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Ulcerative Dermatitis, Thrombocytopenia, and Neutropenia in Neonatal Foals

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This report describes transient ulcerative dermatitis, severe thrombocytopenia, and mild neutropenia in 6 foals from 4 mares from geographically diverse regions of the United States. The foals presented at <4 days of age with oral and lingual ulcers, and crusting and erythema around the eyes, muzzle, and perineal, inguinal, axillary, trunk, and neck regions. There was a severe thrombocytopenia (0–30,000 platelets/μL), leukopenia (1,900–3,200 white blood cells/μL), and mild neutropenia (500–1,800 neutrophils/μL). Four of the 6 foals had petechiae and ecchymotic hemorrhages and 3 had bleeding tendencies. Results of examination of a bone marrow biopsy from 1 foal were normal and results of a platelet surface immunoglobulin test in another were negative. Histopathology of the skin in all foals showed subepidermal clefting with subjacent vascular dilation, dermal hemorrhage, and superficial papillary necrosis. The foals were treated supportively with broad-spectrum antibiotics (5/6), corticosteroids (3/6), gastric ulcer prophylaxis (6/6), whole-blood transfusion (4/6), and platelet-rich plasma (1/6). The skin lesions and thrombocytopenia (>50,000 platelets/μL) improved in 2 weeks (4/6). Two foals had a decline in their platelet counts when the steroids were decreased and needed protracted treatment. All foals survived and were healthy as yearlings. Two mares that had 2 affected foals each, upon subsequent pregnancies to different stallions, had healthy foals when an alternate source of colostrum was given. The findings in the cases in this report suggest a possible relationship between colostral antibodies or some other factor in the colostrum and the thrombocytopenia and skin lesions, although further investigation is warranted to confirm or refute this hypothesis.

Key words: Dermatopathy; Horse; Neutrophil; Platelet; Skin.

The purpose of this paper is to describe a syndrome of transient ulcerative dermatitis, severe thrombocytopenia with bleeding tendencies, and neutropenia in neonatal foals. The physical examination, clinicopathologic, clinical progress, and histopathology of skin biopsy findings of 6 neonatal foals from geographically diverse regions of the United States will be presented.

Materials and Methods

The medical records of 6 neonatal foals examined between 1998 and 2002 with a transient ulcerative dermatitis and severe thrombocytopenia were summarized. The foals were seen at 3 referral hospitals throughout the United States, including Cornell University Hospital for Animals, Ithaca, NY (n = 2), Washington State University Veterinary Teaching Hospital, Pullman, WA (n = 2), and Peterson and Smith Equine Hospital, Ocala, FL (n = 2). A CBC and skin biopsy were performed on all foals. The skin biopsies were fixed in formalin and the slides were evaluated by 1 dermatologist (WHM) retrospectively for the purposes of publication. Data collected from the record included the signalment and parity of the mare and events (medications, illness, and vaccinations) that occurred during pregnancy and parturition, the health of the placenta, as well as the signalment of the foal and events (type of navel dip; colostrum ingestion and immunoglobulin G [IgG] concentration; and administration of vitamin E and selenium, tetanus antitoxin, antibiotics, or other medication) from birth to the onset of clinical signs. The findings of physical examination, hematologic and serum biochemistry, and other diagnostic tests, such as coagulation panel (n = 4), Coombs test (n = 4), bone marrow biopsy (n = 1), skin biopsy (n = 6), and platelet surface immunoglobulin test (n = 1), were evaluated. The clinical course of the disorder along with treatments and outcome were recorded. Similar data from unaffected foals in later years was obtained from mares that had had previously affected foals.

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Results

All mares (n = 4) were multiparous and 2 mares had 2 affected foals from different sires in sequential years, accounting for 4 of the involved foals. No common events were identified that occurred during pregnancy, parturition, and from birth to the onset of clinical signs in these foals, except that all foals received adequate colostrum and were female. All mares were vaccinated during pregnancy and 1 mare was treated during each pregnancy. In that mare, trimethoprim-sulfa was administered for a skin wound during the 1st pregnancy and trimethoprim-sulfa and pentoxyfilline for a suspect placentitis during the 2nd. Each foal was of full gestational age and 1 foaling was prolonged. The placentas of all foals were normal. All foals were fillies and were less than 4 days of age at the time of examination. There were 4 Thoroughbred and 2 crossbred Paint and Warmblood foals. Vitamin E and selenium was administered intramuscularly at birth to 2 foals. Four foals had their navels dipped with chlorhexidine and 2 with iodine. Tetanus antitoxin was administered to 2 foals and 2 foals were treated with procaine penicillin G before the onset of clinical signs. All foals had evidence of adequate transfer of passive immunity with an IgG >800 mg/dL at 24 hours of age.

Generally, foals were bright, alert, and responsive at initial examination. Two foals were mild to moderately lethargic and 1 foal with marked oral lesions had a decreased appetite. Two foals had slightly increased rectal temperatures (102.1°F and 102°F), and the pulse and respiratory rates were within reference ranges. All foals had oral and lingual ulcers, as well as crusting and erythema around the eyes, muzzle, and perineal, inguinal, axillary, trunk, and neck regions. Many (4/6) of the foals had petechiae and

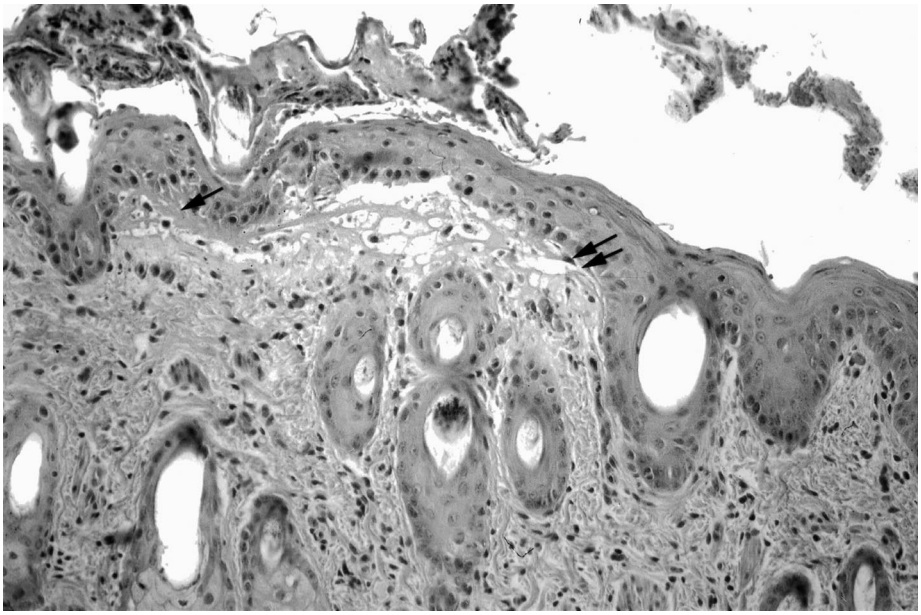

Fig 1. Histopathologic examination of formalin-fixed skin biopsy of foal 1 from mare 1 stained with hematoxylin and eosin at 40×. Notice the subepidermal vesicular change, superficial dermal edema, vascular congestion, and superficial hemorrhage (double arrow), and more advanced lesions showing dermoepidermal separation with fibrin, cellular debris, and red blood cells filling the cleft (single arrow).

ecchymotic hemorrhages and 3 exhibited bleeding tendencies with hematoma formation after venipuncture, mild bleeding from the gums, and bilateral epistaxis.

A severe thrombocytopenia (0–30,000 platelets/μL, reference range 200–339 × 10^3 platelets/μL)[1] without platelet clumping was noted on blood collected in ethylenediaminetetraacetic acid tubes from all foals. The thrombocytopenia was confirmed by a manual count in all foals and 3 foals had the severe thrombocytopenia documented by using sodium citrate as an anticoagulant. A leukopenia (1,900–3,200 white blood cells [WBC]/μL, reference range 4,500–11,000 WBC/μL)[2] and neutropenia (500–1,768 neutrophils/μL, reference range 3,040–9,570 neutrophils/μL)[2] was noted in all foals, with a mild left shift and mild toxic changes in 5 and 3 foals, respectively. The prothrombin time (13.6 seconds, reference range 10.3–11.5 seconds)[1] and partial thromboplastin time (118.1 seconds, reference range 50.5–63.1 seconds)[1] was prolonged in 1 of 4 foals. Results of a Coombs test were negative in all 4 foals tested. Results of a blood culture, equine herpes virus isolation on whole blood, as well as equine viral arteritis titer were negative in 1 foal. Examination of a bone marrow biopsy from 1 foal did not reveal abnormalities. Results of a platelet surface–associated immunoglobulin test were negative for IgG antibodies in another foal (0% IgG antibodies, compared to similarly aged foals [n = 7] measured at the same time, which had 2–16% IgG antibodies bound to the platelets).[a]

Several punch biopsies of the skin lesions were taken from each foal. The skin biopsy procedure was delayed in most cases (5/6) because of the clinical evidence of bleeding tendencies and thrombocytopenia. The biopsies were done between days 3 and 6 of hospitalization, except for 1 foal in which the biopsy was performed shortly after admission because no evidence was found of a bleeding tendency on physical examination and the results of the platelet count were pending. Therefore, the 6 foals provided a skin sample from various stages of the disorder. All foals showed similar histologic abnormalities. The epidermis exhibited multifocal ulcerations with abnormalities at the dermoepidermal junction adjacent to the ulceration. Early changes were characterized by subepidermal vesicular change, superficial dermal edema, vascular congestion, and superficial dermal hemorrhage (Fig 1, single arrow). In more developed lesions, there was dermoepidermal separation with fibrin, cellular debris, and red cells filling the cleft (Fig 1, double arrow).

Most (5/6) of the foals were treated with broad-spectrum antibiotics and all (6/6) were given H2 blockers for ulcer prophylaxis. Corticosteroids were administered to 3 of the foals. Four foals were administered a whole-blood transfusion and 1 received platelet-rich plasma (PRP). Granulocyte colony-stimulating factor (G-CSF)[b] was administered to 1 foal on day 4 and the neutrophil count changed from 1,870 to 20,254 segmented neutrophils/μL accompanied by a marked left shift (2,470 bands/μL) and mild toxic changes within 24 hours. The platelet count in that foal before G-CSF was 3,000 platelets/μL and the following day was 6,000 platelets/μL. Foal 3 developed *Clostridium difficile*–associated enterocolitis and oral candidiasis on day 14 of hospitalization and another foal (foal 6) returned to the hospital 2 weeks later with a septic arthritis of the left stifle. Immunosuppressive doses of corticosteroids and multiple antimicrobial regimes (potassium penicillin G and amikacin followed by ceftiofur) had been administered to the foal that developed clostridiosis.

Platelet count gradually increased in most cases within 7–10 days (Fig 2). Two foals underwent repeated declines in their platelet counts at the same time that changes in corticosteroid administration occurred (Fig 2). Neutrophil counts in all foals returned to within the reference range

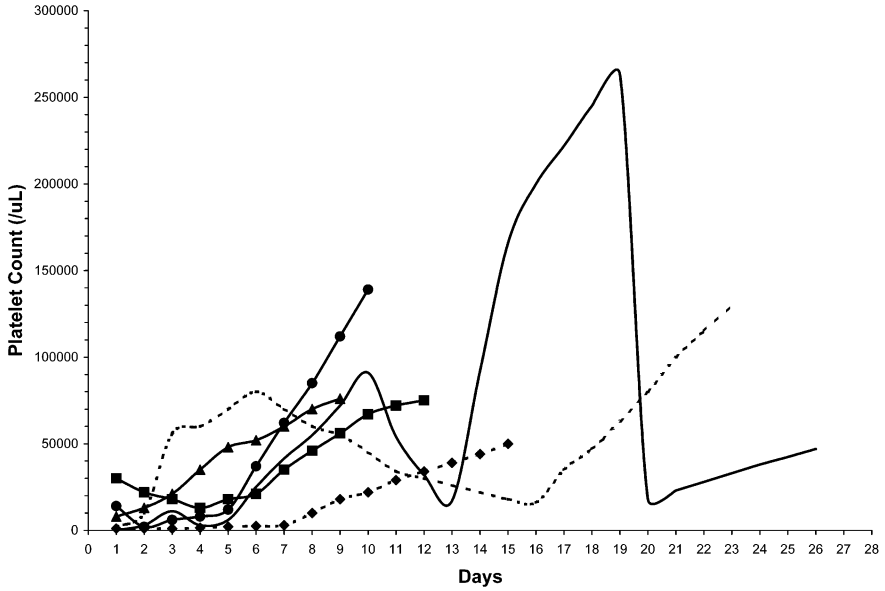

Fig 2. Platelet counts throughout hospitalization and after discharge in 6 neonatal foals with thrombocytopenia and ulcerative dermatitis. Foal 3 (———) was treated with dexamethasone sodium phosphate[c] at 0.1 mg/kg q24h on days 1, 4, 5, 6, and 7, then decreased to 0.05 mg/kg q24h on days 8, 9, and 10, a higher dosage of 0.1 mg/kg q12h on days 13 and 14, and then 0.1 mg/kg q24h from day 15 to day 19. Foal 4 (– – –) was administered dexamethasone sodium phosphate at 0.1 mg/kg q24h on days 1, 2, 3, 4, and 5 and 0.05 mg/kg q24h on days 6, 7, 8, and 9, and 0.07 mg/kg q24h on days 16–18. Foal 5 was treated with prednisolone sodium succinate[d] 2 mg/kg IV on day 1 and was continued on prednisolone sodium succinate at 1 mg/kg q24h until day 7 and then switched to dexamethasone sodium phosphate 0.1 mg/kg q24h for days 8 and 9.

within 3–9 days after hospitalization. CBCs were not performed at the same time in the 2 foals that had relapsing thrombocytopenia; therefore, we are unable to comment on whether the neutropenia recurred in these foals. The skin lesions resolved within 10–14 days and all foals were healthy 5 months to 2 years later.

Two mares had 2 foals affected in spite of being sired by different stallions. On subsequent offspring consisting of 2 fillies and 1 colts, an alternate source of colostrum was provided and these foals did not develop this syndrome. The foals were muzzled for 24 hours and frozen colostrum from other mares on the farm was given. None of the subsequent foals developed clinical signs similar to the previous foals and a CBC on the 1st few days of life showed platelet and neutrophil counts within the reference ranges.

Discussion

This report describes a transient ulcerative dermatitis, thrombocytopenia, and neutropenia in neonatal foals where the ulcerative dermatitis and thrombocytopenia are especially pronounced. Previously reported causes of thrombocytopenia in neonatal foals include neonatal bacterial septicemia and disseminated intravascular coagulation,[3–5] viral infection (equine herpes virus and equine arteritis virus), and neonatal alloimmune thrombocytopenia.[6–8] The repeated occurence of this thrombocytopenia in foals from the same mare, and its transient nature, suggest that this condition might be similar to neonatal alloimmune thrombocytopenia, but the ulcerative dermatitis is distinct. Because all foals developed clinical signs at <4 days of age, an autoimmune-mediated disease was considered unlikely, given the foal's naive immune system. The gradual improvement in platelet count over 2–6 weeks might be supportive of a decline in platelet antibody from the colostrum.[9,10]

Diagnostic tests that can differentiate between excessive platelet consumption versus lack of production of platelets in the bone marrow include mean platelet volume,[11] platelet factor 3,[12] bone marrow biopsy, flow cytometric analysis detecting thiazole orange–positive (reticulated) platelets,[13] and flow cytometric assay for platelet surface IgG.[14–16] In this case series, 1 bone marrow biopsy was examined and no increase or decrease was found in the megakaryocyte line, which along with the clinical course of the disease, tends to support a consumptive process. An attempt to identify IgG on the surface of the platelets by using flow cytometry was done in 1 foal at 4 days of age (day 2 of hospitalization when the foal had a platelet count of 2,000 platelets/μL) and the result was negative.[a] The day after the platelet surface antibodies test was performed there were 8,000 platelets/μL, after which the platelet count continued to increase rapidly (see Fig. 2, foal 6). The foal had not been treated with steroids. The negative results of flow cytometry do not exclude maternal antibodies as the cause of the thrombocytopenia in this instance. The thrombocytes coated with maternal antibodies may have already been removed from circulation by the reticuloendothelial system, as evidenced by the improving platelet count from this point forward. The sample perhaps was taken too late in the disease process.

The results of the limited platelet tests performed in the foals in this study along with their clinical outcomes support a regenerative thrombocytopenia, but further investigation needs to be performed. Diagnostic evaluation of fu-

ture foals with this syndrome should include flow cytometric analysis for platelet-associated antibodies, direct measurement of antibodies bound to platelets, indirect measurement of binding of mare antibodies to foal platelets by using radiolabeled antiglobulin reagent staphylococcal protein A or anti-equine IgG as a cause, or a combination of these.[14–16] Other supportive data would include testing of stallion platelets with mare plasma and colostrum, testing the foal platelets against the mare colostrum, and confirming that the mare did not have antibodies bound to her own platelets. In humans, most autoantibodies to platelets are directed against platelet glycoprotein IIb-IIIa, the most abundant and immunogenic platelet surface glycoprotein.[17] Defining the allotypes of equine platelets and equine platelet antigens, and comparing maternal and neonatal types would further understanding of neonatal alloimmune thrombocytopenia in horses and mules. The fact that the mares were bred to different stallions and produced thrombocytopenic foals on each occasion argues against typical neonatal alloimmune thrombocytopenia. Instead, the mares may have been exposed to a cross-reacting antigen or a foreign platelet antigen that was highly immunogenic and prevalent in the population.

Three aspects of these cases support neonatal alloimmune thrombocytopenia as the most probable cause of the profound thrombocytopenia: all mares were multiparous and 2 of the mares had 2 affected foals from different stallions; subsequent foals from these 2 mares did not develop clinical disease when given an alternate source of colostrum; and the thrombocytopenia was self-limiting with return of the platelet count toward the reference range with 2–3 weeks of supportive therapy, which corresponds to the half-life of maternal IgG in neonatal foals (24 days).[9,10]

Interestingly, all of the foals in our report are fillies, which could suggest a sex linkage. However, another mare seen by ambulatory clinicians at Peterson & Smith Equine Hospital had 3 foals with this syndrome, 1 of which was a colt. These foals were thrombocytopenic and had skin lesions but were not included in the case series in this report because a skin biopsy was not performed.

Septicemic foals are frequently thrombocytopenic but rarely or ever as severe as the thrombocytopenia in these 6 foals.[3–5] Half of the foals in this study had sepsis scores $\geq$11.[18,19] The neutropenia, left shift, and toxic changes observed in most of these foals suggests septicemia. However, petechiations in all 3 of these foals may have falsely contributed to a positive sepsis score (total of 3 points) and may have had a different pathophysiology than septicemia. In fact, the sepsis scores for these 3 foals would be $<$11 (8, 10, and 10) if points due to petechiae were omitted from the calculation. One foal recovered rapidly without antibiotic therapy. Three of 4 foals had coagulation times within the reference range and the other was only mildly abnormal, which does not support a consumptive coagulaopathy such as disseminated intravascular coagulation as a cause of the thrombocytopenia. A blood culture was performed on 1 foal and its result was negative; however, blood cultures are not sensitive. Although some laboratory evidence of sepsis was found, we do not believe septicemia was the cause of the severe thrombocytopenia in these foals because of IgG concentrations within the reference range in all foals, normal coagulation profiles in 3 of 4 foals, the severity of thrombocytopenia did not correspond to the degree of possible sepsis, absence of tachycardia, repeated disease in foals from the same mare, the slow increase in platelet counts and skin lesions over 2–6 weeks, and recovery in 1 foal without antimicrobial therapy.

All foals were neutropenic (500–1,768 neutrophils/μL) compared to healthy foals (reference range 4,500–11,500 neutrophils/μL)[1–3] and we are unsure of the cause. Etiologies of neutropenia in neonatal foals can be categorized similarly to those of thrombocytopenia: decreased production or increased consumption or loss or both. By far the most common cause of neutropenia in neonatal foals is septicemia and toxemia followed by viral disease (equine herpes virus 1 and equine viral arteritis).[18,20] About 70% of septicemic foals have neutrophil counts $<$4,000 neutrophils/μL[18] and foals with equine herpes virus 1 tend to have $<$3,000 WBC/μL.[20] As previously discussed, we do not necessarily believe that these foals were initially septicemic, although, like the thrombocytopenia, the neutropenia, left shift, and toxic changes contribute 3–7 points to the sepsis scores of these patients.[19] A recent report has described neonatal alloimmune neutropenia in an Arabian foal[21]; however, immune-mediated destruction of neutrophils with profound neutropenia ($<$200 neutrophils/μL) has rarely been reported in animals.[22–25] The neutrophils in the foals in this study also may have been involved in a reaction with maternal antibodies, although the neutrophil numbers were not as profoundly affected (none $<$500 neutrophils/μL) as platelets. Based on the small number of foals, as well as the individual variation in half-life of neutrophils and platelets in horses, and how these cells might have been affected by maternally derived antibodies, it is difficult to determine if the changes in the platelet and neutrophil numbers shared a similar pattern, although most foals (4/6) had improvement in neutrophil numbers that corresponded to increases in platelet counts throughout the first 3–9 days of therapy. It would have been interesting to see if the neutrophil count decreased when the thrombocytopenia relapsed in foals 3 and 4 (see Fig 2), but those data were not obtained. It is possible that the neutropenia in these 6 foals could have been due to a combination of immune-mediated destruction similar to the thrombocytopenia and secondary sepsis, or even possibly associated with the skin lesions. Other causes of neutropenia in foals in previously published reports do not fit with what was seen in the foals in this study with concurrent thrombocytopenia and skin lesions.[26,27] The mild neutropenia may have been from margination of the neutrophils to the dermis-epidermis and contributed to the inflammation there, although a marked neutrophilic infiltrate was not seen in the skin biopsies. Flow cytometric analysis of neutrophils in these foals compared to age-matched controls[21] is needed to rule out immune-mediated destruction of neutrophils by maternal antibodies in future cases.

We are especially perplexed to explain the pathogenesis of the skin lesions and exactly how they are related to the severe thrombocytopenia and ecchymosis. We could find no comparable human or animal model for this conclusion. The skin lesions may have been a separate entity (but unlikely in 6 of 6 foals), and in that case, the clinical progress and histopathology of the skin in these foals could support

a transient epidermal bullous dermatosis. An idiosyncratic or chemical reaction to drugs given systemically to the mare and foal (penicillin, pentoxifylline, trimethoprim-sulfa, vitamin E, or selenium), or to topically administered products such as navel dips (iodine or chlorhexidine) could have contributed. No single medication, topical or systemic, was administered to all foals. An iodine reaction was implicated as a cause of transient subepidermal bullous disease without thrombocytopenia in an Appaloosa foal given an iodine navel dip.[28] Only 2 foals in the group in this study were given an iodine navel dip.

The thrombocytopenia, skin lesions, and neutropenia in all foals at a similar age and recovery over a similar time period suggests the hypothesis of a common pathophysiology. One would like to make this presentation of clinical signs into 1 disease process and relate the skin lesions with the thrombocytopenia. Two of the mares with affected foals had a total of 3 sequential healthy foals when an alternative source of colostrum was given, making maternal antibodies or some factor within the mare's colostrum a likely cause of the ulcerative dermatitis, thrombocytopenia, and possibly neutropenia. The destruction of platelets and neutrophils by colostral antibodies could be accompanied by an immune-complex, small-vessel, superficial vasculitis and inflammation resulting in the epidermal necrosis seen on the skin biopsies of these foals.

Foals with thrombocytopenia, neutropenia, and ulcerative dermatitis should be maintained quietly in a safe environment to avoid the risk of external trauma that may result in uncontrolled hemorrhage. Supportive therapy, such as a PRP transfusion, can be used to briefly increase the functional platelet count above the minimum level for adequate hemostasis (approximately 30,000 platelets/μL).[29–32] Treatment of equine thrombocytopenia with PRP is uncommon, probably because benefits are of short duration and cost and technical production of PRP may not be readily available. Administration of PRP, or the more easily prepared whole blood generally result in only mild to moderate increases in platelet counts in other species.[33]

Corticosteroid therapy appeared to be efficacious in increasing platelet counts in some of these foals. Of 3 foals treated with corticosteroids, 2 had a marked decline in their platelet counts when corticosteroids were discontinued or dosage was decreased. A corresponding increase in the platelet count occurred when corticosteroid therapy was reinstituted or the dosage was increased in these 2 foals. This response to treatment with corticosteroids suggests an immune-mediated process (alloimmune thrombocytopenia or other causes of immune-mediated thrombocytopenia) with consumption of platelets. However, these findings may be coincidental. Foals with neonatal isoerythrolysis have been treated with corticosteroids and use of corticosteroids has been recommended in severe cases to decrease destruction of the antibody-laden red blood cells by the reticuloendothelial system.[34–38] To date, corticosteroids have not been used in foals and mules with neonatal immune-mediated thrombocytopenia, but the mechanism of action would be similar to that of steroid treatment for neonatal isoerythrolysis.[6,7] Three foals were not treated with corticosteroids and improved, and, therefore, corticosteroids may not be necessary for the treatment of this condition and in fact, caution is advised when administering immunosuppressive doses of corticosteroids in neonatal foals at risk of septicemia or secondary bacterial infections.

G-CSF was used in 1 of the foals in this study because of the severe neutropenia, and the neutrophil count increased by 10-fold within 24 hours (from 1,800 to 20,254 neutrophils/μL). However, band neutrophils also increased (2,470 neutrophils/μL) and toxic changes increased, suggesting that the changes in the leukogram may have been multifactorial, with both the G-CSF and septicemia contributing. Minimal improvement occurred in the peripheral platelet count after the G-CSF (3,000–6,000 platelets/μL in 24 hours) in the foal in this study and in healthy foals given G-CSF.[39]

Footnotes

[a] Clinical Immunology Lab, Kansas State University, College of Veterinary Medicine, Manhattan, KS

[b] Granulocyte colony-stimulating factor, Neupogen, Amgen Inc, Thousand Oaks, CA

[c] Dexamethasone sodium phosphate, Azium, Schering-Plough Animal Health Corp, Union, NJ

[d] Prednisolone sodium succinate, Solu-Delta-Cortef, Pharmacia & Upjohn Company, Kalamazoo, MI

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References

1. Barton MH, Morris DD, Crowe N, et al. Hemostatic indices in healthy foals from birth to one month of age. J Vet Diagn Invest 1995; 7:380–385.

2. Harvey JW, Asquith R, McNulty PK, et al. Haematology of foals up to one year old. Equine Vet J 1984;16:347–353.

3. Barton MH, Morris DD, Norton N, Prasse KW. Hemostatic and fibrinolytic indices in neonatal foals with presumed septicemia. J Vet Intern Med 1998;12:26–35.

4. Brianceau P, Divers TJ. Acute thrombosis of limb arteries in horses with sepsis: Five cases (1988–1998). Equine Vet J 2001;33: 105–109.

5. Bentz AI, Wilkins PA, MacGillibray KC, et al. Severe thrombocytopenia in 2 Thoroughbred foals with sepsis and neonatal encephalopathy. J Vet Intern Med 2002;6:494–497.

6. Traub-Dargatz JL, McCLure JJ, Koch C, Schlipf JW. Neonatal isoerythrolysis in mule foals. J Am Vet Med Assoc 1995;206:67–70.

7. Buechner-Maxwell V, Scott MA, Godber L, Kristensen A. Neonatal alloimmune thrombocytopenia in a quarter horse foal. J Vet Intern Med 1997;11:304–308.

8. Ramirez S, Gaunt SD, McClure JJ, Oliver J. Detection and effects on platelet function of anti-platelet antibody in mule foals with experimentally induced neonatal alloimmune thrombocytopenia. J Vet Intern Med 1999;13:534–539.

9. Lavoie J, Spensley MS, Smith BP, Mihalyi J. Absorption of bovine colostral immunoglobulins G and M in newborn foals. Am J Vet Res 1989;50:1598–1603.

10. McGuire TC, Crawford TB. Passive immunity in the foal: Mea-

surement of immunoglobulin classes and specific antibody. Am J Vet Res 1973;34:1299–1302.

11. Sullivan PS, Manning KL, McDonald TP. Association of mean platelet volume and bone marrow megakaryocytopoiesis in thrombocytopenic dogs: 60 cases (1984–1993). J Am Vet Med Assoc 1995; 206:332–334.

12. Sellon DC. Thrombocytopenia in horses. Equine Vet Educ 1998;10:133–139.

13. Russell KE, Perkins PC, Grindem CB, et al. Flow cytometric method for detecting thiazole orange-positive (reticulated) platelets in thrombocytopenic horses. Am J Vet Res 1997;58:1092–1096.

14. Nunez R, Gomes-Keller MA, Schwarzwald C, Feige K. Assessment of equine autoimmune thrombocytopenia (EAT) by flow cytometry. BMC Blood Disord 2001;1:1–13.

15. McGurrin MKJ, Arroyo LG, Bienzle D. Flow cytometric detection of platelet-bound antibody in three horses with immune-mediated thrombocytopenia. J Am Vet Med Assoc 2004;224:83–87.

16. Davis EG, Wilkerson J, Rush BR. Flow cytometry: Clinical applications in equine medicine. J Vet Intern Med 2002;16:404–410.

17. George JN, El-Harake MA, Raskob GE. Chronic idiopathic thrombocytopenic purpura. N Engl J Med 1994;331:1207–1211.

18. Koterbra AM, Brewer BD, Tarplee FA. Clinical and clinicopathological characteristics of the septicaemic neonatal foal: Review of 38 cases. Equine Vet J 1984;16:376–383.

19. Brewer BD, Koterbra AM. Development of a scoring system for the early diagnosis of equine neonatal sepsis. Equine Vet J 1988; 20:18–22.

20. Perkins G, Ainsworth DM, Erb HN, et al. Clinical, haematological and biochemical findings in foals with neonatal equine herpesvirus-1 infection compared with septic and premature foals. Equine Vet J 1999;31:422–426.

21. Davis EG, Rush B, Bain F, et al. Neonatal neutropenia in an Arabian foal. Equine Vet J 2003;35:517–520.

22. Chickering WR, Prasse KW. Immune mediated neutropenia in man and animals: A review. Vet Clin Pathol 1981;10:6–16.

23. Maddison JE, Hoss B, Johnson RP. Steroid responsive neutropenia in a dog. J Am Anim Hosp Assoc 1983;19:881–886.

24. McManus PM, Litwin C, Barber L. Immune mediated neutropenia in 2 dogs. J Vet Intern Med 1999;13:372–374.

25. Brown MR, Rogers KS. Neutropenia in dogs and cats: A retrospective study of 261 cases. J Am Anim Hosp Assoc 2001;37:131–139.

26. Toribio RE, Bain FT, Mrad DR, et al. Congenital defects in newborn foals of mares treated for equine protozoal myeloencephalitis during pregnancy. J Am Vet Med Assoc 1998;212:697–701.

27. Kohn CW, Swardson C, Provost P, et al. Myeloid and megakaryocytic hypoplasia in related Standardbreds. J Vet Intern Med 1995;9:315–323.

28. Ginn PE, Hillier A, Lester GD. Self-limiting subepidermal bullous disease in a neonatal foal. Vet Dermatol 1998;9:249–256.

29. Byars TD, Greene CE. Idiopathic thrombocytopenic purpura in the horse. J Am Vet Med Assoc 1982;180:1422–1424.

30. Morris DD, Whitlock RH. Relapsing idiopathic thrombocytopenia in a horse. Equine Vet J 1983;15:73–75.

31. Larson VL, Perman V, Stevens JB. Idiopathic thrombocytopenic purpura in two horses. J Am Vet Med Assoc 1983;183:328–330.

32. Humber KA, Beech J, Cudd TA, et al. Azathioprine for treatment of immune-mediated thrombocytopenia in two horses. J Am Vet Med Assoc 1991;199:591–594.

33. Hohenhaus AE. Bloodbanking and transfusion medicine. In: Ettinger SJ, Feldman EC, eds. Textbook of Veterinary Internal Medicine. Diseases of the Dog and Cat, 5th ed, Vol 1. Philadelphia, PA: WB Saunders; 2000:348–356.

34. Becht J. Neonatal isoerythrolysis. In: Robinson N, ed. Current Therapy in Equine Medicine 2. Philadelphia, PA: WB Saunders; 1987: 244–247.

35. Rutherford CJ, Frenkel EP. Thrombocytopenia. Issues in diagnosis and therapy. Med Clin North Am 1994;78:555–575.

36. Zaruby JF, Hearn P, Colling D. Neonatal isoerythrolysis in a foal, involving anti-Pa alloantibody. Equine Vet J 1992;24:71–73.

37. David JB, Byars TD, Braniecki A, et al. Kernicterus in a foal with neonatal isoerythrolysis. Compend Cont Educ Pract Vet 1998;20: 517–522.

38. Perkins GA, Divers TJ. Polymerized hemoglobin therapy in a foal with neonatal isoerythrolysis. J Vet Emerg Crit Care 2001;122: 141–146.

39. Zinkl JG, Madigan JE, Fridmann DM, et al. Haematological, bone marrow and clinical chemical changes in neonatal foals given canine recombinant granulocyte-colony stimulating factor. Equine Vet J 1994;26:313–318.