline soft tissue sarcoma, were also treated with adjuvant chemotherapy (3,36). Generally, the protocol for neoadjuvant chemotherapy is identical to that for adjuvant chemotherapy (41). No significant differences in adverse effects were observed between the neoadjuvant and adjuvant chemotherapy groups. A similar result was observed in the present case.

In both human and veterinary medicine, hydroxyurea is well tolerated, with only reversible dose-dependent myelosuppression observed as a side effect (5,25). In humans, hydroxyurea is well tolerated by most patients with meningiomas (20,29). In large-scale human studies, the only consistently reported ad-

verse effect is hematological toxicity (20). Hydroxyurea is well tolerated in dogs, similar to humans (10). However, unusual dermatological toxicity was reported in two dogs (23). In that study, onychomadesis was observed in two dogs receiving long-term hydroxyurea treatment. Discontinuation of hydroxyurea treatment or dose tapering of hydroxyurea was required to treat the nail lesions. Another case study described long-term chemotherapy with hydroxyurea in a dog with suspected meningioma (17). In that study, no significant adverse effects were observed during the treatment period, and hydroxyurea was well tolerated. A few reports have described the long-term administration of hydroxyurea in cats. Recently, long-term hydroxyurea chemotherapy for intracranial meningiomas was reported in one cat (42). In that report, one cat with a meningioma survived for 408 days after chemotherapy with hydroxyurea and corticosteroids. Chemotherapy with hydroxyurea was initiated (25 mg/kg PO once daily) and tapered to once every alternate day. Only mild anemia occurred; no other adverse effects were observed during the treatment period. In our study, neoadjuvant and adjuvant chemotherapies were well tolerated. No clinical signs of hematological toxicity were observed. Neutropenia was observed 74 days after adjuvant chemotherapy. This was classified as Grade I according to the Veterinary Cooperative Oncology Group (VCOG) Common Terminology Criteria for Adverse Events (22). In our study, the administered dose of hydroxyurea was 25 mg/kg PO once daily. However, it was adjusted according to hematological toxicity and tapered once every alternate day for maintenance purposes. Hydroxyurea, as used in this regimen, was well tolerated by the patient. No chemotherapy-associated adverse effects were observed during the treatment period. Hematological toxicity is most commonly observed, with a reduction in hemoglobin, white blood cells, and platelets in both human and veterinary medicine (20,23,29). Thus, periodic complete blood cell counts to identify any adverse effects of hydroxyurea during chemotherapy are recommended.

The limitations of this study are that only one case was investigated and the follow-up period was relatively short. Therefore, further studies are required to investigate the effects of hydroxyurea as a neoadjuvant and adjuvant chemotherapy in a larger number of feline meningioma cases. Based on the patient's quality of life and minimal adverse effects observed in our study, neoadjuvant and adjuvant chemotherapy with hydroxyurea can be considered for the management of feline meningiomas, along with other treatments such as surgical resection and anti-inflammatory drugs. Although the long-term benefits of neoadjuvant chemotherapy in feline meningiomas have not yet been extensively elucidated, it appears to be relatively safe and well tolerated in cats.

Conclusions

In this case report, we have described the use of neoadjuvant and adjuvant chemotherapy for a feline meningioma. Although neoadjuvant and adjuvant chemotherapy have not been well documented in either human or veterinary literature, neoadjuvant and adjuvant chemotherapy with hydroxyurea appear to be well tolerated. Hence, they may be considered as palliative treatment options for feline meningiomas. Further large-scale studies are required to establish guidelines for neoadjuvant and adjuvant chemotherapy in cats with meningiomas.

Source of Funding

This study received no external funding.

Acknowledgements

This research was supported by the National Research Foundation of Korea and funded by a grant from the Korean Government (NRF-2022R1G1A1003682113148209264010 1). This study is also supported by the Basic Science Research Program through the NRF, funded by the Ministry of Education (RS-2023-00219710314820926400 01).

Conflicts of Interest

The authors have no conflicting interests.

References

1. Blonski M, Pallud J, Gozé C, Mandonnet E, Rigau V, Bauchet L, et al. Neoadjuvant chemotherapy may optimize the extent of resection of World Health Organization grade II gliomas: a case series of 17 patients. J Neurooncol 2013; 113: 267-275.
2. Bots GT. The influence of preoperative administration of methotrexate on the outgrowth of meningiomas and astrocytomas in tissue culture. Acta Neurochir (Wien) 1980; 54: 201-204.
3. Bray J, Polton G. Neoadjuvant and adjuvant chemotherapy combined with anatomical resection of feline injection-site sarcoma: results in 21 cats. Vet Comp Oncol 2016; 14: 147-160.
4. Cameron S, Rishniw M, Miller AD, Sturges B, Dewey CW. Characteristics and survival of 121 cats undergoing excision of intracranial meningiomas (1994-2011). Vet Surg 2015; 44: 772-776.
5. Dogruel M, Gibbs JE, Thomas SA. Hydroxyurea transport across the blood-brain and blood-cerebrospinal fluid barriers of the guinea-pig. J Neurochem 2003; 87: 76-84.
6. Fisher B, Bryant J, Wolmark N, Mamounas E, Brown A, Fisher ER,

et al. Effect of preoperative chemotherapy on the outcome of women with operable breast cancer. J Clin Oncol 1998; 16: 2672-2685. Corrected and republished in: J Clin Oncol 2023; 41: 1795-1808.
7. Fisher ER, Wang J, Bryant J, Fisher B, Mamounas E, Wolmark N. Pathobiology of preoperative chemotherapy: findings from the National Surgical Adjuvant Breast and Bowel (NSABP) protocol B-18. Cancer 2002; 95: 681-695.
8. Forterre F, Fritsch G, Kaiser S, Matiasek K, Brunnberg L. Surgical approach for tentorial meningiomas in cats: a review of six cases. J Feline Med Surg 2006; 8: 227-233.
9. Forterre F, Tomek A, Konar M, Vandevelde M, Howard J, Jaggy A. Multiple meningiomas: clinical, radiological, surgical, and pathological findings with outcome in four cats. J Feline Med Surg 2007; 9: 36-43.
10. Forward AK, Volk HA, Cherubini GB, Harcourt-Brown T, Plessas IN, Garosi L, et al. Clinical presentation, diagnostic findings and outcome of dogs undergoing surgical resection for intracranial meningioma: 101 dogs. BMC Vet Res 2022; 18: 88.
11. Gillespie S, Gilbert Z, De Decker S. Results of oral prednisolone administration or ventriculoperitoneal shunt placement in dogs with congenital hydrocephalus: 40 cases (2005-2016). J Am Vet Med Assoc 2019; 254: 835-842.
12. Gordon LE, Thacher C, Matthiesen DT, Joseph RJ. Results of craniotomy for the treatment of cerebral meningioma in 42 cats. Vet Surg 1994; 23: 94-100.
13. Greco JJ, Aiken SA, Berg JM, Monette S, Bergman PJ. Evaluation of intracranial meningioma resection with a surgical aspirator in dogs: 17 cases (1996-2004). J Am Vet Med Assoc 2006; 229: 394-400.
14. Hechler AC, Moore SA. Understanding and treating Chiari-like malformation and syringomyelia in dogs. Top Companion Anim Med 2018; 33: 1-11.
15. Ijiri A, Yoshiki K, Tsuboi S, Shimazaki H, Akiyoshi H, Nakade T. Surgical resection of twenty-three cases of brain meningioma. J Vet Med Sci 2014; 76: 331-338.
16. Jung DI, Kim HJ, Park C, Kim JW, Kang BT, Lim CY, et al. Long-term chemotherapy with lomustine of intracranial meningioma occurring in a miniature schnauzer. J Vet Med Sci 2006; 68: 383-386.
17. Jung DI, Lim CY, Kang BT, Kim JW, Yoo JH, Park HM. Long-term chemotherapy with hydroxyurea in a dog with suspected intracranial meningioma. J Vet Clin 2008; 25: 514-517.
18. Keyerleber MA, McEntee MC, Farrelly J, Thompson MS, Scrivani PV, Dewey CW. Three-dimensional conformal radiation therapy alone or in combination with surgery for treatment of canine intracranial meningiomas. Vet Comp Oncol 2015; 13: 385-397.
19. Kim J, Kim KH, Kim YZ. The clinical outcome of hydroxyurea chemotherapy after incomplete resection of atypical meningiomas. Brain Tumor Res Treat 2017; 5: 77-86.
20. Kim MS, Yu DW, Jung YJ, Kim SW, Chang CH, Kim OL. Long-term follow-up result of hydroxyurea chemotherapy for recurrent meningiomas. J Korean Neurosurg Soc 2012; 52: 517-522.
21. Körner M, Roos M, Meier VS, Soukup A, Cancedda S, Parys MM, et al. Radiation therapy for intracranial tumours in cats with neurological signs. J Feline Med Surg 2019; 21: 765-771.
22. LeBlanc AK, Atherton M, Bentley RT, Boudreau CE, Burton JH, Curran KM, et al. Veterinary COOPERATIVE ONCOLOGY GROUP-Common Terminology Criteria for Adverse Events (VCOG-CTCAE v2) following investigational therapy in dogs and cats. Vet Comp Oncol 2021; 19: 311-352.
23. Marconato L, Bonfanti U, Fileccia I. Unusual dermatological toxicity of hydroxyurea in two dogs with spontaneously occurring tumours. J Small Anim Pract 2007; 48: 514-517.
24. Matiasek LA. Intracranial meningiomas in cats. Vet Times 2010; 40: 24-26.
25. Miller MK, Zimmerman SA, Schultz WH, Ware RE. Hydroxyurea therapy for pediatric patients with hemoglobin SC disease. J Pediatr Hematol Oncol 2001; 23: 306-308.
26. Mochizuki T, Tanabe K, Saito R, Ota H, Yamamoto Y, Saeki Y, et al. Perioperative management of polycythemia vera with advanced gastric cancer: a case report. Int J Surg Case Rep 2019; 58: 224-227.
27. Motta L, Mandara MT, Skerritt GC. Canine and feline intracranial meningiomas: an updated review. Vet J 2012; 192: 153-165.
28. Nakaichi M, Taura Y, Nakama S, Takeuchi A, Matsunaga N, Ebe K, et al. Primary brain tumors in two dogs treated by surgical resection in combination with postoperative radiation therapy. J Vet Med Sci 1996; 58: 773-775.
29. Newton HB, Slivka MA, Stevens C. Hydroxyurea chemotherapy for unresectable or residual meningioma. J Neurooncol 2000; 49: 165-170.
30. Olsen JA, Thomson M, O'Connell K, Wyatt K. Combination vinblastine, prednisolone and toceranib phosphate for treatment of grade II and III mast cell tumours in dogs. Vet Med Sci 2018; 4: 237-251.
31. Rajan R, Poniecka A, Smith TL, Yang Y, Frye D, Pusztai L, et al. Change in tumor cellularity of breast carcinoma after neoadjuvant chemotherapy as a variable in the pathologic assessment of response. Cancer 2004; 100: 1365-1373.
32. Saito R, Chambers JK, Kishimoto TE, Uchida K. Pathological and immunohistochemical features of 45 cases of feline meningioma. J Vet Med Sci 2021; 83: 1219-1224.
33. Sessums K, Mariani C. Intracranial meningioma in dogs and cats: a comparative review. Compend Contin Educ Vet 2009; 31: 330-339.
34. Spugnini EP, Ruslander D, Bartolazzi A. Extraskeletal osteosarcoma in a cat. J Am Vet Med Assoc 2001; 219: 60-62, 49.
35. Tomek A, Cizinauskas S, Doherr M, Gandini G, Jaggy A. Intracranial neoplasia in 61 cats: localisation, tumour types and seizure patterns. J Feline Med Surg 2006; 8: 243-253.

36. Torrigiani F, Romanelli G, Roccabianca P, Treggiari E. Neoadjuvant and adjuvant doxorubicin chemotherapy in a case of feline soft tissue sarcoma. JFMS Open Rep 2019; 5: 2055116919857870.
37. Troxel MT, Vite CH, Van Winkle TJ, Newton AL, Tiches D, Dayrell-Hart B, et al. Feline intracranial neoplasia: retrospective review of 160 cases (1985-2001). J Vet Intern Med 2003; 17: 850-859.
38. Wang H, Mao X. Evaluation of the efficacy of neoadjuvant chemotherapy for breast cancer. Drug Des Devel Ther 2020; 14: 2423-2433.
39. Wasser K, Sinn HP, Fink C, Klein SK, Junkermann H, Lüdemann HP, et al. Accuracy of tumor size measurement in breast cancer using MRI is influenced by histological regression induced by neoadjuvant chemotherapy. Eur Radiol 2003; 13: 1213-1223.
40. Watanabe K, Ishikawa S, Kimoto T, Nosaka K, Kajikawa H. [Production and absorption rate of cerebrospinal fluid in the spinal subarachnoid space of the dog (author's transl)]. No Shinkei Geka 1976; 4: 351-358. Japanese.
41. Wustefeld-Janssens B, Smith L, Wilson-Robles H. Neoadjuvant chemotherapy and radiation therapy in veterinary cancer treatment: a review. J Small Anim Pract 2021; 62: 237-243.
42. Yun T, Koo Y, Kim H, Lee W, Kim S, Jung DI, et al. Case report: long-term chemotherapy with hydroxyurea and prednisolone in a cat with a meningioma: correlation of FDG uptake and tumor grade assessed by histopathology and expression of Ki-67 and p53. Front Vet Sci 2021; 8: 576839.
43. Zee CS, Chen T, Hinton DR, Tan M, Segall HD, Apuzzo ML. Magnetic resonance imaging of cystic meningiomas and its surgical implications. Neurosurgery 1995; 36: 482-488.