Importance of Host Response in Resistance to Nematode Parasites

Jorge F. González, Departamento de Patología Animal, Facultad de Veterinaria, Universidad de Las Palmas de Gran Canaria, Trasmontaña s/n, Arucas, Las Palmas, 35413. Spain

Introduction

Gran Canaria is one of the seven volcanic islands of the Canarian Archipelago. It is located in the Atlantic Ocean about 150 km from Northwest cost of Africa. Although it is a tiny island, with only 1,560 km^2, it is popularly called "miniature continent" due to the different climates and diversity of landscapes founds on it. Variation in local weather is mainly the consequence of the global effect of the Alisios winds, local sea current, big mountains (volcanoes) and the proximity to the Sahara desert. Two basic climatological zones have been proposed: the dry and the temperate. They are further subdivided to give a total of four isoclimates zones organized in concentric circles on the Island: dry desert, dry steppe, temperate mild and temperate cold (Rodriguez-Ponce et al, 1995).

Obviously, this great difference in weather has an impact on small ruminant parasite prevalence. In general, there are more gastrointestinal nematodes (gi) in sheep and goats in temperate than in dry areas, and also worm species are different depending on isoclimate zones (Molina et al, 1997; Hernández et al, 2012).

Two main local breed of sheep has been exploited by local farmers almost exclusively: the Canaria Hair Breed (CHB) and the Canaria sheep (CS). The CHB sheep are short haired breed sheep predominantly reared for meat and manure production while the CS are predominantly utilized for milk production. Differences in trichostrongylid egg counts in faeces between breeds have been consistently observed in routine analysis carried out for the Parasitology Unit of the Veterinary Faculty of Las Palmas de Gran Canaria University, even though animals from both breeds were co-habited the same grazing areas. In last few years, we have carried out several trials in order to demonstrate differential resistance to *Haemonchus contortus* in this two breed of sheep.

In these trials, several animals (8-11 months old) have been inoculated with 20,000 L3 of an *H. contortus* strain donated by Dr. Knox and Dr. Bartley (Moredum Research Institute, Edinburg, Scotland). Animals have been slaughtered at different days post infections. Several parasitological and immunological techniques have been carried out. Some of the results obtained in these trials are presented herein.

Results and Discussions

Mean egg per gram (EPG) and number of eggs in female worm in uterus have been significantly lower in CHB sheep than in CS. There were also clear trends for a reduction in adult worm burden. Adult worm burden was 50% lower when compared with mean worm counts in CS at 28 dpi, although it was not statistically significant (p=0.06) (González et al, 2008). These data suggest that CHB sheep is more resistant than CS to *H. contortus* infections. Interestingly, there were no significant differences between breeds in larval counts and length at 7 dpi which suggest that protective mechanism(s) in resistant (CHB) sheep were mainly directed against the adult parasite (González et al, 2011).

In the susceptible (CS) breed, at 28 dpi, there was a significant and positive correlation between worm burden and length, as well as between eggs in uterus and worm length. EPG were also correlated with adult worm counts. These correlations have been shown in several experimental infections in sheep in both *Teladorsagia circumcincta* (Stear and Bishop, 1999) and *H. contortus* (Lacroux et al, 2006) infections. In all these studies, the early parasitic stages are proposed as the target of immunity. However, no such correlations were observed in resistant CHB sheep, in which the adult stage seems to be the target of the immune response. These suggest that resistance mechanism(s) in this sheep breed may be different to those previously studied in commercial breed of sheep (González et al, 2011).

No quantitative differences between breeds were observed in immune cell populations quantified at the abomasal wall at different killing points (7, 21 and 28 dpi). The only exception was the eosinophil. A significant reduction in this granulocyte population was detected only in the susceptible breed of sheep at 28 dpi. Abomasal eosinophil number was two-fold higher in the resistant CHB than in CS at 28 dpi, suggesting that CHB sheep have increased recruitment of eosinophils in abomasal tissues, when adult parasites are present. Eosinophils have been demonstrated to surround larvae *in vivo* and to damage larvae *in vitro*, and this cell is probably involved in a delayed-larvae rejection (Rainbird et al, 1998; Meeusen and Balic, 2000; Balic et al, 2006). There is no clear evidence in its role against adult to date.

A significant negative correlation between abomasal CD4+T cells with worm burden and length at 28 dpi was observed in the CS breed, suggesting that this cell may be relevant in modulating parasite establishment, in agreement with several previous studies (Gill et al, 1993; Peña et al, 2006). However, no such significant correlative response was found in the CHB sheep. In contrast to CS breed, eosinophil and □□ T cells were negatively correlated with epg at 28 dpi only in CHB sheep, but not with worm burden or length, suggesting that these cells may play a role in modulating fecundity against *H. contortus* (González et al, 2011).

Conclusions

In conclusion, with these trials, we have demonstrated disparate immune responses between two breeds of sheep native to the Canary Islands. These results –in addition to other experiments developed with other local breeds of sheep- strongly suggest that ancient breeds may hold the key to identify the resistance pathways of host against parasitic diseases. This information may be potentially useful for identify new pharmacological targets or immunization strategies. Obviously, first step is preserved this endangerment resource. Local and national government and international agencies must promote and protect these indigenous animal breeds (Piedrafita et al, 2010).

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