Crossed Fat Embolism in a Cow with Tetralogy of Fallot

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ABSTRACT. A 10-month-old, female Holstein-Friesian cow with tetralogy of Fallot died during surgery for ameliorating pulmonary stenosis. Necropsy revealed no fracture of bones. Microscopically, fat emboli in the capillaries were detected in the brain, kidney, lung, adrenal gland and pituitary. In the kidney, many fat emboli were present in the glomeruli. No significant changes of the neurons were found throughout the brain, and perivascular hemorrhage and/or necrosis were rarely seen accompanying with fat emboli in the cerebral cortex. The trigger for fat embolism might be cæstotomy, and right-to-left shunt due to heart malformation might be attributed to crossed and systemic distribution of the fat emboli.—KEY WORDS: bovine, cardiac malformation, embolism.


Fat emboli have been found histopathologically in almost all patients dying soon after fracture of large bones or after disruptive adipose tissue trauma or burns [2]. They were also identified in a variety of non-traumatic conditions such as diabetes mellitus, sickle cell anemia, decompression sickness and pancreatitis in human [2, 7]. There were a few reports on this pathologic condition in domestic animals. In dogs, fat embolism following surgery for the fracture of the femur or pelvis was reported [5]. Unusual glomerular lipid emboli were also described in a diabetic dog [1]. This report describes systemic fat embolism in a cow with congenital heart disease which died during surgery.

A 10-month-old, female Holstein-Friesian cow weighing about 120 kg was admitted to the Azabu University Veterinary Teaching Hospital with cyanosis, weakness, anorexia, dehydration, cough and purulent nasal discharge. Hematological examination indicated polycythaemia (red blood cell count: 12.6×10⁶/μl, packed cell volume: 50.5%) and leukocytosis (white blood cell count: 10,000/μl). The value of plasma fibrinogen (1,200 mg/dl) and serum creatin kinase (416.3 IU/l) was high. Ultrasonography and phonocardiography indicated tetralogy of Fallot. Urinalysis revealed mild proteinuria. Ten days after the first admission, patch graft surgery was performed to ameliorate pulmonary stenosis under systemic anesthesia with halothane. The animal died during the operation, approximately two hours after cæstotomy in which two costae had been resected by the surgical saw for thoracotomy.

Necropsy confirmed tetralogy of Fallot characterized by interventricular septal defect, pulmonic stenosis, overriding of the aorta and hypertrophy of the right ventricle. Various-sized vegetations caused by bacterial infection were also found in the bicuspid, tricuspid, aortic and pulmonary valves. The lung showed congestive edema with ecchymotic and suffusive hemorrhage. Kidneys were congested with petechiae, and some infarcts were present in the cortex. There were no evidences of fracture of major bones. Tissue specimens were fixed in 10% neutral buffered-formalin and embedded in paraffin. The sections were stained with hematoxylin and eosin (H-E). Periodic acid-Schiff reaction (PAS) and Klüver-Barrera’s stain were also applied on the sections of kidney and brain, respectively. Immunohistochemical examination was made on the kidney and brain using paraffin sections. The kidney sections were digested with 0.25% trypsin for two hr at 37°C followed by incubation with rabbit anti-bovine IgG (Organon Teknika Corporation, PA, U.S.A.). The brain sections were reacted with rabbit anti-human glial fibrillary acidic protein (GFAP) antibody (Bio-Science, Emmenbrucke, Switzerland) or rabbit anti-human von Willebrand factor (VWF) antibody (Dakopatts a/s, Glostrup, Denmark). The latter antibody was applied on the sections digested by 0.1% trypsin for one hr at 37°C. The visualization of the immunoreaction was accomplished by biotynilated goat anti-rabbit IgG and peroxidase conjugated streptavidin (Histofine SAB-PO Kit, Nichirei Corporation, Tokyo, Japan). Small cubes of formalin-fixed kidney specimens were osmicated to stain lipids.

Microscopically, various-sized fat emboli, which appeared as black globules in the sections of osmicated tissue, were present approximately in 30% of the glomeruli in both kidneys (Figs. 1 and 2). Glomeruli in the superficial cortex were predominantly involved. Most glomeruli except sclerotic ones were enlarged with severe congestion and mesangial expansion due to increased matrix and hypercellularity. No IgG-deposition was present in the glomeruli. Some necrotic foci, microabscesses, fibrosis and mononuclear cell infiltration in the interstitium were present. In the lung, a few fat emboli were detected in the septal capillaries (Fig. 3). On the other hand, many heart failure cells were seen in the alveoli associated with edema and hemorrhage. The alveolar walls were thickened due to marked congestion, cellular infiltration and fibroplasia. Neutrophilic infiltration with occasional fibrin depositions was also seen in the alveolar and bronchial lumens. The fat globules were occasionally found throughout the brain, especially in the cerebral cortex (Fig. 4). Sometimes the vascular structure around the fat globules was obscure. However, the globules were surrounded by VWF-positive flattened cells (Fig. 5), which were attached or surrounded by GFAP-positive cellular processes (Fig. 6). Superficial cerebral cortex was edematous, and small hemorrhagic foci were scattered throughout the brain. Perivascular hemorrhage and/or necrosis associated with fat emboli were rarely found in the cerebral cortex (Fig. 7). There were no ischemic
Fig. 1. Multiple fat emboli in the renal glomerulus. Note the vacuoles occluding the capillary lumens and mesangial hypercellularity. PAS. × 228.

Fig. 2. Osmiophilic fat emboli (arrows) in the renal glomeruli. Osmicated renal tissue. H-E. × 224.

Fig. 3. Intracapillary fat globules (arrows) in the thickened alveolar septa. H-E. × 500.

Fig. 4. Fat emboli in the cerebral cortex. H-E. × 448.

Fig. 5. Fat globule surrounded by VWF-positive endothelium (arrow). Immunostaining. × 448.

Fig. 6. Fat globule attached by GFAP-positive cellular proceces. Immunostaining. × 448.

Fig. 7. Hemorrhage and necrotic change around the capillary with fat emboli. H-E. × 328.
changes of the neurons, gliosis and spongy status in the brain. A few fat emboli were also seen in the adrenal cortex and pituitary without any significant lesions.

Mild extramedullary hematopoiesis in the spleen and hydropic degeneration of the hepatocytes were observed. The epithelium of the forestomachs showed mild hyperand parakeratosis. Focal myocardial necrosis with or without cellular reaction and fibrosis was scattered in the heart.

The fat embolism has been attributed to the release of lipids from damaged adipose tissue or bone marrow, where the fat was aspirated into venules or sinusoids [7, 12, 13]. The masses of myeloid tissue in the pulmonary vessels were occasionally found as well as fat globules [7, 9]. However, there is some controversy regarding the origin of the fat. In some instances, the amount of fat in the pulmonary vessels was far more than what might be released from the site of injury [7]. The agglomeration of chylomicrons and fatty acid in the circulation following the release of fat from local sites has been proposed [2]. The trigger of the entry of the fat into the circulation in the present case might be a cecostomy followed by systemic fat embolism during the operation. In the cecostomy, four sites of the two ribs were cut by surgical saw, so that bone marrow tissue might be crushed and be forced to enter into the circulation. In human, fetal intra-operative fat embolism occurred during total hip replacement [6, 8].

For many years the clinical importance of fat embolism has been controversial. The fat embolism syndrome consists of the triad of neurological dysfunction, respiratory insufficiency and petechiae, which occur in only 0.5 to 5% of traumatic cases in human [2]. The overall mortality rate for this condition is 5 to 15% [4]. The obstruction of the cerebral vessels by fat emboli might be important for the cause of death. The release of vasoactive amines and other vasoconstrictive substances from platelets due to activation of coagulation system associating with fat embolism could further contribute to the hypoxemia and cerebral hypoxia [2]. In the present case, we did not perform the special stains for fat on brain tissue. However, immunohistochemical examinations confirmed that the vacuoles occupied the capillaries, suggesting fat embolism as seen in the other organs. In the patients with intracardiac right-to-left shunt, the fat emboli might be of acute clinical importance and cause hyperacute or fulminating symptoms because of the risk of the embolism in vital organs such as brain [3, 9]. Systemic distribution of fat emboli in the present case might be caused by right-to-left shunt due to heart malformation. The significance of fat embolism as a cause of death was not clear in the present case. Bacterial endocarditis and renal abscesses seen in the present case indicated sepsis, which was suggested to be one of the aggravating or triggering pathologic conditions for clinical symptoms in fat embolism [13]. Multifocal myocardial necrosis which might be due to dissemination of septic thrombi from the heart and pulmonary lesions caused by infection and heart failure might be the most important causes of the death of the animal. Systemic anesthesia and tracheotomy might agglomerate the respiratory and circulatory disturbance caused by pulmonary and cardiac lesions.

There was diffuse and global mesangial expansion without IgG deposition on the renal glomeruli in the present case, which might be a secondary manifestation of cyanotic congenital heart disease as previously described in man [11] and in a cat [10].

REFERENCES