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Case report

MAMMARY ADENOMA ASSOCIATED WITH CHRONIC MASTITIS IN A WILD BOAR *(SUS SCROFA)*

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Mammary gland tumor is rare and only a few cases have been reported in wild animals. Moreover, most etiologies of the known cases in veterinary medicine are related to age, diet, obesity, and excessive sex hormones in domestic animals while few etiologies are reported in wild animals. An unknown-aged female wild boar was presented to the Department of Veterinary Pathology, Kyungpook National University with a well-demarcated, and firm-to-elastic mammary gland mass. The cut-surface of the mass was pink-reddish, and homogeneous. Microscopically, the mass was mainly composed of well-differentiated neoplastic glandular epithelial cells characterized by a single-layer, columnar to cuboidal shapes, and small and central nuclei and nucleoli. Any evidence of invasiveness or metastases of the neoplastic cells were not observed. Interestingly, infiltration of chronic inflammatory cells such as plasma cells and macrophages was observed along with a large quantity of gram-negative and positive bacterial colonies in the mammary glands. Moreover, accompanied fibrosis of stroma was observed, as well. Based on the gross and microscopic findings, the present case was diagnosed as mammary simple adenoma caused by chronic mastitis progressing to fibrotic condition. To the authors' knowledge, this is the first study describing the histopathological aspects of mammary gland tumors associated with chronic mastitis accompanied by fibrosis in wild animals.

Key words: Adenoma, fibrosis, mammary gland, mastitis, wild boar

INTRODUCTION

Mammary gland tumor is one of the most frequently diagnosed tumors in companion animals such as dogs and cats [1,2]. In veterinary medicine, the development of mammary gland tumor is usually known to be associated with middle-to-older age, excessive hormone exposure, and high-meat diets, and obesity [2]. Therefore, in these animals, mammary gland tumor is likely caused by a frequent ingestion of meat, humanized lifestyle, and increased life expectancy due to advanced medical-care services. In contrast, a low incidence of mammary gland tumors has been reported

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in industrial animals, including cows, mares, ewe, as most of these animals eat low-fat and high-fiber diet and are raised for food or fiber production [2,3]; therefore, they do not reach an age at which mammary gland tumors tend to develop [2]. In wild animals, very few cases of mammary gland tumors have been reported despite their huge population probably due to their short life span caused by infection, wound, or starvation. Moreover, it is challenging to check them for long periods of time since they look for other habitats. Therefore, most of the known cases in wild animals have been reported in captive animals, such as lion, tiger, jaguar, or cougar [4], and only little histopathological aspects have been reported.

Wild boars (*Sus scrofa*) are widely distributed worldwide. Therefore, they have been regarded as the reservoir of many infectious diseases, such as African swine fever, *brucellosis, trichinellosis, tuberculosis*, and *leptospirosis* [5]. Ironically, despite their huge population, very few cases of tumor, including B-cell lymphoma, have been reported [6]. None of the mammary gland tumors have been reported in wild boars, and their etiologies in this animal species are unknown. In this case, a wild boar was diagnosed with mammary adenoma induced by chronic mastitis progressing to fibrosis. Considering the lack of information about mammary gland tumors in wild boars, the present case may contribute in the histopathological aspects and pathological etiology of mammary gland tumors in wild animals. Thus, in this study, we report the first case of mammary adenoma in a wild boar.

CASE PRESENTATION

An unknown-aged female wild boar weighing 60 kg with mammary gland tumor was transferred for post-mortem examination. Grossly, in the mammary glands of the wild boar, a characteristic neoplastic change was seen (Figure 1A, 1B) diffusely in subcutaneous layer (Figure 1C). However, any exudate from the mass was not observed. The mass was well-encapsulated and had a very firm-to-elastic texture with a size of 17 cm × 13 cm. The cut-surface of the mass was homogeneous, pink-reddish, and had well-demarcated lobules (Figure 1C). There was no evidence of invasiveness into the muscular layer. Moreover, no significant lesions related to mammary neoplasia were observed in other organs. The excised mass was processed for further histopathological analysis. The mass was fixed in 10% neutral buffered formalin and routinely processed for paraffin-embedded blocks. All tissue sections were cut into 4 μm-thick sections and stained with hematoxylin & eosin (H&E) stain, Masson's trichrome stain, or Gram stain for further analyses.

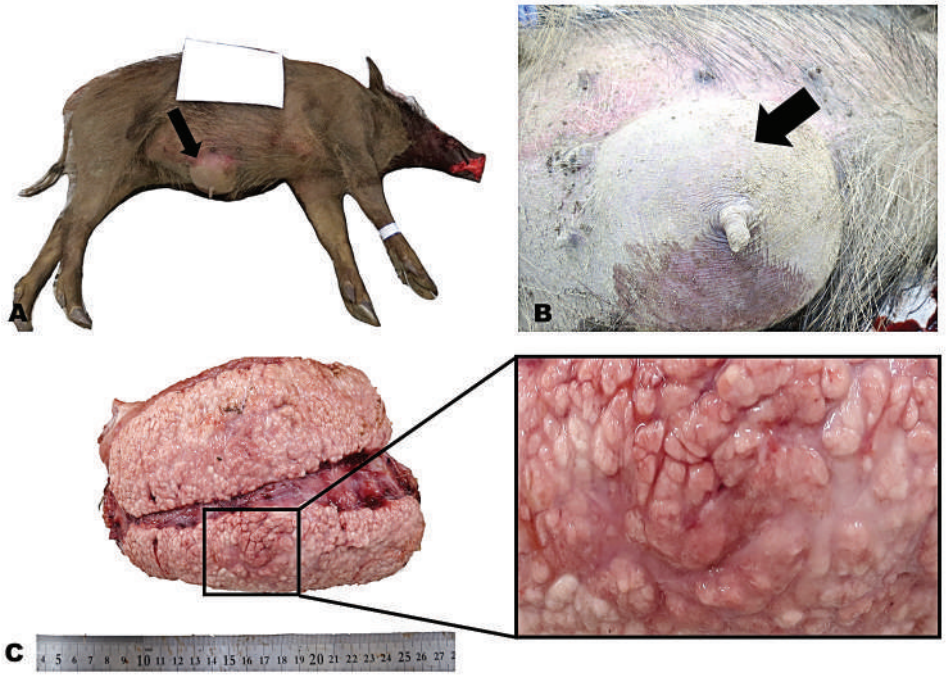

Figure 1. Mammary gland mass of an unknown-age female wild boar (*Sus scrofa*). **(A and B)** A 17 x 13 cm mass of mammary gland tumor. The mass was very firm-to-elastic without any exudate. **(C)** The mass was well-encapsulated and had a homogeneous pink-reddish cut surface. Well-demarcated mammary lobules were observed (inset).

Microscopically, the subcutaneous layer was mainly composed of neoplastic mammary glands separated by thick fibrous connective tissues (Figure 2A). The architecture of the mammary glands was well-maintained (Figure 2A). The glandular epithelial cells, which line these neoplastic mammary glands, were well-differentiated (Figure 2B), single-layered, cuboidal to columnar, and had a low-to-moderate cellularity and eosinophilic cytoplasm (Figure 2B). Most of the cells had small and central nuclei and nucleoli (Figure 2B). Mitotic figures were not observed. Invasion into blood vessels or lymphatic ducts was not observed. Myoepithelial cells were inconspicuous and did not exhibit neoplastic changes (Figure 2B). A diffuse infiltration of chronic inflammatory cells, such as plasma cells, around the neoplastic glandular epithelial cells and in the surrounding connective tissues was observed (Figure 2C). Moreover, extensive stromal fibrosis was also noted in Masson's trichrome staining (Figure 2D). Interestingly, a

large quantity of gram-negative and gram-positive, rod-shaped, bacterial colonies and macrophages phagocytizing these bacteria were observed in the blood vessels and fibrotic connective tissues of the mammary glands based on both H&E and Gram staining (Figure 3A, 3B). In conclusion, the present case was diagnosed as mammary adenoma.

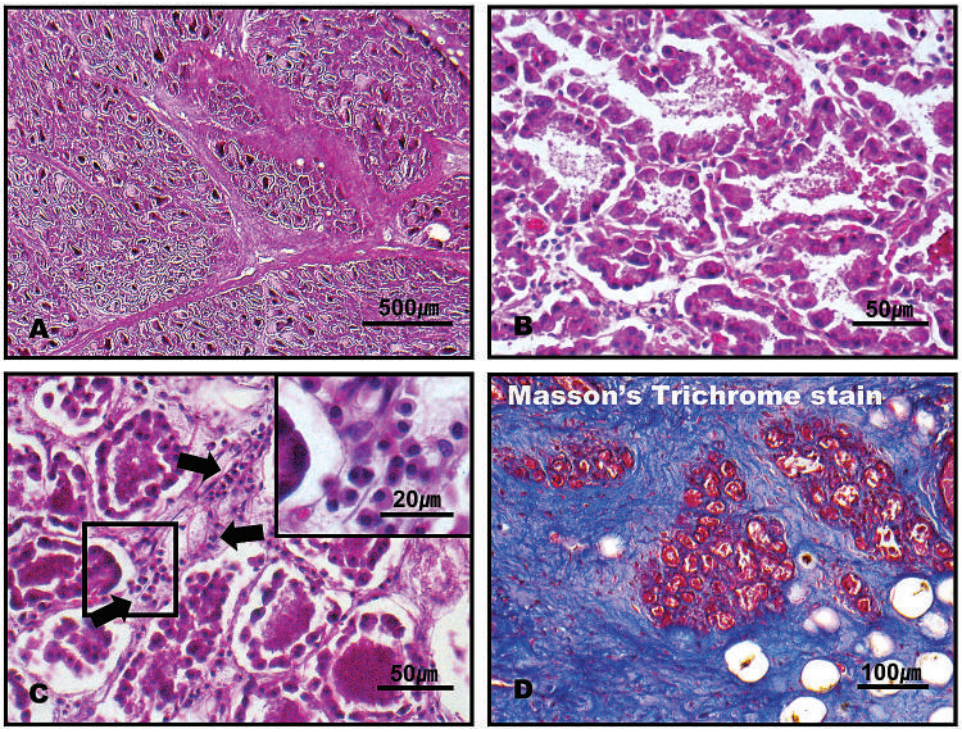

Figure 2. Representative images of microscopic findings. **(A)** The architecture of the mammary glands was well-maintained, and the neoplastic glandular epithelial cells were well-separated by thick fibrous connective tissues. Hematoxylin & eosin (H&E) stain. Bar=500 μm. **(B)** Well-differentiated neoplastic glandular epithelial cells. These neoplastic cells were single layered, cuboidal to columnar, and had central nuclei and nucleoli. Neoplastic changes in myoepithelial cells were not observed. Hematoxylin & eosin (H&E) stain. Bar=50 μm. **(C)** Infiltration of chronic inflammatory cells (inset, arrows) in the mammary glands. Hematoxylin & eosin (H&E) stain. Bar=50 μm. Inset, Bar=20 μm. **(D)** Extensive fibrosis in mammary glands in Masson's Trichrome staining. Bar=100 μm.

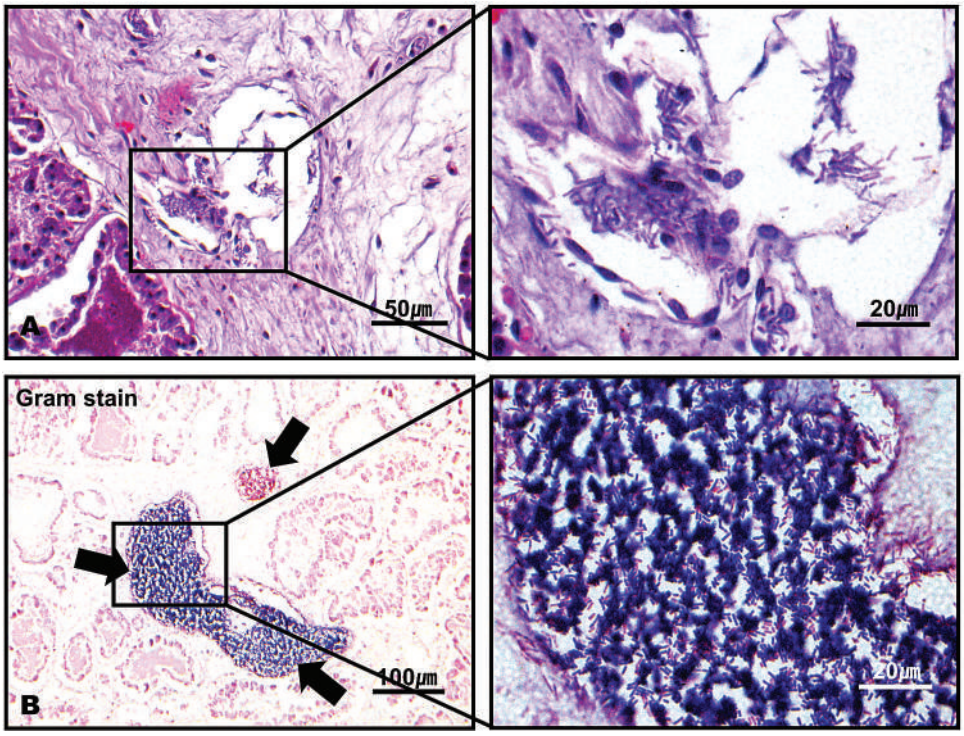

Figure 3. The representative images of microscopic findings and Gram staining. **(A)** A large quantity of bacterial colonies was observed around the neoplastic glandular epithelial cells, blood vessels and stroma of fibrotic connective tissue surrounding the glands. Macrophages phagocyting bacteria were also observed (inset). Hematoxylin & eosin (H&E) stain. Bar= 50 μm. Inset, Bar=20 μm. **(B)** A large quantity of gram-negative and -positive rod-shaped bacteria were observed in the mammary glands. Gram stain. Bar=100 μm. Inset, Bar=20 μm.

DISCUSSION

Breast cancer is one of the most commonly occurring cancers found in humans [7], and diet having high portion of fat, obesity, and excessive exposure to sex hormones have been suggested as major causes of this cancer [8,9]. Similarly, mammary gland tumors have been reported as one of the most prevalent tumors found in companion animals such as dogs and cats [1,2]. Diet, obesity, and sex hormones are also the major risk factors in the development of mammary tumors in companion animals [2]. The mammary gland tumors found in companion animals share a lot of similar aspects of those found in humans since their environment and lifestyles have been adapted to humans [10,11]. Moreover, in other animals including industry animals and wild animals, few cases of mammary gland tumors have been reported [2,3,11]. Interestingly, zoo captive wild animals show similar morphologic aspects shown in humans, and higher risk of mammary tumor development than that of free ranging wild animals, and the excessive nutrition with high fat, obesity, and excessive progestin

treatment, such as melengesterol acetate, followed by recurrent high estrogen exposure during folliculogenesis have been suggested as one of the risk factors for tumor development [11]. Since there are a lot of environmental differences between captive and free ranging wild animals, the other causes need to be considered in the mammary gland tumor development in this wild boar.

Inflammation could also be a critical cause of tumor development [12]. Because of persistent inflammation induced by bacterial or viral infection, trauma, or immune-mediated response, repair processes occur in mammary glandular epithelial cells, resulting in cell hyperplasia and metaplasia which can be accompanied by stromal fibrosis [12,13]. However, most of the known cases of mammary gland tumors in veterinary medicine are related to age, diet, obesity, and excessive sex hormone exposure since these cases are mainly reported in domestic animals. In the present case, the wild boar had a large quantity of gram-positive and gram-negative bacterial infections in the mammary glands. A diffuse infiltration of chronic inflammatory cells, such as plasma cells and macrophages, were also observed. Moreover, the extensive stromal fibrosis was observed with the bacterial colonies and inflammatory cells. This fibrosis in the regions indicates that these bacterial infections resulted in chronic mastitis and fibrosis, which ultimately led to the proliferation and neoplastic changes in glandular epithelial cells.

Many gram-positive and gram-negative bacteria have been suggested to be the cause of mastitis or inflammation associated with fibrosis in sows. For instance, *Trueperella pyogenes* is a gram-positive, rod-shaped bacterial species that can cause mastitis in sows [14], while class of coliforms such as *Escherichia* and *Klebsiella* are gram-negative, rod-shaped bacteria reported to be associated with mastitis [15]. Considering that these bacteria are easily found in nature and are resident flora of sows, these bacteria probably caused the mastitis and fibrosis in this wild boar.

Since mammary gland tumors are one of the most frequently diagnosed tumors in veterinary medicine, there have been many sub-categories for this diagnosis [2]. The histopathological criteria to differentiate benign from malignant mammary tumors include well-circumscribed margins, monomorphic nuclei, or absence of lymphatic or vascular invasion or metastases which were consistent with the present case [2]. Due to the lack of a histopathological grading system for wild animals, the criteria for the diagnosis of canine and feline mammary gland tumors have been used in this case. Based on the criteria suggested by Goldschmidt et al. [2], the differential diagnoses for the mammary tumor in this wild boar included mammary hyperplasia and mammary adenoma. Mammary hyperplasia is defined as an increase in the numbers of normal ducts and acini per lobules, and the proliferation of these components results in multinodular irregular masses [2,16]. In contrast, mammary adenoma is a well-circumscribed mass with firm and homogeneous cut-surface and consisted almost entirely of well-differentiated glandular epithelial cells [2,16]. In the present case, based on gross examination, the mass was well-demarcated with firm-to-elastic texture and had a homogeneous pink-reddish cut-surface. On microscopic examination, a

uniform proliferation of glandular epithelial cells without ductal proliferation was observed, which are the characteristics of mammary adenoma. Based on the gross and histopathological examination, the present case was diagnosed as a mammary adenoma caused by chronic mastitis accompanied by fibrosis.

Although few cases of mammary gland tumors in captive wild animals have been reported, to the authors' knowledge, mammary gland tumors in free ranging wild boars have not been reported yet. Moreover, a mammary gland tumor induced by chronic mastitis with bacterial infection in wild animals has not been suggested either. Thus, a detailed histopathological description of this mammary gland tumor may provide a clue for the diagnosis and mechanisms of tumor development caused by chronic bacterial infections in wild animals. Since there have been very limited data on mammary gland tumors in wild animals, and none has been reported in a wild boar, we hereby present this first case report of mammary adenoma induced by chronic mastitis in a wild boar.

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Author's contributions

SMB was involved in data collection, data interpretation, and wrote the manuscript. SWL was involved in data collection. JKP supervised the whole progress within data collection, data analysis and interpretation, reviewed and revised the manuscript, and is responsible for the integrity of the work as whole. All authors read and approved the final manuscript.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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ADENOM MLEČNE ŽLEZDE POVEZAN SA HRONIČNIM MASTITISOM KOD DIVLJE SVINJE *(SUS SCROFA)*

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Kod divljih životinja, tumori mlečne žlezde se retko nalaze i opisuju u literaturi. Kod domaćih vrsta životinja kod opisanih slučajeva, većinom su povezani sa starošću, načinom i kvalitetom ishrane, gojaznošću i sa velikim koncentracijama polnih hormona međutim, kod divljih vrsta životinja nema podataka o etiologiji ovog oboljenja. Na Departmanu za veterinarsku patologiju, Kyungpook nacionalnog Univerziteta, dopremljena je divlja svinje nepoznate starosti, kod koje su uočene dobro demarkirane čvrste do elastične mase u mlečnoj žlezdi. Površina preseka novotvorevine bila je ljubičasto-crvene boje i homogene strukture. Mikroskopskim pregledom uočeno je da se masa uglavnom sastojala iz dobro diferenciranih neoplastičnih glandularnih epitelnih

jednoslojnih ćelija, peharastog do kuboidnog oblika sa centralno položenim malim jedrima i jedarcima. Nisu uočene bilo kakve invazivne osobine ili metastaze neoplastičnih ćelija. Interesantan je nalaz infiltracije hroničnih zapaljenskih ćelija kao što su plazma ćelije i makrofagi zajedno sa nalazom brojnih kolonija gram negativnih i gram pozitivnih bakterija u mlečnoj žlezdi. Isto tako, pored ovog nalaza, uočena je i fibroza strome. Na osnovu makroskopskih i mikroskopskih promena, postavljena je dijagnoza: jednostavni adenom mlečne žlezde izazvan hroničnim mastitisom koji je progredirao u stanje fibroze. Prema saznanju autora, radi se o prvoj studiji kojom se opisuju histopatološki aspekti tumora mlečne žlezde povezanim sa hroničnim mastitisom koji je praćen fibrozom, kod divljih životinja.