Case Report

A Case of Pemphigus Folliaceus Treated with Homeopathy in a Horse

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Abstract

A 6-year-old Dutch Warmblood dressage horse mare was presented with an 8-month history of blisters, scales, and edema all over the body. A skin biopsy from 2.5 months earlier supported the diagnosis of pemphigus foliaceus. At presentation for homeopathic treatment, the mare had been maintained on prednisolone (600 mg q 24 hr) for 2.5 months because attempts to decrease the dose (300 mg q 24 hr) resulted in an immediate relapse of clinical signs. Frequent doses of the homeopathic medicine Phosphorus 200K allowed for the dose of prednisolone to be decreased after 5 days; after 5 weeks, the prednisolone was discontinued. The signs of pemphigus foliaceus resolved after 63 days of homeopathic treatment, and the mare remained free of skin lesions at the 2-year follow-up.

Introduction

Pemphigus foliaceus, the most common autoimmune skin disease in horses, is associated with the production of autoantibodies directed against keratinocyte surface proteins that mediate intercellular adherence (1). These autoantibodies bind to the surface of the keratinocytes and stimulate acantholysis. This disease is characterized by the presence of vesicles and pustules that may wax and wane. It is rare to find primary pustules in the horse because the lesions rapidly progress and leave crusted erosions. Alopecia, scaling, and crusting are the most common clinical signs, with variable presentations of pruritus, pain, edema, and fever. Lesions may begin on the face or limbs and spread to the rest of the body. There is also a localized form that is restricted to the coronary bands (1).

Pemphigus is identified in adult and young horses less than 1 year of age (2, 3). Young horses often have a better prognosis for remission without relapse than adult horses. Initial case reviews reported that the risk of developing pemphigus foliaceus was higher in Appaloosas, but more recent reviews do not support that finding and state that Quarter Horses and Thoroughbreds may be more predisposed (2–4). No gender predilections were found, and 80% of cases had the first lesions appear between September and February (2, 4). The timing may be associated with insect exposure or preventive medicine practices, such as deworming and vaccination, which occur at specific times of the year. The reviews state that the most common clinical signs are edema and crusting followed by pain, pruritus, and fever. In addition to the cutaneous lesions, systemic signs may include depression, poor appetite, weight loss, and fever (2, 4).

Pemphigus foliaceus should be considered in all cases of skin disease that present with scaling and crusting. Differential diagnoses include dermatophytosis, dermatophilosis,
systemic granulomatous disease, and primary keratinization disorders. Before making this diagnosis, the pathologic changes associated with pemphigus foliaceus should be evident from the gross skin lesions, cytology, and histology results. Cytology can be taken from intact pustules or erosive-crusted lesions. Often, single or rafts of acantholytic cells are found on Wright or Diff-Quik staining. Generally, few or no bacteria are found from intact pustules, and only extracellular bacteria are found from erosive, crusted samples. Optimally, biopsies should be taken from primary vesicles or pustules to identify acantholytic cells histologically, but intact pustules are rarely found, making biopsies from crusted lesions the next best choice. These areas should not be surgically prepared because this may remove the crusts that contain the diagnostic acantholytic cells and affect the diagnostic value of the biopsy. Direct immunofluorescence and immunohistochemistry are rarely performed in equine cases but could reveal a diffuse intercellular deposition in the epidermis of immunoglobulins IgG, IgM, and occasionally complement. One study that applied indirect immunofluorescence testing found circulating anti-keratinocyte autoantibodies in 5/9 (56%) of horses with pemphigus foliaceus; most of these horses had skin-fixed intercellular epidermal IgGs (3). Although diagnostic emphasis is on histopathology, other potential abnormal laboratory findings include mild normocytic normochromic anemia, neutrophilia, mild hypoalbuminemia, and hypergammaglobulinemia (1).

High dosages of glucocorticoids are the standard treatment for pemphigus foliaceus. Prednisolone is preferred over prednisone in horses because the efficacy of prednisone is limited by its poor absorption and biotransformation in horses (5). Prednisolone is generally effective at high induction doses (1.5–2.5 mg/kg q 24 hr for 7–10 days). This is tapered over several weeks to a maintenance dose (0.5–1 mg/kg q 48 hr). Occasionally, other forms of glucocorticoids, such as dexamethasone, may be needed at tapering doses (1).

Injectable gold salts, specifically aurothioglucose, have been used successfully in horses with pemphigus foliaceus, but this is no longer available. An alternative is aurothiomalate. In a protocol extrapolated from the human literature, test doses of injectable gold salts (20 mg and 50 mg weekly) are given to evaluate for potential deleterious side effects including eosinophilia and cutaneous reactions. If there are no abnormal reactions, weekly intramuscular injection can be administered; there is a long lag phase of 6 to 12 weeks before a response may be seen. It is recommended to monitor for bone marrow suppression (in particular, thrombocytopenia), drug reactions, and proteinuria (1).

There are reports in the literature of using azathioprine for various autoimmune skin diseases in horses. However, the use of azathioprine in horses may be cost prohibitive for many clients (6, 7). Horses have low levels of thiopurine methyltransferase, the enzyme that is responsible for the metabolization of azathioprine, necessitating monitoring for potential side effects of thrombocytopenia, leukopenia, and anemia (8). Azathioprine can also be used in an attempt to decrease the amount of steroid required for long-term management. Other adjunctive treatments with variable success rates include pentoxifylline and omega-3 and omega-6 fatty acids (1).

The management of pemphigus foliaceus requires patience and support because this disease may take weeks to months to control and can wax and wane. In young horses, the prognosis is generally good, and some cases can go into complete remission without ongoing therapy. In adult horses, a small percentage of cases do not achieve adequate control of clinical signs. In a retrospective study, 5 of 13 horses (38%) were euthanized for either lack of response to treatment or development of steroid-induced acute laminitis; 4 of 11 horses (36%) remained in remission for more than 1 year after immunosuppression therapy (2). In another study, follow-up information from 7 out of 15 horses indicated that 1 horse was euthanized due to financial constraints, 1 horse achieved long-term remission in the absence of treatment, and the other horses achieved remission with prednisone, prednisolone, or aurothioglucose treatments (4).

**Case report**

A 6-year-old Dutch Warmblood mare was presented for homeopathic treatment for pemphigus foliaceus.
The initial cutaneous lesions were noted 8 months prior to presentation for homeopathic treatment and were characterized by some crusts on the legs and urticaria on the body. The horse had been vaccinated for influenza and tetanus (a) 1 month prior to the appearance of the skin lesions. The veterinarian presumed this was a case of mycosis and treated the horse with enilconazole (b). Treatment with enilconazole was repeated when the lesions became worse. The horse had a severe reaction characterized by severely edematous legs and large, warm nodules on the skin.

A biopsy was then taken of a hard, parchment-like cutaneous lesion on the left shoulder. Histopathology found a large serocellular crust with acantholytic keratinocytes and large numbers of degenerate and intact neutrophils; a mainly intact epidermis with mild hyperplasia; a mild, mainly perivascular infiltration of the dermis with mononuclear inflammatory cells, mild to focally severe edema, and regions of well-developed adnexa. The findings were supportive of a diagnosis of pemphigus foliaceus.

The skin lesions resolved when the mare was treated with prednisolone (600 mg q 24 hr) for 2.5 months, but after 1 week on a tapered dose (300 mg q 24 hr), the scales, crusts, and edema returned. The owner refused to give lifelong medication and was considering euthanasia if homeopathic therapy was not successful.

On presentation for homeopathic treatment, the mare was slightly emaciated with a range of hard and soft circinate blisters, scales, and crusts all over her body with a left sided distribution predominating, and edema of the legs (Figure 1, see page 45). The lesions were mildly pruritic and slightly sensitive to touch.

Subjectively, the mare was overreactive with startling or jumping away to every sight and sound when she was with a new rider, sensitive to touch with jumping to all sides when grains of sand touched her body at a trot; and girthing had to be done with care. Her lean and athletic appearance was impressive, as were her gaits and shiny skin. She had a thin skin but liked to be brushed and caressed.

Prednisolone was continued (300 mg q 24 hr) because the pemphigus lesions were present at that dose, enabling any change in clinical signs to be attributed to the addition of the homeopathic medicine to the current protocol. Detoxification was initiated with Lymfedrainage (c) at 2.5 ml twice daily.

The skin lesions were significantly worse 1 week later. Phosphorus 200K (d) was prescribed (1 pellet dissolved in 10 ml of water and 3 gtt of 70% ethanol; 10 succussions then 3–5 drops applied directly to the oral mucous membranes q 24 hr).

On day 3 of homeopathic treatment, the owner discontinued the homeopathic therapy because the mare was exhibiting dull mentation.

By day 5, the lesions were slightly less swollen, but the mare was still pruritic. The mare was also experiencing limb stiffness, and the hind limbs were more edematous and warm. The decision was made to increase the frequency of administration of the Phos 200K (3 doses q 1 hr) because of the improvement in the skin lesions even though other clinical signs were worse.

The next day, the mare was more lively. A new cutaneous lesion appeared on the right side of her body, but the existing lesions looked better and were less swollen. Her legs were still edematous. The Phos 200K solution was continued at the same dose noted for day 5.

On day 7, the initial cutaneous lesions were continuing to resolve and were smoother. Crusts were removed with brushing. An edematous region developed in front of the udder. The dosing of Phos 200K was maintained.

By day 11, the lesions at the front of the body had resolved; although some spots were smoother, others became larger. The legs were less edematous. The dose of Phos 200K was continued; the dose of prednisolone was decreased (300 mg every other day).

One week later, the owner reported that all the lesions were significantly improved except the ones that remained on the neck; interestingly, the neck was the site where the lesions first appeared. The Phos 200K dosing was continued; the dose of prednisolone was decreased further (300 mg q 3 days).
Figure 1: The mare at the beginning of homeopathic treatment.
By day 40, the mare was much improved. A few small lesions remained on her neck, but her legs were clear (Figure 2, above). The Phos 200K was continued; the prednisolone was discontinued.

On day 49, a few new, mild spots developed on her shoulder, but overall, the skin was clear. The owner started to ride her again. The dosing of Phos 200K was decreased to every other day. On day 63, the owner reported that the skin was fine except for a spot on the shoulder where the biopsy had been taken.

Treatment with Phos MK (e) (SID for 7 days) was initiated because the improvement in the skin lesions had plateaued and only the biopsy-spot with rough hair on the shoulder still existed. The lesion on the shoulder did not change by day 77 (Figure 3, see page 47) and had the appearance of a biopsy scar. At this point, the horse returned to full training and dressage shows. Phos MK was discontinued.

At a recheck 1 year later, the skin was fine except for the rough haircoat at the biopsy site on the shoulder. By 2 years later, the last remaining sign on the shoulder had resolved. The horse never experienced a relapse of pemphigus foliaceus signs.

Discussion

The prognosis for horses with pemphigus foliaceus is guarded. Prolonged treatment with prednisolone is often necessary and, if possible, the dose of prednisolone should be decreased very carefully. The horse owner needs to make an informed decision and recognize the commitment required to optimize response to treatment. Young horses have a better prognosis than older horses. Euthanasia was considered for the horse described in the case report because clinical signs recurred immediately after a couple of attempts to decrease the dose of prednisolone. Homeopathy was the last option for the horse.

The homeopathic medicine Phos was chosen to treat this horse (Figure 4, see page 47). Her overreactivity to all impressions and physical appearance were all signs that, according to homeopathic rules, indicated Phos.

A rule of thumb in classical homeopathy is to administer the lowest dose of the indicated homeopathic medicine. However, in severe cases, it is acceptable to induce a reaction by administering the medication more frequently. In this horse, Phos 200K gave a slight reaction when given once daily, but a good healing response was achieved when the frequency was increased to 3 doses a day separated by 1 hour. It was clear that the resolution of clinical signs was the...
result of homeopathic therapy because the skin lesions resolved immediately after the addition of frequent doses of Phos 200K to the prednisolone treatment that the horse had been receiving.

The owner chose to maintain the frequent doses of Phos 200K out of concern for a relapse if the dose was decreased. It is the writer’s experience that some patients with severe pathology recover more quickly with repetitive dosing than less frequent dosing.
In a successful homeopathic cure, it is expected that an increase in the patient’s vitality will be one of the earliest indicators that cure is occurring. In this case, the mare’s increase in vitality was noted the day following the increase in dosing frequency. In addition, and often in contrast to conventional therapies, in successful homeopathic treatment the oldest signs will disappear last. The regression of signs in the horse in this case did indeed move in this direction, with the original lesions on the neck being the last to resolve (Figure 5, above).

Pemphigus foliaceus remains a challenging autoimmune disease with a guarded prognosis in the horse. Given the significant euthanasia rate and side effects related to the currently available conventional therapies, homeopathic treatment should be considered when appropriate in the equine patient.

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Endnotes
(a) Equip FT, Zoetis, Belgium
(b) Imaverol, Elanco Animal Health, Belgium
(c) Lymfedrainage, Apotheek Denys, Gent, Belgium
(d) Phosphorus 200K, Dolisos/Unda, Belgium
(e) Phosphorus MK, Dolisos/Unda, Belgium
(f) Repertorization from Radar 10.5.003

References