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Acute Respiratory Distress Syndrome Related with Blood Transfusion in a Dog with Chronic Kidney Disease

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Abstract : An 11-year-old intact male Yorkshire terrier had intermittent vomiting, anorexia and depression for a month. Clinical laboratory works showed azotemia and anemia. Chronic kidney disease with developing anemia was diagnosed clinically. Clinical signs were resolved but anemia was deteriorated and blood transfusion was performed. On 10 hours after transfusion, the dog showed acute respiratory distress. Transfusion related acute respiratory distress syndrome (ARDS) was diagnosed based on acute clinical signs, risk factors of transfusion, bilateral alveolar infiltration on thoracic radiographs, and PO_2:FiO_2 ratio less than 200 on arterial blood analysis. The dog died within 2 hours after ARDS diagnosis.

Key words : chronic kidney disease, blood transfusion, acute respiratory distress syndrome, dog.

Introduction

Acute lung injury (ALI) or acute respiratory distress syndrome (ARDS) is characterized by acute injury to the lungs that results in impaired gas exchange and alveolar pulmonary edema (4,24). ALI or ARDS can be commonly triggered by bacterial pneumonia, aspiration pneumonia, sepsis, or shock in dogs (16,17). Among predisposing factors of ALI or ARDS, blood transfusion related ALI or ARDS is an uncommon but fatal syndrome characterized by the sudden onset of respiratory failure within hours of the blood transfusion (12,20). This case report describes the development and clinical characteristics of ARDS after transfusion in a dog with chronic kidney disease.

Case

An 11-year-old intact male Yorkshire terrier with 2.52 kg was admitted with a history of intermittent vomiting and depression for over a month. The hematologic and clinical chemistry works showed increased WBC of $21200 \times 10^3/\mu L$ (normal: $6000\sim17000 \times 10^3/\mu L$), blood urea nitrogen (BUN) level of 97 mg/dl (normal: 7~27 mg/dl), creatinine level of 3.8 mg/dl (normal: 0.5~1.3 mg/dl), and phosphorus level of 6.6 mg/dl (normal: 3~6.2 mg/dl). Hematocrit was decreased with 23.9% (normal: 37~55%). There was electrolyte imbalance with Na^+ 163.6 mmol/L (normal: 135~155 mmol/L), K^+ 4.35 mmol/L (normal: 3.5~5.8 mmol/L), and Cl^- 133.9 mmol/L (normal: 105~120 mmol/L). Other clinical blood including albumin level of 2.4 g/dl and total protein 5.2 g/dl

were within normal limits. Urinalysis showed lower urine specific gravity of 1.012 (normal: 1.015 to 1.040) without proteinuria. Urine protein to creatinine (UP/C) ratio was under 0.2. Abdominal ultrasonographs revealed bilateral irregular small kidneys with hyperechoic cortex. Therefore chronic kidney disease (Iris staging 3) and normochromic normocystic anemia developing from decreased renal synthesis of erythropoietin were diagnosed clinically. The dog was hospitalized and had supportive care including daily maintenance fluid, force feeding through nasoesophageal tube, darbepoietin alfa (0.45 ug/kg sc once weekly) as an erythropoiesis stimulating agent, metoclopramide (0.25 mg/kg bid) as an antiemetics, and famotidine (0.25 mg/kg bid) as a H2 receptor antagonist. For four days of hospitalization, vomiting was resolved and appetite was recovered and creatinine level was slightly decreased with 3.5 mg/dl. However anemia was deteriorated with manual PCV 18. Blood transfusion was performed. Blood type of this dog was DEA 1.1. Transfusion with packed RBCs of canine DEA 1.1 was performed after cross matching. There were no any complications, such as weakness, vomiting, allergic reaction, fever, or hemolysis during and after intensive monitoring of transfusion. PCV was 30 after transfusion. However, on 10 hours after transfusion, this dog showed acute respiratory distress. This dog had O_2 therapy through oxygen collar method in the sternal recumbency. Thoracic radiographs revealed severe diffuse homogeneous alveolar infiltration in the bilateral lung lobes (Fig 1). There were no remarkable findings, such as hemorrhage or ascites, on abdominal radiographs and ultrasonographs. Hematology and clinical chemistry were still not remarkable except mildly decreased creatinine with 2.53 mg/dl. The analysis of arterial gas showed low PaO_2 40 mmHg (normal: 90~100 mmHg), pH 7.27 (normal: 7.36~7.44), HCO_3

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21.7 mmol/L (normal: 24~26 mmol/L), tHb 7.4 (normal: 12~18), and SO_2 60% (normal: 93~100%). PCO2 51 mmHg (normal: 36~44 mmHg), anion gap 31.5 mmol/L (normal: 8~25 mmol/L), and Na+ 165 mmol/L (normal: 144~160 mmol/L) were increased. Increased arterial PCO_2 and decreased pH indicated acute respiratory acidosis. FiO_2 was considered to be 0.3~0.7 based on the oxygen supply method in this dog. Calculated PO_2:FiO_2 ratio was 57.1~133.3 mmHg. Therefore, ARDS was diagnosed through acute respiratory signs, risk factors of transfusion, bilateral alveolar infiltration of the thorax on radiographs, and PO_2:FiO_2 ratio of less than 200 on arterial blood gas analysis. The dog was deteriorated rapidly in spite of intensive oxygen therapy under sternal recumbency. During preparing mechanical ventilation, the dog died within two hours of ARDS diagnosis.

Discussion

Acute lung injury (ALI) or acute respiratory distress syndrome (ARDS) is acute, severe, life-threatening clinical syndrome of impaired gas exchange, which results in bilateral pulmonary inflammation and edema (4,24). ARDS is the most severe form of ALI and defined by a ratio of arterial oxygen to fraction of inspired oxygen of 200 mmHg or less (4,24). The predisposing factors of ALI or ARDS can divide direct pulmonary insult and extrapulmonary systemic disease. Primary lung injury includes pneumonia (9,16,17), pulmonary trauma (9), lung lobe torsion (15), inhalant toxicosis (e.g., smoke) (16,17). Secondary lung injury includes sepsis (16,17), shock (16,17), pancreatitis (11), toxicosis (e.g., bee envenomation) (21), disseminated intravascular coagulation (16,17), and transfusion (20). Transfusion related ALI or ARDS are uncommon in both human and veterinary medicine, but may be leading cause of transfusion related mortality (12,20). Transfusion related ALI is classified into classic and delayed patterns in human medicine (12). Classic pattern is characterized by time onset within two hours, resolving course in 48~96 hours, and relatively low mortality. While delayed pattern shows time onset of 6~72 hours, slow resolving course or progressive development of severe ARDS, and relatively high mortality (12). Pathophysiology of classic and delayed patterns may be antineutrophil antibodies and bioactive mediators, respectively. Antineutrophil antibodies react with pulmonary microvascular neutrophils and these lead to endothelial damage and vascular leakage into the alveolar space. Hypothesis of bioactive mediators suggests that lipids or other mediators, such as CD40L, activates neutrophils and contributes to endothelial damage, especially in patients with accumulation of neutrophils in the pulmonary microvasculature as result of preexisting systemic inflammation. These lead to vascular leaks and pulmonary edema (10,12,22). This dog showed time onset of 10 hours after transfusion, progressive development of ARDS, and death in spite of intensive care. Therefore delayed pattern of transfusion related ARDS was considered and main pathophysiology could be bioactive mediators in this dog. Critically ill patient may have higher risk of development of ALI and ARDS with poor prognosis (3,16,17). This dog had chronic kidney disease with developing anemia by failure of renal synthesis of erythropoietin. These conditions of this dog may predispose rapid deterioration of ARDS and death.

The diagnosis of ALI and ARDS is based on the following criteria in human and veterinary medicine: acute onset of respiratory distress within 72 hours, identifiable risk factors including direct or secondary pulmonary injury, bilateral or diffuse infiltration on thoracic radiographs or computed tomography without evidences of cardiogenic pulmonary edema, and analysis of arterial blood gas; a PaO_2:FiO_2 ratio of less than 300 indicates ALI, while a PaO_2:FiO_2 ratio of less than 200 is diagnostic of ARDS (4,24). Thoracic radiographic signs are variable depending on the severity and staging of ARDS. The most common findings are bilateral or diffuse alveolar infiltration (8,13,19,23). In human medicine, the early exudative phase of ARDS (about 1~7 days of time onset) have bilateral homogeneous alveolar infiltration and a central perihilar ("bat-wing") consolidative appearance with sparing of lung periphery (8,13,19,23). Abnormal radiographic signs of ARDS remains usually static for the long periods. In the proliferative or intermittent phase of ARDS (about 8~14 days of time onset), thoracic radiographs have diffuse coarse reticular interstitial pattern. During this period, new alveolar infiltration is likely to represent superadded infection or other complications besides ARDS process. Most pulmonary infiltrations begin to resolve in fibrotic or late phase of ARDS (above 15 days of time onset), showing variable duration and speed (8,13,19,23). This dog also had severe bilateral homogeneous alveolar infiltration and central consolidative appearance with sparing of lung periphery. These findings can represent severe early exudative phase of ARDS. Other possible causes of alveolar infiltrations, such as pneumonia, diffuse alveolar hemorrhage, pulmonary thromboembolism, or other non-cardiogenic pulmonary edema, were clinically ruled out because there were no additional risk factors or any change of hematologic and chemistry before and after transfusion. Thoracic radiographs of pulmonary thromboembolism show usually normal and uncommonly arterial dilation, hyperlucency, pleural based wedge shaped infiltration, or patchy regional alveolar interstitial pattern (5). Therefore, acute severe bilateral homogeneous alveolar infiltration with sparing of lung periphery in this dog can represent ARDS. Computed tomography (CT) provides more detailed information in pulmonary lesions in human medicine. CT is an effective modality of confirming the diagnosis of ARDS, evaluating the staging of ARDS, and identifying complications of ARDS. CT may have a potential role as a means of prognosticating in ARDS (19). In veterinary medicine, CT has not been used for routine diagnostic tool of ARDS, but may become an important modality by increased recognition and management of ARDS soon.

No drug has proved effective in the prevention or treatment of ARDS. In human medicine, prone position (ventral recumbency) helps to improve oxygenation and respiratory mechanics, to homogenise the pleural pressure gradient, alveolar inflation, and ventilation distribution, to increase lung volume and reduce the amount of atelectatic regions, to facilitate the drainage of secretions, and to reduce ventilator-associated lung injury (18). In veterinary medicine, sternal recumbency also increases PaO_2 significantly (14). Mechani-
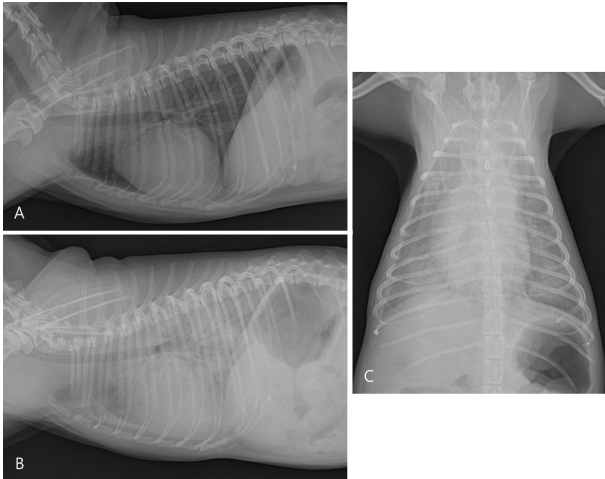
Fig 1. Thoracic plain radiographs. A: right lateral view, the dog has a nasoesophageal tube before transfusion, B and C: right lateral (B) and ventrodorsal (C) views, there are bilateral alveolar infiltration and central distribution with sparing of periphery after transfusion.

cal ventilation may be the most beneficial treatment for ARDS (1,2,6,7,9). Pulmonary protective ventilator strategies include lowering tidal volume, limiting driving pressures to less than 20 cmH$_2$O above the selected PEEP values, lung recruitment maneuvers, permissive hypercapnia, and preferential use of pressure-limited ventilatory cycles. Alveolar over-distension and end-expiratory collapse should be prevented during mechanical ventilation because these can lead to poor patient outcome (1,2,6,7,9). Unfortunately, mechanical ventilation was not performed in this dog because of rapid deterioration of lung injury.

The prognosis of ALI and ARDS may depend on timely diagnosis, the severity of lung injury, and intensive care. However, very few dogs have reported as survivors from ARDS in veterinary medicine. Especially critically ill patients have reported more poor prognosis (3,16,17). However, recently, survivors from ARDS have increased with early recognition, timely diagnosis, and prompt intensive care in veterinary medicine (9).

In conclusion, ARDS should be considered in cases showing clinical signs of acute respiratory distress by risk factors of primary or secondary lung insult. Thoracic radiographs of bilateral alveolar infiltration with central distribution helps to diagnose tentatively. Intensive oxygen therapy or pulmonary protective mechanical ventilation should be needed promptly. This case describes transfusion related ARDS and may help further diagnosis and management in veterinary medicine.

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만성신장질환 개에서 수혈과 관련된 급성호흡곤란증후군

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요　약 : 한달간 간헐적인 구토, 식욕부진과 침울을 보인 11살의 중성화하지 않은 수컷 요크셔 테리어견이 내원하였다. 혈액검사상 질소혈증과 빈혈을 나타내었으며, 만성신장질환과 이로 인한 빈혈 상태로 진단이 되었다. 임상 증상 및 질소혈증은 다소 감소하였으나 빈혈은 악화되었기 때문에 수혈을 실시하였다. 수혈 동안 환자의 상태는 양호하였으나, 수혈 후 10 시간째 환자는 급성 호흡곤란 증상을 보였다. 이 환자는 급성 호흡곤란의 임상 증상을 보인점, 수혈의 위험 요인들, 흉부 방사선사진에서 좌우 미만성의 폐포 침윤, 동맥혈 분석에서 200 미만의 PO_2:FiO_2 비율을 바탕으로 수혈과 관련된 급성호흡곤란증후군으로 진단이 되었으며, 이 증상을 보인후 2시간후 폐사하였다.

주요어 : 만성신장질환, 수혈, 급성호흡곤란증후군, 개