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Sertoli Cell Tumor Accompanied by Pancytopenia in a Dog

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Abstract : 11 year old male Yorkshire terrier was referred to Haemaru Referral Animal Hospital with signs of hematuria, petechia, and gynecomastia. Blood works revealed severe leukopenia, moderate anemia and severe thrombocytopenia. On ultrasonography and radiography, mixed echo texture mass was found in abdomen. The abdominal mass was surgically removed, and submitted for histopathology. Histopathologic features of the tissues were consistent with malignant Sertoli cell tumor. Bone marrow aspirates were hypocellular. Serum estrogen concentration was 72.80 pg/ml (normal range for females <15 pg/ml) after surgery. Clinical signs of feminization and hemorrhagic diathesis were attributed to hyperestrinism caused by the tumor. The dog was put on fluid therapy, antibiotics and palliative drugs and survived 2 more weeks after surgery without clinical improvement.

Key words **:** Sertoli cell tumor, pancytopenia, dog

Introduction

Common tumors arising from canine testicles include seminoma derived from germ cells and Sertoli cell tumor and interstitial (Leydig) cell tumor both from sex-cord stroma (1).

Although these tumors can develop in normal testicles, these tumors are predisposed to cryptochidism and according to a report, incidence of Sertoli cell tumor in cryptochid was 20 times higher than in scrotal testes (2). Mixed tumors can also occur (1).

Sertoli cell tumors may be hormonally active and cause signs of hyperestrinism in approximately 20-30 % of the patients with these tumors, which includes feminization, gynecomastia, atrophy of the contra-lateral testicle, squamous metaplasia within the prostate gland, alopecia, and bone marrow suppression (1). It is not proved that estrogen is solely responsible for these signs because in some dogs with signs of apparent hyperestrinism increased serum estrogen can not be demonstrated (3). Bone marrow suppression was reported in about 15 % of hormonally active Sertoli cell tumors (4,5). Prognosis is always grave for dogs with pancytopenia due to myelotoxicity (6).

This report describes a case of malignant Sertoli cell tumor in a cryptochid accompanied by pancytopenia along with typical signs of hyperestrinism.

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Case

11 year old male yorkshire terrier dog was referred to Haemaru animal hospital with a history of gynecomastia, hematuria, and skin petechia. At local hospital the dog was found cryptochidic. At presentation, the appetite of the dog was good without vomiting or diarrhea. Subcutaneous hemorrhage was found in inguinal area, and mammary glands were enlarged (Fig 1).

Blood works revealed severe pancytopenia, which included leukopenia (670/μl; reference range, 5500 - 16900/μl), anemia (4.10 $\times$ $10^6/\mu l$; reference range, 5.50 - 8.50 $\times$ $10^6/\mu l$), and thrombocytopenia (1000/μl; reference range, 175 - 500 $\times$ $10^3/\mu l$). Regeneration was poor (reticulocyte count 9600/μl; reference range, <80 $\times$ $10^3/\mu l$). In blood smear examination there was no platelet clumps found. Serum chemistry results were all within reference limits. On ultrasonography, intra-abdominal mass containing multiple pseudocysts was found (Fig 2). The mass was clearly margined. Because there was no cryptochid found, the mass was considered arising from the cryptochid. There was no evidence of distant or pulmonary metastasis on radiography.

Before surgery the patient was put on antibiotics to prevent septicemia and whole blood transfusion were performed to increase platelet numbers. At surgery the mass was surgically removed (Fig 3) and resected mass was fixed in 10 % neutral buffered formalin, and submitted to Antech Diagnostics for histopathology. During surgery, a bone marrow aspiration from the femoral head was performed and

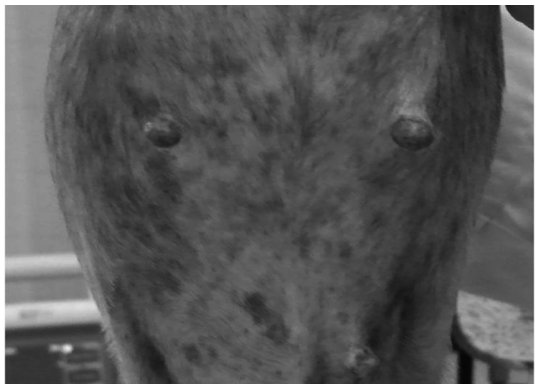

Fig 1. Petechia and ecchymoses on the abdomen with enlarged mammary glands.

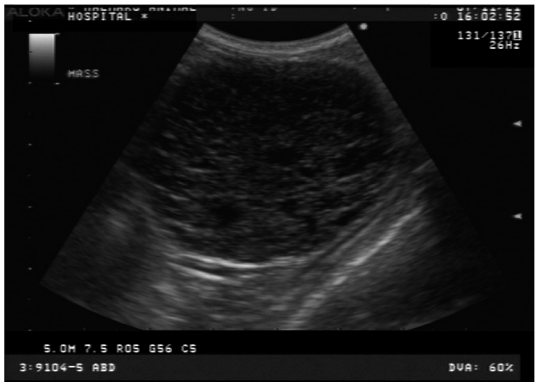

Fig 2. Abdominal ultrasonography revealed a large mass in the abdomen.

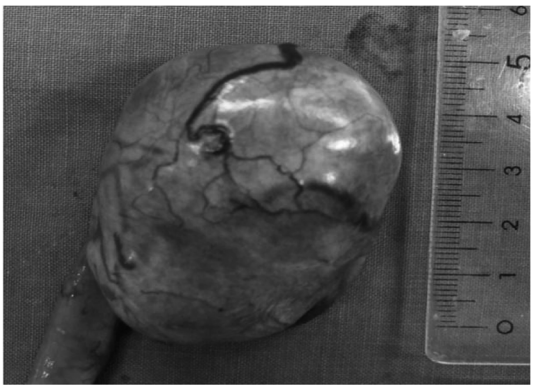

Fig 3. The large abdominal mass at surgery.

evaluated cytologically. Serum sample was also submitted for serum estradiol analysis.

Serum estradiol concentration was 72.80 pg/ml (reference range, <15 pg/ml). Bone marrow smears were hyopcellular and hematopoietic cells were lacking, consistent with pancytopenia. The major cell types seen included mast cells, macrophages, lymphocytes and plasma cells (Fig 4). On histopathologic assessment the mass was composed of cellular islands of varying size separated by abundant dense fibrous stroma. Tumor cells were arranged perpendicular to adjacent fibrous stroma. The tumor cells were polygonal to

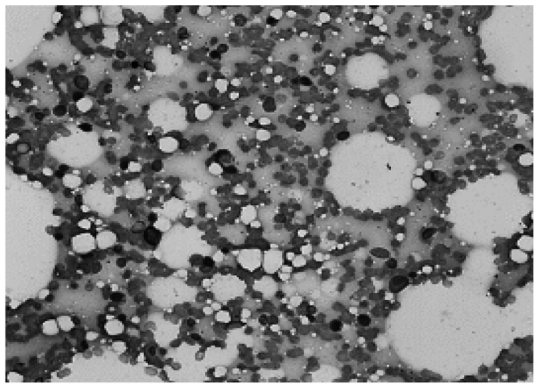

Fig 4. Bone marrow aspirate. Hematopoietic cells are lacking. Marophage, plasma cell and mast cells are evident (Diff-Quik stain, ×40).

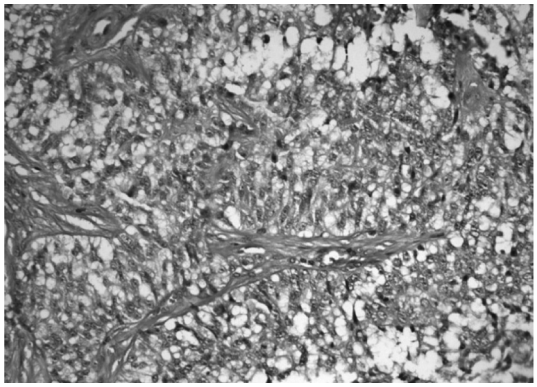

Fig 5. Histology of Sertoli cell tumor. Polygonal to elongate cells were arranged perpendicular to adjacent fibrous stroma (H&E, ×400).

elongate with amphophilic cytoplasm that was sometimes vacuolated. Nuclei were round to ovoid with fine dispersed chromatin and 1 or 2 nucleoli that were prominent (Fig 5). There was mild-moderate anisokaryosis. Neoplastic cells were within the lumen of a small intratumoral vein. Based on these findings the tumor was diagnosed as malignant Sertoli cell tumor.

After surgery, the dog was maintained with antibiotics and palliative drug, but 8 days after surgery, petechia recurred in muzzle, ear and distal ends of legs. On the next day, pleural effusion began to accumulate and the dog became dyspneic and deteriorated. At the owner's request, the dog was euthanized on the 12 th day after surgery.

Discussion

Pancytopenia can develop by various causes that include infectious diseases (parvovirus infection, monocytic ehrlichiosis), medications (estrogen, phenylbutazone, meclofenmic acid, cephalosporin, trimethoprim-sulfadiazine, albendazole, griseofulvin, and quinidine), toxins, exposure to radiation, and tumors (7). There has been some case reports that the identification of the causative factors was not detected, and were

deemed idiopathic (8). In a retrospective study of 9 aplastic pancytopenia cases the underlying causes were ehrlichiosis, Sertoli cell tumor, drugs (griseofulvin, chloramphenicol, antibiotics) and unidentified factors (9). In this report estrogen secreting Sertoli cell tumor was the causative factor. Because estrogen myelotoxicity can be shown in dogs with Sertoli cell tumor and less frequently with Seminoma or interstitial cell tumor (10), testicular tumors should be considered as one of the major differentials of pancytopenia. The exact mechanism that pancytopenia occurs in estrogen is still uncertain, but estrogen may interfere with stem cell differentiation, alteration of iron utilization by erythrocyte precursors and inhibition of the production of circulating erythrocyte-stimulating factor (5).

In myelotoxic dogs, high serum estrogen concentration can be demonstrated but not all dogs with myelotoxic signs show hyperestrogenism (6,10). This may be attributable to the fact that estrogen assays by most laboratories detect only estradiol concentration of the three major forms of estrogen (estrone, estradiol-17β and estriol). Some authors suggested estrogenic materials of unknown structure (3). Recently it has been reported that clinical signs of feminization syndrome were more closely correlated not with serum estradiol concentration but with testosteone/estradol ratios (11). In the present case serum estrogen concentration was approximately 5 times greater than the reference limit, but the testosterone/estradiol ratio was not determined. In cases where serum estrogen concentration is not elevated, testosterone/estradiol ratio may be useful to evaluate the myelotoxicity. In the present case, the increased serum estradiol concentration was after surgical removal of the mass. In previous cases surgical removal of the mass resulted in decreased serum estradiol concentration, but in the present case serum estradiol concentration was still high. This may due to metastasis of the maliganant Sertoli cell tumor, although physical examination and radiography did not detect any metastatic foci.

For treatment the tumor mass, source of estrogen, must be surgically removed (11). To stabilize the patient fluid therapy, whole blood transfusions, platelet rich plasma infusions and broad spectrum bactericidal antibiotics can be given. Other therapeutic options include glucocorticoids, anabolic steroids and hemtinics although the beneficial effects of these drugs are not well known (11). So far whatever the treatment options used, prognosis for dogs with myelotoxicity due to Sertoli cell tumor has been always grave (6). If severe thrombocytopenia persists more than 2 weeks, prognosis is even worse (10). Lithium has been reported to be successful in some cases for treating pancytopenic dogs (12,13). Lithium stimulates division of pluripotent stem cells by an unknown mechanism. The responses may depend on the reserve of bone marrow stem cells (10). In this case it was considered as one of treatment options, but the drug was not available in Korea. In a report cisplatin was responsive to aggressive testicular tumors (14), but it was uncertain whether this drug can reverse myelotoxic effects of estrogen. In the present case, symptomatic therapy was initiated before and after surgery, but the dog's condition did not improved, and the owner elected euthanasia.

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