Salvage of *Theileria* infected calves with clinical manifestation of exophthalmia

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Abstract Two crossbred female calves aged between 30 and 35 days were presented with bilateral exophthalmia, inappetence, pyrexia and cachexia since last 15 days. Clinical examination revealed mainly bilateral exophthalmia with dry and pulpy cornea, generalized enlargement of superficial lymph nodes, pallor mucous, petechiae, high rectal temperature and sternal recumbency. The calves were severely infested with *Hyalomma anatolicum anatolicum* ticks and thin layer blood smears revealed presence of piroplasm in the RBCs, while lymph nodes aspirate smear examination revealed presence schizonts in the mononuclear cells. The calves were treated with bu-parvaquone; meloxicam, nandrolone decanoate and vitamins A, D₃, E and H. From day second post-therapy a remarkable improvement in the clinical condition was noticed and substantial reduction in the both protruded eyeballs was noticed by 7 days post-therapy in the both calves. Further at day 47 post-therapy the one calf was free from the parasite on blood smear examination and right eye was retracted in its orbits with full of sight. Moreover the left eye was also retracted in its orbit but there was loss of sight and opacity developed in this eye. While, the other calf also revealed remarkable improvement in the clinical condition and both eye balls retracted completely into the orbit at day 30 post-therapy. But, at day 86 the calf developed microphthalmia and complete loss of sight in

both eyes. It can be concluded that adjunction of antioxidants and hematopoietic agents may salvage the calves suffering from fatal theileriosis.

Keywords Calf theileriosis · Exophthalmia · Nandrolone · *Theileria* · Vitamins A, D₃, E and H

Introduction

Calf mortality is one of the major impediments to the livestock upgrading programmes in the Indian subcontinent. The protozoan parasites, *Theileria annulata* endowing the tick-borne disease, bovine tropical theileriosis (BTT) in calves, intricate enormous morbidity and mortality in the endemic areas. BTT bestowed calves mortality has been demonstrated by various scientific workers (Godara et al. 2009; Sudan et al. 2012a). An estimate stated that BTT costs the Indian livestock sector about US\$384.3 million annually (Minjauw and McLeod 2003). The clinical manifestations of BTT diverge from per-acute to acute or sub-acute to chronic. It mainly depends upon the damaging effect of the pathogen on lymphoid tissues and susceptibility of the host. The major clinical manifestations of experimental and natural acute calf theileriosis are pyrexia, generalized lymphadenopathy, anaemia, anorexia, cachexia, respiratory distress, petechiae in conjunctiva, oral and nasal mucosa and unilateral or bilateral exophthalmia (Sengupta et al. 1993; Branco et al. 2010; Sudan et al. 2012b). Calf theileriosis with ocular manifestation of exophthalmia has been anticipated with grave prognosis (Mallick et al. 1986; Mallick 1993). There are no scientific reports demonstrating salvage of the calves with theileriosis bestowing clinical manifestation of exophthalmia to the best of the author's knowledge in published electronic data, albeit standard

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therapeutic interventions were instituted (Sudan et al. 2012b). The present report demonstrates the commendable salvage of two calves with theileriosis bestowing clinical manifestation of exophthalmia.

Clinical examination, results and discussion

Two crossbred female calves aged between 30 and 35 days were presented with bilateral exophthalmia, inappetence, pyrexia and cachexia since last 15 days at Teaching Veterinary Clinical Complex, College of Veterinary Science and Animal Husbandry, DUVASU, Mathura. The owners reported instillation of ocular preparation containing antibiotics in the both eyes since last 7–10 days without any improvements. The calves were not administered with any anti-haemoprotzoal and corticosteroids previously. Clinical examination revealed mainly bilateral exophthalmia with dry and pulpy cornea (Figs. 1, 2), generalized enlargement of superficial lymph nodes, pallor mucous, petechiae, high rectal temperature (105–106 °F) and sternal recumbency. The calves were severely infested with *Hyalomma anatolicum anatolicum* ticks. Further, blood smears were prepared from the marginal ear vein, stained with Leishman stain and examined under the oil immersion lens of a light microscope. Blood smear and lymph nodes aspirate smear examination revealed presence of piroplasm in the RBCs and schizonts in the mononuclear cells (Fig. 3). Approximately, 2.5 ml blood was also obtained in EDTA containing tubes from the jugular vein and used for hematological examinations. At day 0, the values of hematological panels of the calf 1 revealed $3.41 \times 10^6/\mu\text{l}$ total erythrocyte count (TEC), 6.4 g/dl hemoglobin (Hgb), 22 % hematocrit (Hct), 64.5 fl mean corpuscular volume (MCV), 18.7 pg mean corpuscular hemoglobin (MCH),

Fig. 1 Calf 1 with bilateral exophthalmia and dry cornea

Fig. 2 Calf 2 with bilateral exophthalmia and dry cornea

Fig. 3 Lymph nodes aspirate smear examination revealing presence of schizonts in the mononuclear cells

and 29.1 g/dl mean corpuscular hemoglobin concentration (MCHC). While, total leukocyte count (TLC) was $20.5 \times 10^3/\mu\text{l}$ and granulocytes, lymphocytes and monocytes counts were 14.9×10^3 , 2.97×10^3 and $2.63 \times 10^3/\mu\text{l}$, respectively. In chorus, the hematological panels of the calf 2 at day 0 revealed $3.44 \times 10^6/\mu\text{l}$ TEC, 4.3 g/dl Hgb, 13.1 % Hct, 38 fl MCV, 12.4 pg MCH, and 32.3 g/dl MCHC. While, TLC was $13.8 \times 10^3/\mu\text{l}$ and granulocytes, lymphocytes and monocytes counts were 11.3×10^3 , 1.07×10^3 and $1.44 \times 10^3/\mu\text{l}$, respectively.

The calves were treated with buparvaquone (Zubion) at a dose rate of 2.5 mg/kg BW intramuscularly and repeated at day 7; meloxicam (Melonex) was given at a dose rate of 0.3 mg/kg intramuscularly daily for 3 days and a total 25 mg nandrolone decanoate (Deca-Durabolin) was given intramuscularly. A total 1 ml of a commercial formulation containing vit. A 2.5 lac IU, vit. D₃ 25,000 IU, vit. E 100 IU, and biotin 12.4 mcg/ml (Intavita–H) was also given intramuscularly at the weekly intervals for three times. Topical application of Flumethrin 1 % Pour-On

Fig. 4 Calf 1 with normal right eye ball fully retracted in the orbit at day 47 post-therapy

preparation (Bayticol Pour-On) over the vertebral column was also advised. From day second post-therapy a remarkable improvement in the clinical condition was noticed by the calf owners. The owners reported the calves regained their normal appetite within 7 days post-therapy and substantial reduction in the both protruded eyeballs was noticed. The calf 1 was examined further at day 47 post-therapy and found to be free from the parasite on blood smear examination. Significant reduction in all superficial lymph nodes was observed. The right eye was completely retracted in its orbits (Fig. 4) and full of sight. Moreover, the left eye was also retracted in its orbit but there was loss of sight and opacity developed in this eye (Fig. 5). The calf 2 was further examined at day 30th post-therapy and revealed no parasite in blood smear examination and remarkable improvement in the clinical condition. Both the eye balls retracted completely into the orbit, but the calf developed opacity and loss of sight of the both eyes. Further, at day 86 post-therapy second calf developed microphthalmia and complete loss of sight in the both eyes (Fig. 6). At day 47th post-therapy of the first calf and at day 30th post-therapy of the other calf, the hematological panels were within the normal reference range.

Fig. 5 Calf 1 with opacity of left eye ball fully retracted in the orbit at day 47 post-therapy

Fig. 6 Calf 2 with fully retracted eye balls in the orbit at day 86 post-therapy

The present report clearly demonstrates the affected calves were severely anemic. Anemia, owing to overproduction of cytokines and reactive oxygen species, is a significant feature of theileriosis (Nazifi et al. 2009; Saleh et al. 2011). Anabolic steroids have been widely used in the past for the treatment of aplastic anemia and other hypoplastic clonal hematological diseases (Tsiara et al. 2004). Pharmacologic doses of anabolic steroids induce an increase in red cell mass by stimulating the endogenous erythropoietin production; hypoxia and anabolic steroids both act synergistically and increase erythropoietin release by the kidney (Neff et al. 1981). In the present report remarkable improvement of anemia might be attributed to the stimulation of endogenous erythropoietin production by nandrolone decanoate and/or antioxidant potential of vitamins A, D₃, E and H (Singh et al. 2012). The anabolic steroid was preferred over the administration iron preparations for the management of anaemia considering the fact that BTT imparts extra-vascular lyses of RBC's and thus the affected calves will not be iron deficient. The second dose of buparvaquone was administered at day 7 considering that the plasma half life of the drug is approximately 7 days. Moreover, the time required for the inoculated sporozoites to develop into macroschizonts in the host mononuclear cells is approximately 6–8 days. Buparvaquone acts mainly on the macroschizonts and intra-erythrocytic piroplasms; thus the sporozoites inoculated by the ticks on day 0 may escape from the first dose of buparvaquone. The second dose administration of buparvaquone at day 7 will kill the escaped sporozoites owing to their development into macroschizonts.

Cells infected with *T. annulata* also produce high levels of inflammatory cytokines, especially tumor necrosis factor alpha (TNF- α) (Brown et al. 1995). This cytokine is a potent inducer of all the major clinical symptoms of acute tropical theileriosis including pyrexia, anaemia, anorexia,

muscle wasting and necrosis (Graham et al. 2001). These symptoms are observed in acute cases of tropical theileriosis. In addition, TNF- α has been implicated in mediating the ulcerative lesions associated with tropical theileriosis and in enhancing the proliferation of infected cells (Forsyth et al. 1999).

Clinical manifestation of edema, proptosis and diplopia in thyroid associated ophthalmopathy are attributed to infiltration of lymphocytes and enlargement of extra-ocular muscle, accumulation of glycosaminoglycan (GAG) (Balázs and Korányi 2011). The activated lymphocytes have been shown to secrete several cytokines including TNF- α , interleukin-1 and interferon gamma which are able to express HLADR antigens and stimulate fibroblasts to proliferate, produces GAG and free oxygen radicals. The pathological changes observed in different organs and tissues of *T. annulata* infected animals are the result of proliferation of infected macrophages, while other clinical symptoms result from pro-inflammatory cytokines produced by these cells, mainly TNF- α (Branco et al. 2010; El-Deeb and Iacob 2012). Thus, it is quite possible that the infiltration of lymphocytes and overproduction of TNF- α be implicated in ophthalmopathy of calf theileriosis. It can be concluded that adjunction of antioxidants and hematopoietic agents can salvage the calves suffering from fatal theileriosis. Moreover, large scale clinical studies are on adjunctive antioxidant, hematopoietic agents and TNF- α blockers is required to provide a novel therapeutic regimen of calf theileriosis.

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