

## Extreme Leukemoid Reaction in a Dog with Pyometra

Jae-Ik Han, Hye-Jin Jang, Kwi-Ho Jun\*, Hyun-Gu Kang and Ki-Jeong Na<sup>1</sup>

Veterinary Medical Center, College of Veterinary Medicine, Chungbuk National University, Cheongju 361-763, Korea

\*Su Animal Hospital, Cheongju 361-750, Korea

(Accepted : November 25, 2009)

**Abstract :** Leukemoid reaction has been rarely encountered in dogs. This report describes a case of leukemoid reaction showing extremely elevated leukocyte count. A 10-year-old female Maltese dog was presented with purulent and bloody vaginal discharge. The CBC revealed severe leukemoid reaction ( $976 \times 10^9$  cells/l, reference range 6 to  $17 \times 10^9$  cells/l) and mild non-regenerative anemia. On the blood smear, elevated leukocytes consist of numerous neutrophils and monocytes only. Radiographic and ultrasonographic examinations revealed generalized enlargement of the uterus, which was filled with a complex fluid. After ovariohysterectomy, *Escherichia coli* was isolated from the uterine fluid. To author's knowledge, it is the new record of extreme leukemoid reaction caused by local bacterial infection in dogs.

**Key words :** leukemoid reaction, dog, pyometra, *Escherichia coli*.

### Introduction

Leukemoid reaction, where the total leukocyte concentrations exceed  $50 \times 10^9$  cells/l, is rarely encountered in dogs and cats (3). Increased granulopoiesis in the marrow, spleen and liver is the primary cause of leukemoid reaction and is usually the result of the release of granulocyte colony-stimulating factor (G-CSF) during infection, inflammation or neoplasia (6-10,13,14). While these extremely elevated leukocyte counts could lead to a misdiagnosis of leukemia, leukemoid reaction can be recognized because the leukogram reveals that the predominant leukocytes are segmented and earlier neutrophils (3).

This case report describes the new record of the leukemoid reaction in a dog with pyometra. Total leukocyte concentration in this case was extremely elevated nearly four times higher than previous report.

### Case

A 10-year-old female Maltese dog was presented with progressive weakness and a purulent vaginal discharge that was mixed with blood. Samples for CBC and serum biochemical analyses were collected from the cephalic vein. The animal had not been treated for the problems prior to presentation.

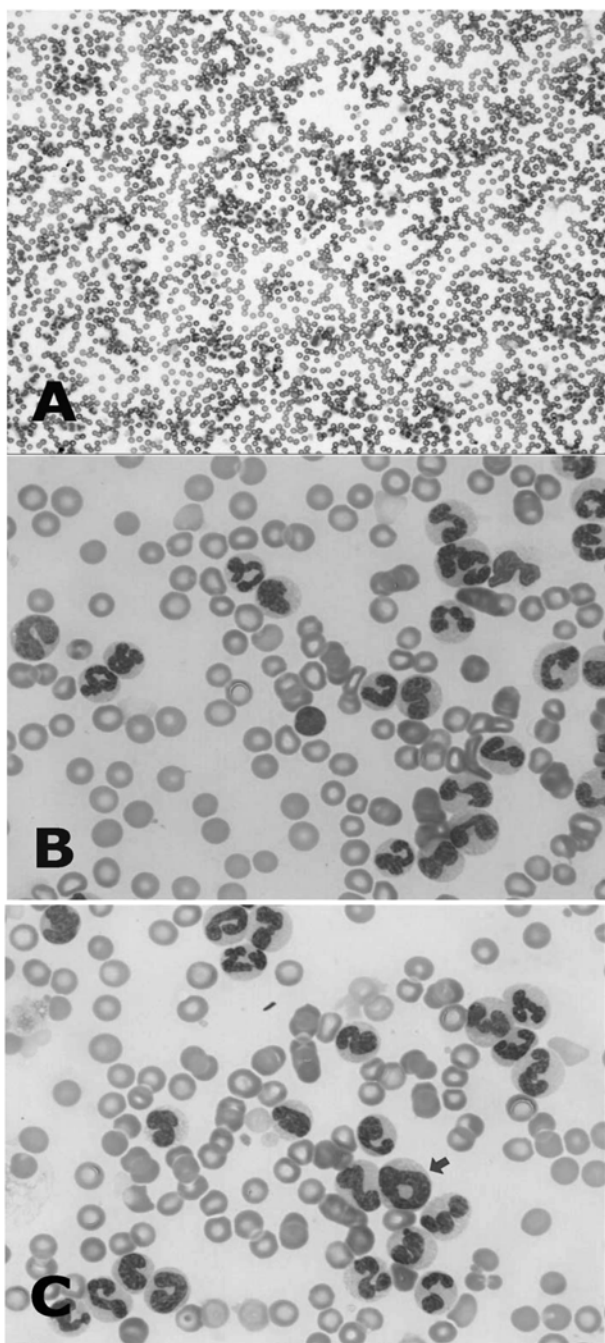
A manual CBC was performed three times because the WBC numbers exceeded the upper limit that could be detected by the HemaVet 850 machine (range 0.1 to  $200 \times 10^9$  cells/l; Drew Scientific, Farmington, CT, USA). The CBC revealed extreme leukocytosis ( $976 \times 10^9$  cells/l, reference range 6 to

$17 \times 10^9$ /l) with neutrophilia ( $790 \times 10^9$  cells/l) and monocytosis ( $136 \times 10^9$  cells/l); mild non-regenerative anemia ( $4.62 \times 10^{12}$  cells/l, reference range 5.5 to  $8.5 \times 10^{12}$  cells/l); and thrombocytopenia ( $1.31 \times 10^{11}$  cells/l, reference range 2.0 to  $5.0 \times 10^{11}$  cells/l). On the blood smear, numerous neutrophils with a left shift and monocytes were observed. Toxic neutrophils and metamyelocytes were occasionally detected, but myeloid or erythroid precursor cells were not found (Fig 1). Serum biochemistry abnormalities (7020 Automatic Analyzer, Hitachi high-Technologies Corporation, Japan) were also detected. They included azotemia (creatinine 48 mg/l, reference range 5-15 mg/l; BUN 2370 mg/l, reference range 70-250 mg/l); hyperbilirubinemia (11 mg/l, reference range 1-5 mg/l); hypoalbuminemia (18 g/l, reference range 26-33 g/l); increased ALP (1501 IU/l, reference range 29-97 IU/l); hyperphosphatemia ( $> 200$  mg/l, reference range 26-62 mg/l); hyponatremia (114 mmol/l, reference range 141-152 mmol/l); and hyperkalemia (6.8 mmol/l, reference range 4.37-5.35 mmol/l).

Analysis of cytologic samples prepared from the purulent vaginal discharge revealed a number of markedly degenerative neutrophils (about 90% of the nucleated cells) and low numbers of macrophages and RBCs. Intracellular and extracellular rod-shaped bacteria were also observed. Radiographic findings included an enlarged intraabdominal organ with the absence of fetal mineralization. Ultrasonographic examination of the abdomen revealed a generalized enlargement of the uterus, which was filled with a complex fluid. Based on the results of these examinations, this case was diagnosed as pyometra with renal dysfunction.

After ovariohysterectomy, the aspirated fluid from the lumen of the uterus was incubated at 37°C for 3 days in Muller-Hinton broth (Becton Dickinson and Company, Cockeysville, MD, USA) in both aerobic and anaerobic conditions. After 3

<sup>1</sup>Corresponding author.  
E-mail : sigol@cbnu.ac.kr



**Fig 1.** Blood smear from the patient with extreme leukocytosis. (A) A number of leukocytes, mainly neutrophils and monocytes, were detected.  $\times 10$  objective. (B) The elevated leukocytes consist of mature or immature neutrophils (band cells and metamyelocytes), and monocytes.  $\times 100$  objective. (C) Occasionally, toxic neutrophils (arrow) were detected.  $\times 100$  objective. Wright-Giemsa stain.

days, the cultured broths were repeatedly pure-cultured and the isolated colonies were subjected to bacterial identification analysis using the Remel RapID™ ONE System (remel, Lenexa, KA, USA). This revealed that the bacteria were *Escherichia coli* (*E. coli*).

## Discussion

In this report, we describe the new record of the leukocyte concentration of extreme leukemoid reaction, which showed nearly four times higher than previous report, caused by local bacterial infection in a dog. In the veterinary literature, inflammatory diseases such as pyometra, pyothorax and acute pancreatitis are the most likely cause of leukemoid reaction (3). In such cases, the maximal total leukocyte concentration has been reported to be  $125 \times 10^9$  cells/l. In canine hepatozoonosis, maximal total leukocyte concentration of  $200 \times 10^9$  cells/l have been reported (8,9). In neoplasia, maximal total leukocyte concentrations of  $250 \times 10^9$  cells/l have been reported (1,3,6, 13). In our case described here, the total leukocyte count reached  $976 \times 10^9$  cells/l, as determined by repeated manual CBC.

On physical examination, purulent vaginal discharge, which is a typical symptom of open type pyometra (12), was observed. Radiographic and ultrasonographic examinations and surgery then revealed a generalized enlargement of the uterus, which was filled with pus, but other abnormalities were not found. Blood smear analysis generated a leukogram characterized by large numbers of neutrophils and monocytes, but myeloid or erythroid precursor cells were not detected. Thus, we ruled out the possibility of leukemia and consequently, pyometra was identified as the cause of the extreme leukemoid reaction in our case.

In our case, serum biochemical analysis revealed severe azotemia and electrolyte imbalances, despite significant clinical signs were not examined. In bacterial identification, we identified that *E. coli* was a causative bacteria of the pyometra. It has been reported that nephropathy can be induced in cases of pyometra because of the release of bacterial toxin from the uterus (5), and several studies have shown that renal dysfunction can occur in dogs with pyometra (2,4,11). Stone *et al.* also found that *E. coli* is the major causative agent in canine cases of renal dysfunction that is secondary to pyometra (11).

In summary, this report showed a new record of leukemoid reaction caused by local bacterial infection. In our case, the leukocyte concentration was nearly four times higher than the previous report. Veterinary clinicians should pay careful attention to interpret the cause of leukemoid reaction in dogs.

## Acknowledgement

The authors are grateful for support from the 2009 Brain Korea Project.

## References

1. Chinn DR, Myers RK, Matthews JA. Neutrophilic leukocytosis associated with metastatic fibrosarcoma in a dog. *J Am Vet Med Assoc* 1985; 186: 806-809.
2. De Schepper J, De Cock I, Capiu E. Urinary gamma-glutamyl transferase and the degree of renal dysfunction in 75 bitches with pyometra. *Res Vet Sci* 1989; 46: 396-400.

3. Gaunt SD. Extreme neutrophilic leukocytosis. In: Schalm's Veterinary Hematology, 5th ed. Philadelphia: Lippincott Williams & Wilkins. 2000: 347-349.
4. Heiene R, Kristiansen V, Teige J, Jansen JH. Renal histomorphology in dogs with pyometra and control dogs, and long term clinical outcome with respect to signs of kidney disease. *Acta Vet Scand* 2007; 49: 13.
5. Kaymaz M, Bastan A, Erunal N, Aslan S, Findik M. The use of laboratory findings in the diagnosis of CEH-pyometra complex in the bitch. *Turk J Vet Anim Sci* 1999; 23: 127-133.
6. Lappin MR, Latimer KS. Hematuria and extreme neutrophilic leukocytosis in a dog with renal tubular carcinoma. *J Am Vet Med Assoc* 1988; 192: 1289-1292.
7. Lobetti RG. Leukemoid response in two dogs with *Babesia canis* infection. *J S Afr Vet Assoc* 1995; 66: 182-184.
8. Macintire DK, Vincent-Johnson N, Dillon AR, Blagburn B, Lindsay D, Whitley EM, Banfield C. Hepatozoonosis in dogs: 22 cases (1989-1994). *J Am Vet Med Assoc* 1997; 210: 916-922.
9. Panciera RJ, Ewing SA. American canine hepatozoonosis. *Anim Health Res Rev* 2003; 4: 27-34.
10. Sharkey LC, Rosol TJ, Grone A, Ward H, Steinmeyer C. Production of granulocyte colony-stimulating factor and granulocyte-macrophage colony-stimulating factor by carcinomas in a dog and a cat with paraneoplastic leukocytosis. *J Vet Intern Med* 2008; 10: 405-408.
11. Stone EA, Littman MP, Robertson JL, Bovee KC. Renal dysfunction in dogs with pyometra. *J Am Vet Med Assoc* 1988; 193: 457-464.
12. Sumner-Smith G. The diagnosis of "open" and "closed" pyometra in the dog and cat-I: clinical aspects and differential diagnosis. *J Small Anim Pract* 2008; 6: 429-435.
13. Thompson JP, Christopher MM, Ellison GW, Homer BL, Buchanan BA. Paraneoplastic leukocytosis associated with a rectal adenomatous polyp in a dog. *J Am Vet Med Assoc* 1992; 201: 737-738.
14. Weltan SM, Leisewitz AL, Goddard A. A case-controlled retrospective study of the causes and implications of moderate to severe leukocytosis in dogs in South Africa. *Vet Clin Path* 2008; 37: 164-172.

## 자궁축농증 있는 개에서의 심한 백혈병성 반응

한재익 · 장혜진 · 전귀호\* · 강현구 · 나기정<sup>1</sup>

충북대학교 동물의료센터 · \*수동물병원

**요 약** : 개에서 백혈병성 반응은 흔하지는 않다. 이 것은 백혈구가 많이 증가하여 백혈병성 반응을 보이는 증례이다. 10년령의 암컷 말티즈로 화농성의 혈액섞인 질 분피물이 있었다. 전체혈구계산에서 백혈병성 반응( $976 \times 10^9$  cells/l)을 나타내고 비 재생성 빈혈이 있었다. 혈액도말검사에서 증가된 백혈구는 호중구와 단핵구만 나타났다. 방사선 및 초음파검사서 자궁은 확장되고 복합적인 액체가 차있는 것이 확인되었다. 자궁절제술 이후에 *E. coli*가 자궁내 액체로부터 분리되었다. 저자의 조사에 의하면 국소감염의 예에서 이와 같이 극도의 백혈병성 변화를 보이는 것은 처음이다.

**주요어** : 백혈병성 반응, 개, 자궁축농증, *Escherichia coli*.