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Pathological studies and therapeutic management of equine cutaneous neoplasms suspected of sarcoids

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Abstract

Cutaneous neoplasms affecting equines is very important condition. The sarcoid is a type of skin tumor that affects the equine family and equine sarcoids remain a frustrating and challenging entity for veterinary practitioners and research scientists alike. The present study was conducted on 6 clinical cases (5 horses and 1 mule) of cutaneous neoplasm suspected of sarcoids. The clinical cases were diagnosed on the basis of clinical and pathological examination of the lesions. The age of animals ranged from 1.5 years to 8 years. Grossly, the lesions were that of nodular, verrucous and occult form of sarcoid appearances which were present on nostrils, lips, neck, shoulder, back and face region. Gross and histopathological findings revealed 4 cases having fibroma like features characterized by whorls or interlacing bundles of fibrous connective tissue which run in all directions, one of squamous cell carcinoma characterized by neoplastic aggregates of pleomorphic epithelial cells with keratinized pearl formation and one of papilloma characterized by lesions of orthokeratotic hyperkeratosis, finger-like papillae with numerous vacuolating cells with eccentrically placed nuclei. The cases were treated by administering anthiomaline (lithium antimony thiomalate) @ 15ml deep I/M on alternate days in adult animals and 7 ml deep intramuscularly on alternate days in young ones along with supportive therapy. Vincristine sulphate at the dose rate of 0.025/kg body weight I/V at weekly intervals for 2 to 4 times was incorporated in the treatment schedule if the cases do not respond to anthiomaline. The efficacy of anthiomaline in the treatment of sarcoid suspected cases was found to be 50% only and all were treated after vincristine administration. The results shows that anthiomaline along with vincristine sulphate is more effective as compared to anthiomaline alone in the treatment of equine sarcoid.

Keywords: Pathological studies, therapeutic management, equine cutaneous neoplasms

Introduction

Cutaneous neoplasms particularly equine sarcoids are considered to be the most common skin tumours in horses, donkeys and mules which can affect the equids of all ages, types and breeds (Ragland *et al.*, 1970; Pascoe and Summers, 1981; Knottenbelt *et al.*, 1995; Goodrich *et al.*, 1998; Goldschmidt and Hendrick, 2002; Bergvall, 2013) [34, 31, 18, 121, 11, 5]. Sarcoids may occur in any part of the body either as solitary or multiple lesions, but the most common regions are the head, ventral abdomen and the limbs and at other body parts that have been previously traumatized (Jackson, 1936 and Ragland *et al.*, 1970) [13, 34]. The fibroblastic wart-like lesions of equine skin show variable manifestations and a variable response to therapy. These tumours may not being life threatening, but can adversely affect the material value of horses and can often compromise the use of the horse because of their location. The present study was carried out to find the morphological and histopathological studies in equines suffering from cutaneous neoplasms suspected of sarcoid and to evaluate the therapeutic efficacy of anthiomaline alone or combination of anthiomaline and vincristine sulphate in equines suffering from sarcoids.

Materials and Methods

The present investigation included six clinical cases of equines (five horses and one mule) suffering from cutaneous neoplasm suspected of sarcoids which were presented to the Department of Veterinary Clinical Complex, Lala Lajpat Rai University of Veterinary and Animal Sciences, Hisar. Complete anamnesis was carried out to record age, sex, any bleeding /ulceration, infection/inflammation and gross appearances. The clinical examination of the affected animals helped in the preliminary diagnosis as it gives information about the type of sarcoid (occult, verrucous, nodular, fibroblastic, malevolent and mixed) the animal is suffering

from. Tissue samples were collected from lesions separately in 10% buffered formalin for histopathological examination.

Histopathological studies

For pathological examination of the tumours, representative tissues pieces of 3-5mm were surgically cut and placed in 10% buffered formalin subsequently processed by paraffin embedding technique as described by Luna, 1968. The histopathological technique involved fixation, washing, dehydration, clearing, embedding, section cutting, staining and microscopical examination.

The tissue samples were washed in running tap water to remove formalin, processed in ascending grades of alcohol for dehydration and cleared in benzene, infiltrated and embedded in paraffin. The paraffin embedded tissues were cut into 3-4 micron thick section using automated microtome and stained with Hematoxylin and Eosin as per procedure of Luna, 1968.

Treatment

Initially, the cases were treated by administrating anthiomaline (lithium antimony thiomalate) at the dose rate of 15 ml deep intramuscularly on alternate days in adult animals and 7 ml deep intramuscularly on alternate days in young ones along with supportive therapy. But in the cases which did not respond to anthiomaline, vincristine sulphate at the dose rate of 0.025/kg body weight intravenously at weekly intervals for 2 to 4 times was incorporated in the treatment schedule.

Results

The details regarding age, sex, location of the tumour and gross appearances of the cases are described in table 1. The results revealed that the age of affected animals ranged from 1.5 years to 8 years. All the affected animals were males. Clinically, the lesions were present on different regions of the body i.e. nostrils, lips, neck, shoulder, back and face region (Fig. 1). In the present study, the lesions were that of nodular, verrucous and occult form of sarcoid.

Table 1: Description of cases of equine suffering from cutaneous neoplasm

S. No	Animal species	Age (year)	Sex	Site of collection	Diagnosis based on histopathological finding
1	Horse	1.5	M	Lips	Squamous cell carcinoma
2	Horse	2	M	Nostrils	Papilloma
3	Horse	1.5	M	Back	Fibroma
4	Horse	8	M	Face	Fibroma
5	Horse	8	M	Chest region	Fibroma
6	Mule	5	M	Neck	Fibroma



Fig 1 (a-e): Gross picture of cases of equines suffering from cutaneous neoplasm

Pathological studies

Histopathological examination revealed that 4 cases were having features of fibroma like sarcoids, one each of squamous cell carcinoma and papilloma. The detailed histopathological findings of these cases are described as follows:

Papilloma

One case of papilloma was found in a two year old male horse. The growth was present on the nostril region with nodular appearance. Histopathologically, the tissue section revealed the changes similar to papilloma tumour which was characterized by orthokeratotic hyperkeratosis, finger-like papillae with numerous vacuolating cells with eccentrically placed nuclei (Fig. 2).

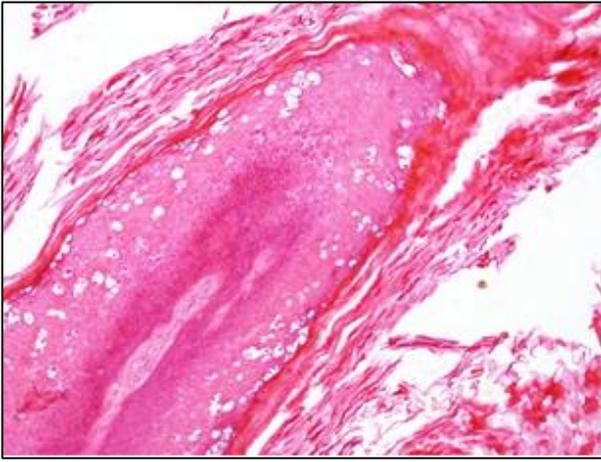


Fig 2: Papilloma characterized by orthokeratotic hyperkeratosis, finger-like papillae with numerous vacuolating cells with eccentrically placed nuclei (H&E x200)

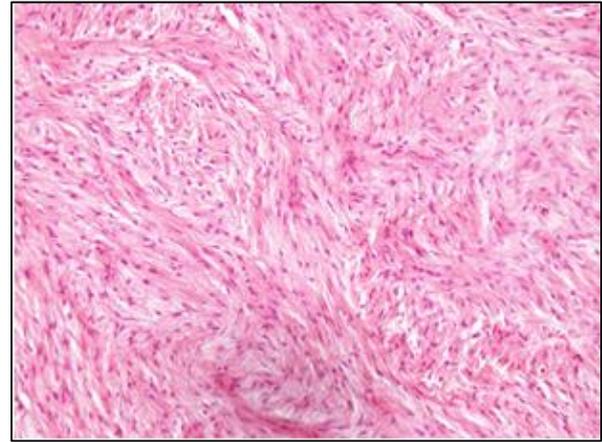


Fig 4: Fibroma characterized by whorls or interlacing bundles of spindle shaped fibroblast like cells in criss-cross pattern with dense collagen tissue (H&E x200).

Squamous cell carcinoma

One case of squamous cell carcinoma was found in 1.5 year old male horse. The growth was of nodular type with cauliflower like appearance present on lip portion. Histopathologically, the tissue section revealed the changes similar to squamous cell carcinoma which was characterized by neoplastic aggregates of pleomorphic epithelial cells with keratinized pearl formation (Fig. 3).

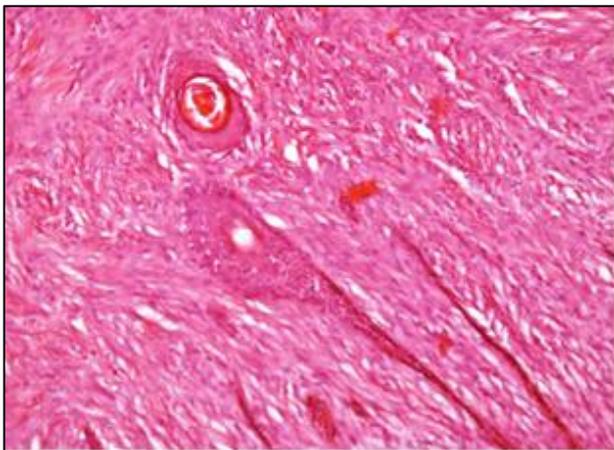


Fig 3: Squamous cell carcinoma characterized by neoplastic aggregates of pleomorphic epithelial cells with keratinized pearl formation (H&E x200)

Fibroma

Four cases were diagnosed as fibroma like sarcoids. The growths in two cases in 8 years horses were present on face and chest region, while in one case in a 1.5 year old horse the growth was present on back region, and in one case in 5 year old mule it was on neck region. The various forms on gross appearances were verrucous, which look like grey, scabby or warty in appearance ; nodular form which look like spherical subcutaneous masses under the skin; occult form which look like as circular or roughly circular, hairless, roughened areas; fibroblastic form like of fleshy masses. Histopathologically, the tissue section revealed the changes similar to fibroma which was characterized by whorls or interlacing bundles of spindle shaped fibroblast like cells of fibrous connective tissue which run in all directions with collagen tissue in between. (Fig. 4). Neoplastic cells revealed variable morphological features varying from slender with elongated to plump cells with large, irregular nuclei.

Therapeutic efficacy

The efficacy of anthiomaline in the treatment of sarcoid suspected cases was found to be 50% as only three cases out of six responded to the treatment by anthiomaline alone and recovered. The rest three cases which did not respond to anthiomaline alone were treated by combination of anthiomaline and vincristine sulphate. The cases recovered after fourth injection of vincristine sulphate and there was no history of recurrence in these cases. This shows that anthiomaline along with vincristine sulphate is more effective as compared to anthiomaline alone in the treatment of equine sarcoid.

Discussion

The sarcoid can be defined as locally aggressive fibroblastic benign tumours of equine skin (Ragland *et al.*, 1970) [34]. It can occur as single or multiple lesions in different forms, ranging from small wart-like lesions to large ulcerated fibrous growths. The sarcoid can be seen as an outbreak in small group of horses (Ragland *et al.* 1969) [33] but most commonly seen in individual horses. In horses breed predisposition can also be there (James, 1968; Lazary *et al.*, 1985; Meredith *et al.*, 1986; Angelos *et al.*, 1988 and Brostrom *et al.*, 1988) [14, 21, 29, 4, 7]. The sarcoid can be classified as verrucous, nodular, fibroblastic type of tumour (Knottenbelt, 2005) [17]. In our study also different forms of fibroma like benign sarcoids were observed. These forms were verrucous, with grey, scabby or warty in appearance ; nodular form like spherical subcutaneous masses; occult form appearing as circular or roughly circular, hairless, roughened areas; fibroblastic form comprising of fleshy masses which bleed easily and malignant form which appear as aggressive lesion with extensive local or wider spread through the skin and subcutaneous tissues. Equine sarcoids have been described as biphasic tumour with dermal and epidermal components. Sections obtained from whole tumours allow for the most accurate histopathological assessment, however, surgical excision for the purpose of diagnosis may lead to a high rate of recurrence (50 - 64%) (Tarwid *et al.*, 1985; Knottenbelt *et al.*, 1995; Martens *et al.*, 2001b) [38, 18, 23]. Even taking a small biopsy of small and flat lesions may trigger rapid growth and ulceration. In the present study 6 cases of cutaneous equine neoplasms were studied. Macroscopically the lesion/growth was present on different parts of the body with variable size and shapes in different forms of sarcoid, similar findings were previously reported (Knottenbelt, 2005; Wobeser *et al.*, 2010; Kainzbauer *et al.*,

2012) [17, 42, 14]. Histopathologically the cases revealed fibroma like sarcoid, papilloma and squamous cell carcinoma with increased density of dermal fibroblast in almost all the cases. These findings are in accordance with earlier reports which suggested the presence of an increased density of dermal fibroblasts (Martens *et al.*, 2000) [24]. Jones *et al.*, (1996) [15] suggested that all connective tissue tumours (fibroma, fibrosarcoma, and neurofibroma) in horse are forms of equine sarcoids. In case of verrucous sarcoid, histopathologically the epidermal component showed hyperkeratotic and hyperplastic changes. Similar findings were observed by Pulley and Stannard, 1990 [32]. Epithelial changes seen in sarcoids are likely the result of growth-promoting factors expressed by the neoplastic fibroblasts that stimulate proliferation of surrounding epithelial cells (Carr *et al.*, 2001b) [23]. Pascoe and Summers (1981) [31] examined 42% of lesions histologically in horses and reported that the most commonly occurring neoplasms were the equine sarcoid, papilloma and squamous cell carcinoma of the eye and external genitalia. In present study, cases of occult and nodular sarcoid showed Histopathologically, epidermal component almost normal with slight amount of granulation tissue and similar findings were observed by Goodrich *et al.*, (1998) [12] and Martens *et al.*, (2000) [24]. Occasionally the epidermal component can be normal, atrophic or even absent (Marti *et al.*, 1993; Lepage *et al.*, 1998 and Martens *et al.*, 2000) [24]. In cases of fibroblastic and malignant sarcoid, changes were observed more in dermal component consisting of bundles of irregularly arranged fibroblasts and variable amount of collagen. Typical changes include dermal proliferation of fusiform or spindle-shaped fibroblasts, forming whorls, interlacing bundles and haphazard arrays with one another (Goodrich *et al.*, 1998) [12]. Fibroblast morphology varies from slender with elongated, pointed nuclei, to plump cells with large, irregular nuclei. The cytoplasmic boundaries are often ill-defined. Fibroblasts are usually spindle-shaped with oval, elongated nuclei, and the mitotic rate may be increased in rapidly growing tumours (Ragland *et al.*, 1970) [34] and in superficial or ulcerated parts (Tarwid *et al.*, 1985) [38]. In spite of the disorder, fibroblasts are normally differentiated, and the anaplasia typical of more aggressive sarcomas is rarely found (Jackson, 1936 and Tarwid *et al.*, 1985) [38, 13].

The cases were treated by administering anthiomaline (lithium antimony thiomalate) along with supportive therapy. Vincristine sulphate was incorporated in the treatment schedule if the cases did not respond to anthiomaline. Other supportive therapy includes administration of injection of vitamin C and B-complex. Three animals out of six responded to the treatment by anthiomaline alone and recovered. Other cases which did not respond to anthiomaline alone were treated by combination of anthiomaline and vincristine sulphate. The cases recovered after fourth injection of vincristine sulphate and there was no history of recurrence in these cases. Previously, there was no history of using anthiomaline and vincristine in cases of sarcoids but several researchers tried these in other species. Vincristine sulphate was used in canines for treatment of mammary tumour by Sandeep, 2013 [35].

Daily topical applications of caustic or antimetabolite drugs such as podophyllum (Metcalf, 1971) [30] and 5- fluorouracil have been advocated for the treatment of small sarcoids (Turrel *et al.* 1985b and Bertone and McClure 1990) [6, 41]. Results of topical chemotherapy have been inconsistent. Implants containing 5- fluorouracil or cisplatin have been

developed for intralesional use and, in a preliminary study; partial remission of sarcoids was seen in 81 of 101 patients treated (Turrel *et al.* 1985b) [41]. Patients required the use of several successive implants for cure, and other therapies were used requires further clinical investigation. Xanthates are derivatives of primary alcohols with antiviral and anti tumoral activity (Amtmann and Sauer, 1987) [1]. They interfere with the action of kinase enzymes (Schick *et al.* 1989) [37]. In transformed hamster embryo fibroblasts they inhibit the replication and transcription of DNA and RNA viruses, including BPV-1 (Sauer *et al.* 1984 and Amtmann *et al.* 1985) [36, 3]. Tricyclodecan-9-yl-xanthogenate (D609) in combination with lauric acid (C12) and human recombinant tumour necrosis factor induced necrosis of human carcinoma xenografts in athymic mice (Amtmann and Sauer, 1990) [2]. Theon *et al.*, 1993 [39] and Theon, 1997 [40] used chemotherapeutic drug such as Cisplatin that can be administered as a sole treatment to small sarcoids, but it was recommended that larger lesions were surgically debulked prior to drug treatment. Other commonly employed treatments include cryotherapy, excision and local immune modulation (Goodrich *et al.*, 1998) [12]. Cryosurgery alone, or in combination with debulking of larger sarcoids has been employed with some success (Laursen, 1987) [20]. Approximately 70% of horses treated appeared to be free from recurrences in most studies, although rates as high as 100% and as low as 60% have been reported (Lane, 1977; Goodrich *et al.*, 1998 and Fretz and Barber, 1980) [12]. Cell death (cryonecrosis) is achieved by repeated freeze-thaw cycles and complications of the technique arise due to damage of adjacent or underlying structures. These include scarring, facial paralysis, haemorrhage and decreased strength of cortical bone (Fretz and Barber, 1980; Genetzky *et al.*, 1983 and McConaghy *et al.*, 1994) [9, 10, 27]. Such potential complications make cryosurgery less suitable for peri-ocular sarcoids and those tumours located on larger vessels, nerves, ligaments or joints.

The present study concluded that the cases of sarcoid in equines are having variable appearances morphologically and histopathologically and it becomes difficult to differentiate them alone on the basis of histopathology and that anthiomaline along with vincristine sulphate is more effective as compared to anthiomaline alone in the treatment of equine sarcoid.

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