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Original Research

Marjolin's Ulcer in Two Horses with Hereditary Equine Regional Dermal Asthenia

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ABSTRACT

Two Quarter Horse mares with hereditary equine regional dermal asthenia (HERDA) were diagnosed with metastatic squamous cell carcinoma (SCC) associated with chronic nonhealing wounds. The lesions were similar to the development of SCC from chronic nonhealing ulcers, known as Marjolin's ulcers in humans. The horses showed recurrent skin wounds in the saddle and paralumbar regions and were confirmed by molecular techniques as having HERDA. Both horses were maintained as research animals for prolonged periods and received regular veterinary care and wound treatment. Both horses were ultimately euthanized because of their chronic progressive wounds, coupled with declining health. At necropsy, the nonhealing wounds were found to be complicated by infiltrative SCC; both horses had metastasis to lungs. Chronically inflamed, recurrent skin wounds that heal slowly and incompletely as a consequence of HERDA are proposed as a major pathogenetic factor in tumorigenesis. Consistent findings with respect to proliferation index (Ki-67) and mutations of p53 tumor suppressor gene were confirmed by immunohistochemistry in one horse. SCC consistent with Marjolin's ulcer has been previously suggested in association with chronic ulcers or burn scars in horses, but this is the first report of an association with chronic poor healing wounds in HERDA horses.

1. Introduction

Hereditary equine regional dermal asthenia (HERDA) is an autosomal recessive disease affecting Quarter Horses and horses of Quarter Horse lineage [1]. Clinical signs typically appear at approximately 1.3 years of age and can progressively worsen with time [2]. HERDA is characterized clinically by loose, thin, and hyperextensible areas of skin that are easily damaged after minor trauma. These areas often develop chronic wounds with slow-healing and atrophic scars [2-5]. Presumptive diagnosis of HERDA is based on history, clinical signs, histological examination of skin biopsies, and pedigree analysis [4]. Definitive diagnosis requires molecular evidence of the c.115G>A

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missense mutation in cyclophilin B (peptidylprolyl isomerase B [PPIB]) [6].

Squamous cell carcinoma (SCC) is a malignant neoplasm of keratinocytes and is the second most common neoplasm observed in equine skin [7]. Prolonged exposure to ultraviolet light, in areas of unpigmented skin with sparse hair coat, is frequently implicated in the pathogenesis of this neoplasia [8]. However, case reports have noted an association between SCC and burn scars or other chronic nonhealing wounds in horses [9-11]. The development of SCC from chronic nonhealing ulcers or scars is well established in humans, and these lesions are known as Marjolin's ulcers [12,13].

This report describes the clinical, laboratory, and pathological findings in two HERDA Quarter Horse mares that developed Marjolin's ulcer associated with chronic wounds.

2. Case Reports

2.1. Case 1

2.1.1. History

A 4-year-old, chestnut Quarter Horse mare was referred to the Veterinary Hospital at São Paulo State University, Botucatu, São Paulo, Brazil, for evaluation of skin wounds in the saddle area and right paralumbar region that had been present for more than 2 years (Fig. 1A). The owners reported that the mare's sire and dam had no clinical skin abnormalities; however, her full brother had similar skin lesions.

Clinical examination revealed an 8 × 8 cm^2 cutaneous ulcer on the right paralumbar region. The owners were unaware of any traumatic incident to cause the lesion. Multiple skin areas along the dorsum appeared more fragile, thin, and loose when compared with normal tissue, and were easily elevated when pinched (i.e., hyperextensible skin). Pain was elicited when the hyperextensible skin was manipulated. Pedigree analysis revealed a common ancestor on both sides of the mare's lineage. Incisional skin biopsies were taken from the lateral neck, dorsum, and abdominal region, and these samples were routinely processed and stained with hematoxylin and eosin and Masson's trichrome. The most remarkable histopathological finding was the presence of thin small collagen fibrils, which created a loose arrangement of collagen fibers within the deep dermis [5]. A presumptive diagnosis of HERDA was made on the basis of the clinical and histopathological findings. On diagnosis, the owners chose to donate the horse to the HERDA herd for research purposes.

The mare was housed in an individual paddock and received daily wound dressing. To avoid myiasis, a repellent insecticide (cypermethrin, 0.4 mg/100 g and dichlorvos, 1.6 g/100 g) was applied daily around the wound. The wound healed after wound care and became an atrophic scar. The skin in the right paralumbar region tore several times in the following years, as did skin in other body regions (Fig. 1B). The same treatment was performed and the wounds always healed well.

Five years after referral to the hospital, the mare exhibited anorexia, progressive weight loss, lethargy, and an extensive right paralumbar wound at the initial site described earlier in the text. Physical examination revealed a cutaneous ulcer (8 × 12 cm^2) with purulent exudate. No evidence of local pain or pruritus was observed. Treatment consisted of wound dressing as previously described, penicillin G benzathine (30,000 IU/kg, intramuscular [IM], once daily) and trimethoprim-sulfadoxine (20 mg/kg, IM, once daily) for 7 days, as well as flunixin meglumine (1.1 mg/kg, intravenous [IV], twice daily) for 3 days.

Fig. 1. Skin wound of a Quarter Horse mare with hereditary equine regional dermal asthenia. (**A**) Atrophic scar at the right paralumbar region after the first topical treatment of the wound; the mare was 4 years old. (**B**) In subsequent years, the skin broke several times at the same region. (**C**) Progressive weight loss and wound deterioration of the mare on the day she was humanely euthanized; the mare was 10 years old.

Despite local treatment, the wound over the right paralumbar region had not healed 12 months later. Physical examination revealed a persistent cutaneous ulceration (18 × 18 cm^2) with thickened areas, necrotic foci, and purulent exudate distributed along the right paralumbar region (Fig. 1C). The mare appeared to be experiencing pain during wound handling, and evidence of self-mutilation of