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Surgical management of perineal squamous cell carcinoma with 5- fluorouracil adjuvant therapy in sixteen mares

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Abstract

Sixteen mares presented with squamous cell carcinoma in perineal region were subjected to cryotherapy followed by surgical resection of growth and adjunct therapy with intralesion 5-fluorouracil in four animals. No reoccurrence was observed in 5-fluorouracil treated mares however, reoccurrence was noticed in three cases subjected to surgical excision alone after 1 year.

Keywords: Mares, perineal growth, squamous cell carcinoma, cryosurgery, 5-fluorouracil

Introduction

Squamous cell carcinoma (SCC) is one of the most common malignant tumour and the second most common cutaneous neoplasm in horses. It can develop at any location on the skin; it occurs most frequently in non-pigmented areas in horses after 10 years of age and older (Ginn *et al.*, 2007) [3]. Eye and the genitalia are the most frequent site for SCC those have squamous epithelium (skin, mouth, nasal cavity/sinuses, stomach). Nonpigmented skin exposed to carcinogens such as smegma (in the case of penile and clitoral forms) and sunlight (in cutaneous and ocular forms) are implicated but there are no scientific studies that confirm this widely held belief (Postey *et al.*, 2007) [11].

Tumours located on the vulva, prepuce, and related areas are far more difficult to treat than corneal tumours. An ulcerative or destructive form and a superficial proliferative are the two forms that results in an expanding tumour mass. Surgical excision is a great choice However it's not always possible to completely remove all malignant cells (Beech, 1999) [1]. Hence, there is a need to use different chemotherapeutic agent as an adjunct to surgical excision. Different chemotherapeutic agents are widely used however toxicity to local healthy cell is a major limiting factor combined with its systemic adverse effect. 5- Fluorouracil on the other hand being an antimetabolite and minimal toxic to the surrounding healthy cell is being increasing popular (Fortier, 1994) [12]. Hence in the present study sixteen mares were surgically managed with or without 5-Fluorouracil and their recurrence studied.

Material and Method

The study was conducted on sixteen non pregnant mares presented with perianal growth. The detailed information about age, sex, duration of illness was recorded followed by estimation of HR, RR, and Temperature. Tissue biopsy of the growth was carried out using sharp dissection with B.P blade under local infiltration with 2 % lignocaine HCL with aseptic precautions. The tissue was then sent for histopathologic examination and stained with H and E stain. The histopathologic interpretation was obtained on light microscope and 100x magnifications.

On the day of presentation, cryosurgery was performed using controlled stream of liquid nitrogen after sedation and local infiltration of 2% lignocaine hydrochloride in all the cases. A x-ray film was used as shield to protect surrounding healthy tissue and spray of concentrated liquid nitrogen was applied. On confirming the biopsy as squamous cell carcinoma the surgical excision was performed in all the cases under low epidural anaesthesia with 2 % lignocaine in standing position. In four cases excision along with intralesional 5-fluorouracil was performed. In all the cases Inj Dicrysticin (5 gm total dose) and Inj. Meloxicam @0.2 mg/kg body weight was given 5 days post operatively along with antiseptic dressing till healing. Telephonic follow up was performed up to 2 years post treatment.

Results and Discussion

Out of 16 cases, seven mares were 10 years old or more, while the rest were around 6 years of age. The incidence increases with age and vulvar forms of squamous cell carcinoma occurs at older age (Ginn *et al.*, 2007, Goldschmidt and Hendrick, 2002, Meuten, 2002) [3, 4, 9].

The same observation has been noticed in this study. Five mares had history of injury and sepsis as well as maggot wound complication before the noticeable growth of squamous cell carcinoma. Albino mares (10/16) were most commonly affected followed by piebald (4/16) and skew bald (2/16). Aetiology of vulvar squamous cell carcinoma might be due to long exposure to ultraviolet light, unpigmented epidermis (Ramos *et al.*, 2007) ^[12] or chronic skin irritation (Smith *et al.*, 2009, Kusewitt and Rush, 2007) ^[7, 14] as 50% of mares having the history of injury and maggot wound which cause irritation and direct exposure of sun light and that can be a aetiology for the SCC as UV light penetrates skin cells to damage DNA, which results in abnormal cellular growth patterns. Depending on injury type, it may become a precancerous cell or fully transform into a malignant, cancerous cell (Muldowney, 1985) ^[10]. but the exact aetiology of equine SCC is still unclear (Hedau *et al.*, 2017) ^[5].

The tumours were mostly of long duration in nature. The average time of illness ranged from four to eight months. The tumours were located at juncture of vulval lips and buttock in most of the cases (11) followed by at ventral commissar of vulva (2) and groin area (3). Certain horse breeds often lack pigmentation at the mucocutaneous junctions where skin meets mucous membranes. These areas like the mouth, within the eye, the vulva, penis, prepuce, and anus are most susceptible to developing squamous cell carcinoma (SCC) (Goldschmidt and Hendrick, 2002) ^[4]. The clitoral form is invariably proliferative. The vulvar forms of SCC are usually proliferative when they develop within the vestibule and ulcerative when they involve the lips of the vulva (Knottenbelt, 2003) ^[6].

Tissue biopsy revealed all the tumors to be squamous cell carcinoma (SCC) on histopathology. The Neoplastic cells had distinct cell borders, abundant eosinophilic granular cytoplasm, occasionally prominent intercellular bridge (desmosomes) and one round to oval, vesiculate nucleus with finely-stippled chromatin and one to two distinct, magenta nucleoli. Multifocally, in many cases, neoplastic cells surrounded variably sized concentric, lamellated eosinophilic material (keratin pearls). SCC is the second most commonly found tumour in equine after sarcoid (Scott and Miller 2003; Hedau *et al.*, 2017) ^[5, 13].

Cryosurgery was well tolerated by all the mares, however, no improvement in the condition and all the mares were surgically operated. Martens *et al.* (2002) ^[8] had reported that cryosurgery alone take more time for recovery of lesion. It can be used as additional treatment with surgical excision and local chemotherapy (Taylor and Halderson, 2012) ^[15].

Surgical excision is the most commonly followed treatment for SCC in mares (Hedau *et al.*, 2017) ^[5]. SCC is known for their rapid growth and high reoccurrence rate even after surgical excision (Beech, 1999) ^[1]. Among the operated mares only 2 mares had complication of infection which was taken care with antiseptic dressing and antibiotic treatment. An uneventful recovery was seen in all the mares given 5-fluorouracil in conjunction with surgical excision, however, reoccurrence of the tumor was observed after one year in three mares undergoing surgical excision alone. Fortier (1994) ^[2] have opined that surgical ablation should be avoided when invasion of local lymph node by the tumor is suspected or there are difficulties with margin definition predisposing it to reoccurrence.

Fortier, (1994) ^[2] have opined 5-FLUOROURACIL to induce a regression in size and advancement rate of the preneoplastic lesions to which it was applied. The effect of fluorouracil may

create a thymine deficiency that provokes unbalanced growth and death of the cell.



Fig 1: Diffuse SCC on valvar lips



Fig 2: Post surgical excision of SCC

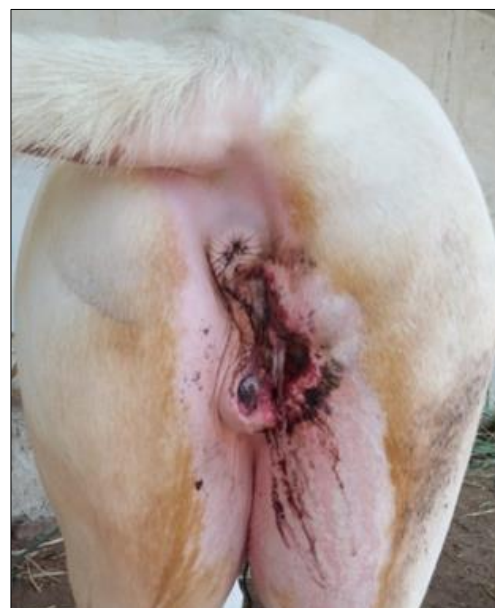


Fig 3: Reoccurrence of perianal SCC



Fig 4: Cryosurgery with liq nitrogen

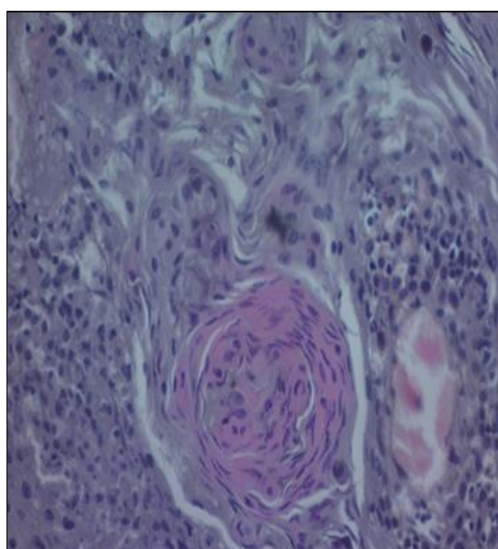


Fig 5: SCC under 100x and H&E stain

In present study 5-FLUOROURACIL was injected locally after surgical excision and no reoccurrence may be indicative of successful remission. Hence, it can be concluded that intralesional use of 5- fluorouracil can be used as a adjunct to surgical excision of genital lesions of horses.

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