

Eyelid Squamous Cell Carcinoma in a Horse in Jeju

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(Accepted: September 26, 2013)

Abstract : An 8-year-old, female, mixed Thoroughbred horse was presented for the evaluation of the left upper eyelid mass with ocular discharge during 4 months. After unilateral surgery, excised eyelid mass and left eye were submitted for diagnosis. Grossly, the removed mass was $6 \times 7 \times 2$ cm in size and dome shape with rough irregular surface. On the cut surface, mass was firm and yellowish white in color. Histopathologically, severely proliferated stratified squamous epithelia were heavily invaginated into dermis, and then formed rete ridge or numerous squamous islands. These neoplastic islands were composed of multiple layers of prickle cells with intercellular bridge and central laminated keratin pearls or necrotic cellular debris. Based on the above results, this case was diagnosed as squamous cell carcinoma in upper eyelid of horse.

Key words : eyelid mass, horse, keratin pearl, squamous cell carcinoma.

Introduction

Squamous cell carcinoma (SCC) is a malignant tumor of squamous epithelium occurring in multiple organs such as the skin, lips, mouth, esophagus, urinary bladder, prostate, lungs, vagina, and cervix in humans and animals (8). SCC in the skin is common in the horse, cattle, cat, and dog, relatively uncommon in the sheep, goats, and pigs (1,8). It most frequently involves male genitalia, ocular and periocular tissue, female genitalia, and the stomach (12). In horses and cattle SCC occurs primarily at mucocutaneous junctions, particularly at the eyelids (1).

SCC is the most common ocular (or periocular) tumor involved in the nictitating membrane, conjunctiva and cornea, and eyelids most frequently affected in horses (3,9). The average age of horses diagnosed with this tumor is between 8 and 13.2 years, with a mean age of 10.8 years in ponies (6,9). Ocular SCCs are malignant, locally invasive and recurrent, and may metastasize (5). According to previous reports, rates of metastasis range from 6 to 18.6% (6).

Several cases of SCC of skin were previously reported in dogs, Pere David deer, and hedgehog in Korea (4,7,14). However there was no available data for the SCC in horse in Korea. In this study, we describe a case of eyelid SCC in a horse reared in Jeju. To the author's knowledge, this is the first case of equine SCC in Korea.

Case

An 8-year-old, female, mixed Thoroughbred horse was presented for the evaluation of the left upper eyelid mass, which had been first noted by the owner 4 months previously. There was a 6-7 cm ulcerated red mass within the left upper eyelid. Severe erythema and crust formation were also presented in the mass. Because of periocular mass, left eye showed severe ocular discharge, corneal opacity, and semi-closed appearance. Blindness was continued for last three months. Due to poor prognosis, complete surgical resection of eyelid mass and enucleation were performed. After unilateral surgery, excised eyelid mass and left eye were fixed in 10% buffered formalin, and submitted to the pathology laboratory at the College of Veterinary Medicine in Jeju National University.

Submitted mass and eye were trimmed, embedded in paraffin, sectioned at $3 \mu\text{m}$, and stained with hematoxylin and eosin (H&E) for light microscopic examination.

Grossly, the removed mass was $6 \times 7 \times 2$ cm in size and dome shape with rough irregular surface (Fig 1). On the cut surface, mass was firm and yellowish white in color. The cornea showed relatively irregular surface, dense neovascularization and corneal scarring with granulation tissue.

Histopathologically, upper area of neoplastic mass showed severe ulceration and beneath suppurative inflammation composed of fibrin and massive neutrophils. Severely proliferated stratified squamous epithelia were heavily invaginated into dermis, and then formed rete ridge or numerous squamous islands (Fig 2). These islands and anastomosing bands of neoplastic epithelial cells were separated by surrounding

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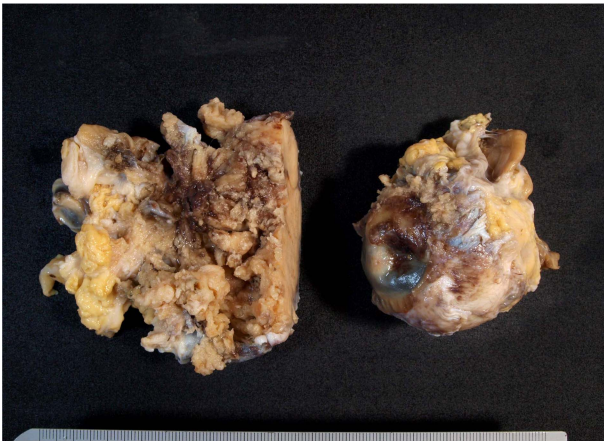


Fig 1. Note upper eyelid mass (left) and left eye (right). Eyelid mass was solid and had irregular surface with hemorrhage. Left eye showed severe corneal opacity.

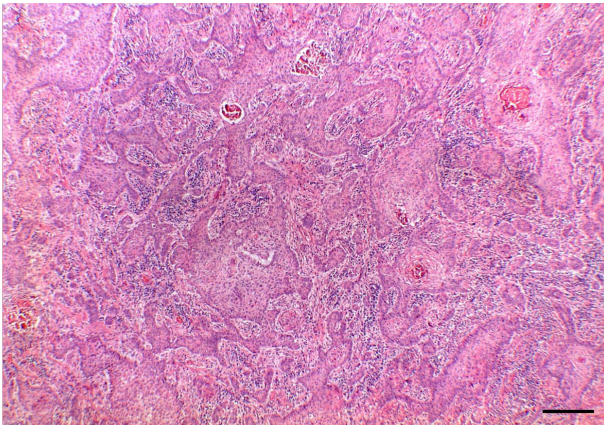


Fig 2. Eyelid mass was composed of islands and trabeculae of well differentiated squamous epithelia. H&E, Bar = 200 μ m.

collagenous tissue. These neoplastic islands were composed of multiple layers of prickle cells in squamous epithelia and/or central laminated keratin pearls or necrotic cellular debris (Fig 3). Neoplastic prickle cells had typical intercellular bridge (= desmosome) and many mitotic figures. Severe multifocal infiltration of lymphocytes and macrophages was also presented throughout the mass. Neoplastic cells had very strong invasive tendency to adjacent tissues such as connective tissue and muscle layer (Fig 4). Cornea of eye showed mild desquamation, severe diffuse hemorrhage, and multifocal mild lymphocytic infiltration. Neoplastic cells extended to limbus, but not invaded into cornea and sclera.

The stratified squamous epithelium of cornea showed multifocal thin epithelial layer with desquamation and erosion. Severe multifocal hemorrhage and chronic inflammatory cells such as lymphocyte and plasma cell infiltration were observed in substatia propria, especially under the erosive area. Some blood vessels showed marked congestion and thrombosis. Other elements of eye including lens, iris, ciliary body, retina, choroid, and optic nerve were within normal limit.

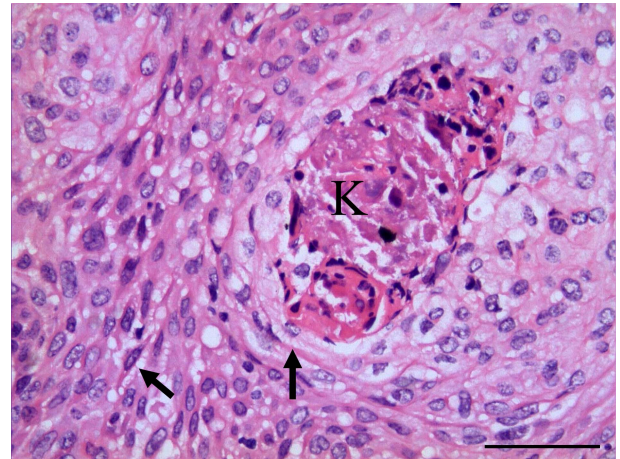


Fig 3. Neoplastic squamous island had central keratin pearl (K). Note typical intercellular bridges (arrows) in prickle cells. H&E, Bar = 50 μ m.

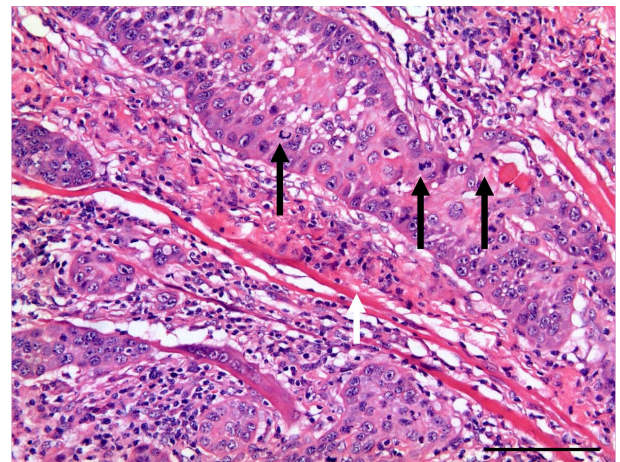


Fig 4. The neoplastic cells showed strong invasion to adjacent muscle (white arrow). Note high abnormal mitoses (black arrows). H&E, Bar = 100 μ m.

Discussion

Based on the clinical, histopathological and gross findings, this case was diagnosed as SCC in the upper eyelid of horse. Differential diagnosis of ocular or periocular mass includes neoplasia such as SCC, sarcoid, papilloma, neurofibroma, basal cell carcinoma, lymphosarcoma, some kinds of adenocarcinoma, and inflammatory lesions such as abscess, granulation tissue, foreign body reaction, or parasitic reactions (11). Two hallmarks including distinct keratin pearls and intercellular desmosomes indicate that this case of ocular mass was derived from squamous epithelium. In addition, neoplastic cells showed strong invasive tendency as malignant potency. According to characteristic histopathologic features, we can make a definitive diagnosis of this tumor as SCC in upper eyelid, and successfully rule out other differential diagnosis. SCC is a locally aggressive neoplasm

that invades surrounding tissues (11). Metastasis of SCC is rare, but it can occur late stage of disease course and involve in mandibular, submaxillary, cranial cervical, and pharyngeal lymph nodes and the thorax (6,11). Eyelid and orbital SCC carry a poor prognosis and increase recurrence than that in the third eyelid, nictitating membrane, and limbus (3).

The etiology of SCC of the ocular or periocular area is not known, but the cause might be associated with the ultraviolet (UV) component of solar radiation, pigmentation status, high levels of nutrition, viral agents and hormonal, genetic and immunological factors (2,6,8). The UV component is the most plausible carcinogenic agent. The association between UV light and skin cancer has been recognized on the basis of clinical, epidemiologic, and laboratory studies both in animals and in man (8). In the US, bovine ocular SCC is more common in the Southwest, purportedly because of the greater exposure to UV radiation (1). According to previous epidemiological study, there is an increased prevalence of ocular SCC in horses with an increase in longitude, altitude, and mean annual solar radiation (2). In contrast, prevalence of SCC increased with a decrease in latitude. In addition, wind and heat have been experimentally shown to enhance solar carcinogenesis (10). Therefore special geographic location, most southern part of Korea, and windy and humid subtropical climate of Jeju island are closely related with the occurrence of ocular SCC in this horse case. Over-expression of the tumor suppressor gene p53, possibly mutated due to UV radiation, play an important role in SCC development in animals (6).

Solar-induced tumors have been higher prevalent in non-pigmented and sparsely haired or hairless areas in domestic animals (2). Close relationship between pigmentation and the development of SCC has been reported in cattle and horses (1,2). Pigment has a substantial inhibitory effect on the development of tumors of the skin and ocular or periocular area. In most breeds of cattle and horses, a lack of pigmentation around the eyelids is an important predisposing factor to the development of SCC (1). Recent survey demonstrated that the mean age of horses with ocular SCC (13 years) was significantly less than that of horses with SCC in skin (15 years), the penis and prepuce (21 years), or vulva and perianal skin (19 years) (13).

Numerous treatment methods, including surgical excision, cryotherapy, radiofrequency hyperthermia, immunotherapy, radiation brachytherapy, carbon dioxide laser ablation, and intralesional chemotherapy have been reported for the periocular neoplasms in horses (3,6,9). However, applicable treatment approach should be selected depend on tumor size, tumor location, availability of equipment and cost of treatment (3,6). Due to the large tumor size up to 7 cm and poor prognosis, we performed complete surgical resection of eye-

lid mass and enucleation in this case. Unfortunately, the occurrence of SCC can not be prevented. Applicable methods to reduce exposure of UV light during the peak hours may decrease the risk of ocular or periocular SCC development in horses, especially in horse rich Jeju Island.

Acknowledgments

We thank professor Joo Myoung Lee of the College of Veterinary Medicine of Jeju National University for submitting the sample.

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제주도의 말에서 발생한 안검 증충편평상피 암종

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요 약 : 8세령의 암컷 갑종 더러브렛 말이 4개월간의 눈물과 함께 좌측 상안검에 종괴가 형성되어 있었다. 편측성 외과적 수술을 실시하여 좌측 안구와 안검 종괴를 절제하여 진단 의뢰되었다. 육안적으로 종괴는 6 × 7 × 2 cm 크기이고 반구형의 모양이며 표면은 불규칙하게 거칠었다. 단면상에서 종괴는 단단하고 유백색조를 띠고 있었다. 병리조직학적으로 심하게 증식된 증충편평상피세포가 진피층으로 심하게 함입되어 있었으며, 무수히 많은 표피 능선(rete ridge)과 증충편평상피 섬(squamous islands)을 형성하고 있었다. 종양세포의 섬들은 중심부에 층판상의 암진주와 괴사된 세포 붕괴물을 가지고 전형적인 세포 간교(intercellular bridge)로 연결된 여러 층의 가시세포로 구성되어 있었다. 이와 같은 결과를 토대로 본 예는 말의 상안검에서 발생한 증충편평상피 암종으로 진단하였다.

주요어 : 안검 종괴, 말, 암진주, 증충편평상피 암종