J Vet Clin 22(3) : 264-267(2005)

Adjuvant Glucocorticoids Therapy in Canine Mast Cell Tumor

Myung-jin Kim, Jae-il Lee, Young-suk Kim, Hwa-young Son, Moo-hyung Jun, Chang-sik Park* and Myung-cheol Kim[1]

College of Veterinary Medicine, Chungnam National University, Daejeon 305-764, Korea
**Division of Animal Science & Resources, Research Center for Transgenic Cloned Pigs, Chungnam National University, 305-764 Daejeon, Korea*

Abstract: A 12-year-old, 8.0 kg, spayed female, mixed-breed dog was presented to the Veterinary Medical Teaching Hospital of Chungnam National University (VMTH, CNU). That case has been growing up mass in her left upper hindlimb about for 2 years and has showed vomiting and anorexia for 3 days. The patient was diagnosed with mast cell tumor on the basis of fine-needle aspiration (FNA) cytology techniques. According to World Health Organization clinical staging system for diagnosing mast cell tumors, it was classified into stage IIIa. The patient was treated by adjuvant corticosteroid therapy, but complete surgical excision was not achieved by owner's request. In the early stage of therapy, the size of the mass was gradually reduced with only adjuvant glucocorticoid therapy, so the patient's general condition was maintained well. But after 53 days later, the treatmant was not effective anymore and mass size was increased. Two months later, she was euthanized because of intermittent vomiting and severe respiratory distress. Splenic mass, duodenal ulceration, liver mass and infiltrated mast cell tumor in upper hindlimb muscle region were found in necropsy examination.

Key words : mast cell tumor, corticosteroid therapy, dog.

Introduction

Mast cell tumors are the most common skin tumors in dogs[3,6-8,12,13]. It has cytoplasmic granules containing several vasoactive substances like histamine, and heparin, which often cause various clinical symptoms such as gastric ulceration and bleeding tendency in the tumor patients[15].

Histopathologic classification and World Health Organization (WHO) clinical staging systems are usually good predictors of lifespan[4]. The best quality of management of local tumor of any grade requires 3 cm surgical margin of surrounding normal tissue with histopathological confirmation of complete excision[1,14]. However, when tumors are not completely excised 3 cm apart from tumor margins, adjunctive chemotherapy with corticosteroids, vincristine, vinblastine, and/or cyclophosphamide and/or radiotherapy is usually applied[2,14].

Corticosteroids usage such as prednisolone and methylprednisolone have been reported for many years because of its effectiveness of reducing local mass size. Glucocorticoid receptors have been identified in the cytosol of canine mast cell tumor (MCT) cells and a recent study demonstrated that corticosteroids inhibits canine mast cell tumor proliferation and probable induces tumor cell apoptosis[14].

This report describes a case of canine mast cell tumor which was medicated with adjuvant corticosteroid therapy.

Case Report

A 12-year-old, 8.0 kg, spayed female, mixed-breed dog was presented to the Veterinary Medical Teaching Hospital of Chungnam National University (VMTH, CNU). That case has been growing up mass in her left upper hindlimb lesion about for 2 years (Fig 1). When she initially presented to local animal hospital, she had clinical signs such as weakness, intermittent vomiting, growing up mass about for 2 years.

On physical examination, the patient had masses in proximal hindlimb, abdominal and forelimb. And moderate cataract and enlargement of inguinal lymph node were also revealed. Diagnostic evaluation included a complete blood count (CBC), serum biochemistry test, survey radiograph and abdominal ultrasound were performed.

Results of the CBC revealed a severe anemia (PCV 20.6%, reference range 37 to 55%) and lymphocytosis (21.78×10^3 cells/μl, reference range 3.0 to 11.8×10^3 cells/μl). The serum

Fig. 1. The figure shows large mass in proximal hindlimb region.

[1]Corresponding author.
E-mail : mckim@cnu.ac.kr

biochemistry profile revealed increase of blood urine nitrogen (50.9 mg/dl, reference range 7 to 20 mg/dl) and moderately elevated glucose (205.2 mg/dl, reference range 60 to 115 mg/dl). There were no other abnormal findings except above problem.

In thoracic radiographs, there were no evidence of metastatic disease. In abdominal radiographs, there were approximately 0.5 cm shotgun bullet in her caudal thigh muscle. Abdominal ultrasound revealed a slightly enlarged spleen and hyperechoic solitary mass in the abdomen.

The dog was diagnosed with mast cell tumor on the basis of fine-needle aspiration (FNA) cytology techniques. Fine-needle aspirates were performed in the proximal forelimb mass with 22-gauge, 3cc syringe needle. According to World Health Organization clinical staging system for mast cell tumors, it was classified into stage IIIa (multiple dermal tumors; large infiltrating tumors with or without regional lymph node involvement, without systemic signs) (Fig 2). When the mass size was measured by a caliper, the biggest mass size was 8.8 by 7.7 cm in length and width.

Due to the history of mast cell tumor, the dog was maintained on intravenous fluid therapy (Lactated Ringer's solution, maintenance 40 ml/kg/day), cimetidine 10mg/kg IV, methylprednisolone 30 mg/kg IV, ampicillin 20 mg/kg IV and sucralfate 1000 mg (after 2 hours meal). All of these drugs were given three times a day.

And corticosteroid injection to intra-tumor was followed for the decrease of local mass size. The dog was still depressed but she had a little appetite. After 2 days later, mass size got smaller (8.0×6.0 cm). After 3 days hospitalization, the dog was discharged.

The therapeutic options of mast cell tumors are surgery and chemotherapy or radiation therapy. These protocols were suggested to the owners, but declined. The dog was medicated with prednisolone 20 mg/m^2 sid PO, cimetidine 10 mg/kg, amoxicillin 30 mg/kg and sucralfate 1 g (after 2 hours meal) tid PO for 2 weeks. Prednisolone dose was reduced in 10 mg/m^2 sid PO for 7 days, and maintained with 10 mg/m^2 PO every other day.

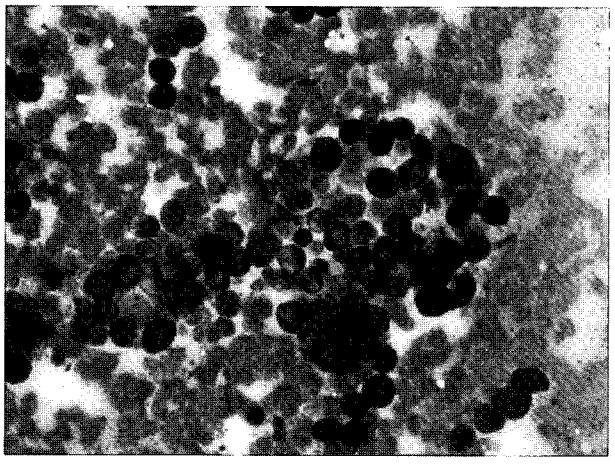

Fig. 2. The figure shows fine needle aspiration (FNA) of a skin nodule reveals poorly differentiated mast cells with metachromatic granules.

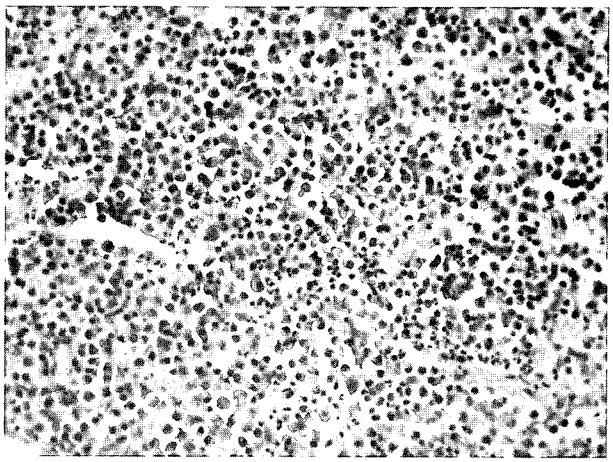

Fig. 3. The figure shows histologically aggregates of poorly-differentiated mast cells in the skin.

She maintained a good appetite and good condition for 2 months. The dog was re-hospitalized because of emergency condition after 2 months. The biggest mass size was 9.7×9.0 cm, and it was very firmly palpated and massively enlarged from the hip to the stifle. And the dog's general conditions got worsen day by day. She was vomited frequently, reluctant to eat, bleed around the tumor and pulmonary distress. The owners chose euthanasia and granted postmortem examination.

At gross necropsy, there was a ovoid, big splenic nodule was identified in the spleen, duodenal ulceration, liver mass and infiltrated mast cell tumor in proximal hind limb muscle region. On histopathology of the skin, the mast cell tumor among dermal collagen fibers generally forms thin cords, showing focal areas of necrosis and aggregates of poorly-differentiated mast cells (Fig 3). Within the spleen, the anaplastic, metastatic and poorly granulated mast cells observed.

Discussion

Well-differentiated or intermediately-differentiated canine cutaneous mast cell tumor often responds to glucocorticoid therapy[15]. Glucorticoids may also contribute to apparent antitumor response by decreasing peritumoral edema and inflammation. It seems to have equal or inhibitory effects on the tumor growth than antineoplastic agents such as cyclophosphamide and vincristine[4]. However, it is thought that poorly differentiated mast cell tumor cells may lose glucocorticoid receptors and therefore may be resistant to glucocorticoid therapy[9]. And intestinal mast cell tumors rarely respond to various treatments including surgery and chemotherapy[10].

In this case, the options of left hindlimb amputation and chemotherapy or radiation therapy were presented to owners, but they denied. They thought that surgery or chemotherapy increased the dog's pain, so they chose on adjuvant corticos-

teroid therapy. Statistically, dogs with grade III and poorly differentiated mast cell tumors typically die of disease within 6 months due to local recurrence or distant metastases[5]. Grade III mast cell tumors are anaplastic and infiltrative, with aggressive local and systemic behavior. Local therapies, such as surgery or radiation therapy alone, are not adequate for dogs with grade III tumors[11].

If the owners had started the initial therapy of mast cell tumors when marked in a grade I or II and histologically well-differentiated, a better prognosis for cutaneous mast cell tumor recovery may be demonstrated a good outcome after surgical amputation of the hindlimb.

Acknowledgements

We thank Dr. Choo Young Jae, Choo Young Jae Animal Hospital to refer us. This work was supported by grant No. R11-2002-100-00000-0 from ERC program of the Korea Science & Engineering Foundation.

References

1. Angela EF, Antony SM, Susan ML, John MG, Amy EB. Radiotherapy of Incompletely Resected, Moderately Differentiated Mast Cell Tumors in the Dog: 37 Cases (1989-1993), J Am Anim Hosp Assoc 1997; 33, 320-324.
2. Chick W, Frances SS, Karin S. Recurrence Rates and Sites for Grade II Canine Cutaneous Mast Cell Tumors Following Complete Surgical Excision. J Am Anim Hosp Assoc 2002; 38, 71-73.
3. David M, Harvey HJ, Lois R, Donald RC. Clostridial peritonitis associated with a mast cell tumor in a dog, J Am Vet Med Assoc 1986; 188, 188-190.
4. David RD, Kenneth MW, John EJ, Ian DR, Peter JI. Vinblastine and Prednisolone as Adjunctive Therapy for Canine Cutaneous Mast Cell Tumors. J Am Anim Hosp Asooc 2004; 40, 124-130.
5. Heather MM, Carolyn JH, Kathleen P, Jeff WT, Michael SB. Cutaneous Mast Cell Tumors in Cats: 32 Cases (1991-1994). J Am Anim Hosp Assoc 1998; 34, 281-284.
6. Howard DM, Daniel DL, Sylvia LL, Elliott RJ. Gastric mast cell tumor in a cougar, J Am Vet Med Assoc 1985; 187, 1258-1260.
7. Jane MT, Barbara EK, Lisa MM, Alain T. Prognostic factor for radiation treatment of mast cell tumor in 85 dogs, J Am Vet Med Assoc 1988; 193, 936-940.
8. Laura DK, David MV, William CK, Gregory KO, Lynn MV. Frequency of argyrophilic nucleolar organizer regions in fine-needle aspirates and biopsy specimens from mast cell tumors in dogs, J Am Vet Med Assoc 1996; 209, 1418-1420.
9. Lisa EM, Laura DG, Brad D, David SB. Spinal Mast Cell Tumor in a Dog. J Am Anim Hosp Assoc 2002; 38, 67-70.
10. Michels GM, Knapp DW, DeNicola DB. Prognosis following surgical excision of canine cutaneous mast cell tumors with histopathologically tumor-free versus non-tumor-free margins. J Am Anim Hosp Assoc 2002; 38, 458-466.
11. Renee AS, GNeal GM, Amiya KP, Karri AM. A prospective Study of Radiation Therapy for the treatment of grade 2 mast cell tumorsin 32 dogs. J Vet Intern Med 1996; 10, 376-378.
12. Ronald LG, Giovanni DG, Caroline BS, Begonia P, Ronald M, David FM, Mari T. Mast Cell tumor destruction by deionized water. Am J Vet Res 1990; 51, 1116-1120.
13. Simoes JP, Schoning P, Butine M. Prognosis of Canine Mast Cell Tumors: A Comparison of Three Methods. Vet Pathol 1994; 31, 637-647.
14. Tamotsu I, Naohiro T, Par G, Eckard H, Akihiro O, Gary RF, Gary LJ, Erwin WG. Mast cell tumor necrosis factor a production is regulated by MEK kinases. Proc Natl Acad Sci 1997; 94, 6358-6363.
15. Tomoko T, Tsuyosi K, Masayuki N, ManabuM, Satoru M, Ryohei N, Nobuo S. Inhibitory Effects of Glucocorticoids on Proliferation of Canine Mast Cell Tumor. J Vet Med Sci 1997; 59, 995-1001.

Canine Mast Cell Tumor에서 Adjuvant Glucocorticoids 치료

김명진 · 이재일 · 김영석 · 손화영 · 전무형 · 박창식* · 김명철[1]
충남대학교 수의과대학
*충남대학교 동물자원학부, 형질전환복제돼지연구센터

요 약: 구토와 식용부진을 3일전부터 나타내고, 2년전부터 좌측 후지 상부에 종괴를 갖고 있는 12년령, 8.0 kg, 난소제거 잡종 암캐 1두가 충남대학교 부속동물병원에 내원하였다. 환자는 fine-needle aspiration (FNA) 세포진단학 검사에 의하여 mast cell tumor로 진단하였다. Mast cell tumor 진단을 위한 WHO clinical staging system에 의하여 stage IIIa로 분류하였다. 환자는 adjuvant corticosteroid 요법에 의하여 투약되었으며, 축주의 요구에 의하여 완전 외과절제는 실시하지 아니 하였다. 초기에 adjuvant corticosteroid 단독 요법에 의하여 종괴의 크기가 점차 감소하였으며, 환자의 전신상태는 호전되었다. 그러나 그 후에는 더 이상 glucocorticoid에 반응을 하지 아니 하였으며, 종괴의 크기가 증가하였고, 2개월 후에 간헐적 구토와 심한 호흡곤란 때문에 안락사 하였다. 비장 종괴, 십이지장 궤양, 간 종괴와 후지 상부 근육부위에 침윤된 mast cell tumor가 부검 시에 발견되었다. Mast cell tumor는 grade I 또는 II에서 그리고 조직학적으로 well-differentiated된 상태에서 외과적 완전절제, 방사선요법, adjuvant corticosteroid 요법, 화학요법을 병용 하여야 양호한 예후를 나타낼 것으로 기대된다.

주요어 : mast cell tumor, corticosteroid 요법, 개.