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CASE REPORT

Is It Possible to Treat Equine Papillomatosis with Ivermectin Given Orally?

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Summary

This case report aims to evaluate the effect of ivermectin in the treatment of a horse with papillomatosis. The horse was a 14-month-old mare, with cutaneous papillomatosis diagnosed by clinical and histopahological examinations. The history revealed that papillomas had developed and progressed in the last 2 months. A single shot of ivermectin (Eqvalan paste®, Topkim, Turkey) at a dose of 200 mcg/kg was orally administered to the horse. The horse was observed at 7th, 15th and 30th days and no other treatment during the recovery period. Papillomas regressed clearly on the 7th day after the administration of ivermectin treatment and regressed nearly 90% on the 15th day and, showed complete remission on the 30th day. The results obtained in this case indicated that ivermectin might be effect in the treatment of equine papillomatosis.

Keywords: *Equine, Ivermectin, Papillomatosis*

Ağız Yoluyla Uygulanan İvermektin ile Equine Papillomatozis Tedavi Edilebilir mi?

Özet

Bu çalışmada papillomatozis'li bir atta ivermektin tedavisinin etkinliğinin değerlendirilmesi amaçlanmıştır. Bu olguyu, klinik ve histopatolojik muayenede papillomatozis olduğu belirlenen ve anemnezde iki aydır papillomdan şikayetçi olduğu öğrenilen 14 aylık kısrak oluşturdu. Papillomatozisli ata tek doz ivermektin (Eqvalan paste®, Topkim, Türkiye) 200 mcg/kg oral olarak uygulandı. Iyileşme periyodu süresince at 7., 15. ve 30. günlerde gözlendi ve bu sürede herhangi bir başka tedavi uygulanmadı. Ivermektin uygulandıktan sonraki 7. günde lezyonların gerilemeye başladığı, 15. günde %90' yakın gerileme olduğu, 30. günde ise tamamen iyileştiği görüldü. Sonuç olarak; equine papillomatozis'te ivermektinin etkili olabileceği düşünülmüştür.

Anahtar sözcükler: *At, İvermektin, Papillomatozis*

INTRODUCTION

Cutaneous papillomas are benign proliferative neoplasms with a complex the etiology and pathogenesis. In animals and men, some forms of cutaneous papilloma are caused by papillomaviruses [1-3]. Cutaneous papillomas in horses occur in acquired and congenital forms. Acquired cutaneuos papilloma in horses is a common viral-induced neoplasm similar to viral papilloma in other species. Viral papillomatosis (warts) and ear papilloma (aural plaque) are recognized as two distinct forms [4-6]. Warts are considered the most common tumors in horses between 1 and 3 years of age [5-7]. Various cutaneous sites, as well as lips, noses, ocular and genital mucous membranes are affected [8]. Papillomas can cause problems due to physical location and esthetics [8,9].

A variety of treatments have been advocated without agreement on the efficacy [10-12]. The variable success and hazards of several attempted therapies (surgery, laser

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surgery, radiation and topical drugs) have led to an interest in immunotherapy. Stimulation of cell-mediated responses by the injection of immunopotentiators has been somewhat successful [9].

Ivermectin an anthelmintic, is used commonly in horses for the treatment of parasitism [13,14]. Ivermectin may also influence the immune system of the laboratory animals and humans [15-17], but the mechanism involved in immunopotentiating effect of ivermectin is unknown. In general, beneficial effects of the use of ivermectin mediated by the immune system have been observed in *Psoroptes cuniculi* [18], *Dipetalonema viteae* [19] and human onchocerciasis infections [20]. Immunohistological studies on macrophages in lymph nodes of oncheriasis in human following treatment with ivermectin indicated that young invading macrophages were found within the cellular infiltrate around damaged microflariae and adhering to the microflariae in lymph nodes. It was also reported that the infiltrating macrophages contained increased amounts of the enzymes lysozyme, a-1-anti-chymotrypsin and a-1-antitrypsin [20]. Blakley and Rousseaux [15] showed that antibody production, T lymphocytes and macrophage-dependent response were enhanced by ivermectin treatment in mice, therefore the immunomodulating effects of ivermectin may provide an alternative approach for treatment of disease problems involving immunosuppression. Elsewhere, it was shown that serum specific antibody activity increased after ivermectin treatment [18,19]. Borku et al.[21] reported that ivermectin was effective in the treatment of bovine cutaneous papillomas. However, it appears that no study concerning the use of ivermectin for the treatment of equine papillomatosis has been reported. Thus, we aimed to evaluate the role of ivermectin given orally in therapeutic dose for the treatment of equine papillomatosis.

CASE HISTORY

A cross breed, 14 months aged horse in Cappadocia, showing cauliflower-like masses of varying sizes, elevated around the lips and nose *(Fig. 1-A)* was evaluated this study. These masses were diagnosed as papillomas following clinical and histopathological examination *(Fig. 1-D)*. Anamnesis revealed that these lesions had appeared 2 months ago, diffused around the lips and the nose and resulted in difficulty in feeding and restraining. At the clinical examination were observed small, circumscribed and overflowed cutaneous horny masses from 0.2 to 1.5 cm in diameter on the lower limb and nose regions. About 50-55 masses in number were detected.

A single shot of ivermectin (Eqvalan paste®, Topkim, Turkey) at the dose of 200 mcg/kg was orally administered to the horse. The horse was observed at 7th, 15th and 30th days and no other treatment during the recovery period.

Skin biopsies containing papillomas were obtained under local anesthesia. Biopsies were fixed in 10% neutral-buffered formalin, embedded in paraffin, sectioned and stained with haematoxylin and eosin (H&E). In histo-pathological examination, uniform epidermal hyper-plasia and expansion of the stratum spinosum were determined. There was parakeratosis and hyper-keratosis in stratum corneum. Acanthosis was seen in stratum spinosum. Stratum spinosum cells were swollen and their cytoplasms contained basophylic granules of various sizes. There were capillary dilatation, hyperemia and lymphocytic infiltration in the propria *(Fig. 1-D)*. Based on the gross and histopathological findings, the case was described as papillomatosis.

Anamnesis revealed that papillomas regressed clearly on the 7th day after the administration of ivermectin treatment. The papillomas were observed to regress and decreased about 5-6 masses in number (nearly 90%) on the 15th day *(Fig. 1-B)* and showed complete remission on the 30th day *(Fig. 1-C)*. After the treatment, no recurrence was learned at the anamnesis.

DISCUSSION

Papillomas are common cutaneous tumors in animals. Growths are pedunculated with a verrucous (wart-like) to cauliflower-like (smoother) surface [7]. Small swollen keratinized papillomas caused by equine papilloma virus are seen widely around the lips and the nose in horses [9]. In this case, a high number of papillomas in various sizes were found around the mouth and the nose.

Papillomavirus infection is the most common cause of papillomas [7]. Papillomavirus is readily detected in these acquired lesions, and the presence of keratinocytes with nuclear atypia, cytoplasmic vacuolization, and kerato-hyaline granule abnormalities (koilocytes) is characteristic. Koilocytes occur only within maturing keratinocytes in the superficial or intermediate layers of the epidermis and must be distinguished from keratinocytes with cytoplasmic vacuolar change due to other causes, such as glycogen accumulation [7,22,23]. The presence of changed keratinocytes known as koilocyte in this case suggested that the papilloma was of a viral origin.

There are various modalities in the treatment of papillomas. In animal papillomas, methods used for treatment include surgery, laser surgery, radiation,

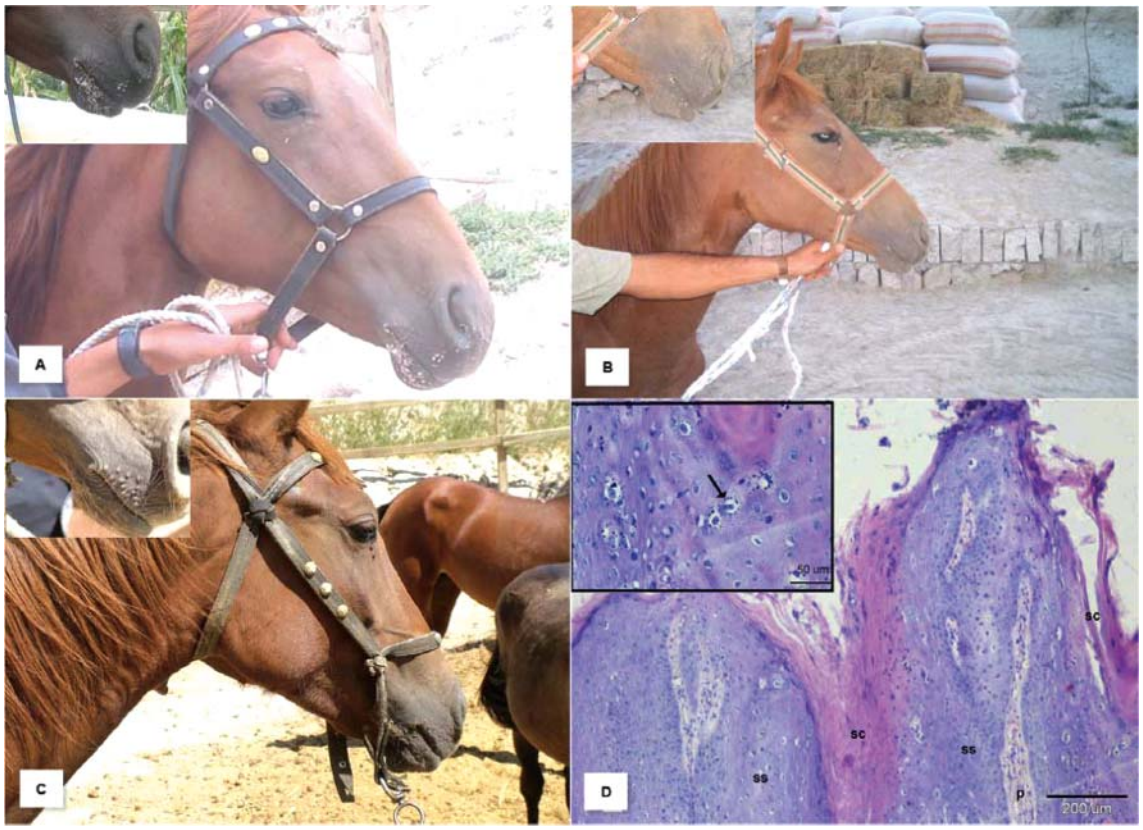

Fig 1. *A*- Horse. Mandibular region. Papilloma. Circumscribed and overflowed cutaneous horny masses. Before ivermectin administration, ***B*-** Mandibular region. On day 15 after ivermectin administration. Evident healing of the nodules, ***C*-** Mandibular region. At 30th day after ivermectin administration. Evident healing of the nodules, ***D*-** Papilloma. Epidermal hyperplasia in stratum spinosum (ss), parakeratosis and hyperkeraratosis in stratum corneum (sc) H-E. Insert: stratum spinosum. Basophylic granules of varying sizes in the cytoplasm of swollen epithelial cells. Hyperemia and cellular infiltration in the propria. p: propria

Şekil 1. *A*- İvermektin uygulaması öncesi atta ağız bölgesindeki yaygın karnabahar görünümlü kornifiye kitleler, ***B*-** İvermektin uygulamasından sonraki 15. günde atta ağız bölgesindeki iyileşen nodüller, ***C*-** İvermektin uygulamasından sonraki 30. günde atta ağız bölgesinde tamamen lezyonların iyileşmesi, ***D*-** Stratum spinosumda (ss) hiperplazi, stratum corneum(sc)'da hiperkeratozis ve parakeratozis. Şişmiş olan epitel hücre sitoplazmasında çeşitli boylarda bazofilik granüller. Propriada (p) hiperemi ve sellüler infiltrasyon

topical drugs etc. Another treatment method is administration of drugs (levamisole etc.) or chemical substances to stimulate the nonspesific immune system [9,23]. It was reported that ivermectin, an anthelmintic drug, increased antibody production, T lymphocyte and macrophage-dependent response, and therefore had an immunomodulator effect [15,18,19]. The effects on immune system of ivermectin using in the different species, application routes and doses is variable. Sajid et al.[24] was reported that the effect of ivermectin on the macrophages engulfment activity was observable when the drug concentration was 600 µg/kg. However, ivermectin was found no increase in the agglutinating antibody titer against Salmonella antigen in rabbits treated with ivermectin at 200 µg/kg [16] and caused a decrease in ability of lymphocytes to divide in response to mitogens in lambs [25]. Borku et al.[21] have found that they achieved success with ivermectin given subcutaneously in therapeutic dose for the treatment of bovine cutaneous papillomas. Therefore, in this study was used ivermectin in the therapeutic dose orally for the treatment of equine papillomatosis. We observed that oral ivermectin treatment in the therapeutic dose brought about a rapid recovery in a horse with papilloma. This case report may contribute as an easy-to-use, effective and noninvasive treatment method for the clinician.

In conclusion, it was observed that oral ivermectin administration might be effective in an equine papillomatosis case. We hope that the data generated here may contribute the current knowledge on the treatment strategies of cutaneous papillomatosis in equine.

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