Diagnostic Exercise

From The Davis-Thompson Foundation*

Case #: 70 Month: July Year: 2016

Answer Sheet

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Morphologic Diagnosis: Eosinophilic granulomatous inflammation, chronic, multifocal, moderate, cecum.

Typical Gross findings: Irregular thickening of the wall of the cecum.

Typical microscopic findings: Multifocal to coalescing eosinophilic granulomas limited to the submucosa of the cecum. At low power (2.9x), these submucosal granulomas could be confused with (and appear similar to) depleted submucosal lymphoid nodules. At higher magnification (20x), each submucosal nodule is clearly a granuloma characterized by epithelioid macrophages, multinucleated giant cells, and prominent infiltration of eosinophils with varying degrees of fibrosis.

Cause: Unknown, but likely a manifestation of spontaneous hypereosinophilic syndrome.

Associated lesion in other organ(s): Chronic vasculitis in associated mesenteric arteries with proliferation of intima can be present, with subintimal infiltration of lymphocytes and eosinophils (see Figure 4), and the early beginning of fibrinoid necrosis (not shown in photos).

Discussion: Eosinophilic granulomas that are limited to the cecum of the Sprague Dawley rat appear to be an entity of unknown etiology. It has been previously reported in a 19-week-old specific-pathogen-free (SPF) Sprague Dawley rat (Li *et al*., 2014), which is an age similar to the 20-week-old Sprague Dawley rat of this case report. The nature of the lesion (eosinophils and granulomatous inflammation) suggests an allergic or parasitic etiology. However, no mast cells (to suggest allergy) and no parasites were found either in the published case of an SPF rat, or in this particular case report. Further, no parasites of laboratory animals are known to cause this particular type of inflammatory reaction. Parasitic infestation/infection of the cecum of laboratory rats include *Eimeria* spp., *Trichomonas muris*, *Giardia muris*, and the pinworm *Syphacia obvelata*, yet these parasites are non-pathogenic and at most cause slight enteritis.

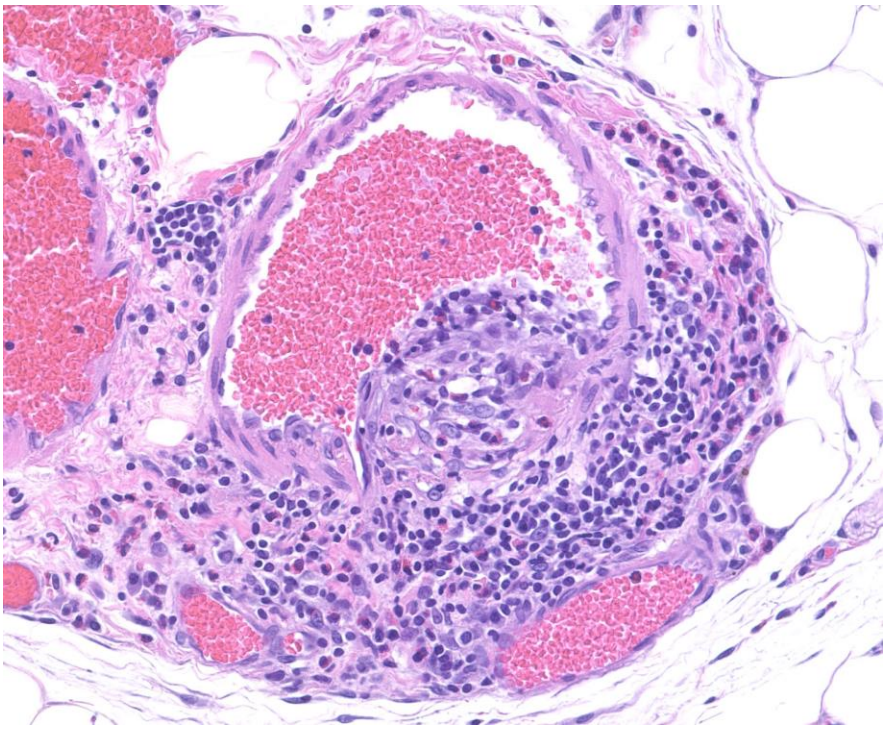

Figure 4. Mesentery (attached to cecum), Rat, 35x objective magnification.

The two cases of eosinophilic granulomas of the cecum reported so far (Li *et al*., 2014 and this diagnostic exercise) are associated with arteritis limited to the mesentery and no systemic lesions. The association, if any, between eosinophilic cecal granulomas and mesenteric arteritis is not clear. Based on the association of granulomas with arteritis in this and the published case of Li *et al*. 2014, and the fact that eosinophilic granule content of cationic proteins and major basic protein is damaging to endothelial cells (Hallgren *et al.,* 1991), there is likely a pathogenic connection between the two inflammatory lesions. The rat in Li *et al*. (2014) had a moderately higher than normal circulating eosinophil count (107 cells/µl compared to the group mean of 75 cells/µl), but the present study did not involve clinical pathology. Similar granulomas have been associated with a rat model for hypereosinophilic syndrome (Sano *et al*., 2001).

References and Recommended literature:

Hallgren, R., Gudbjornsson, B., Larsson, E., Fredens, K. (1991). Deposition of eosinophil cationic protein in vascular lesions in temporal arteritis. Ann. Rheum. Dis. 50:946-949.

Sano, K., Kobayashi, M., Sakaguchi, N., Ito, M., Hotchi, M., and Matsumoto, K. (2001). A rat model of hypereosinophilic syndrome. Pathol Int. 51:82-88.

Matsumoto, K., Matshushita, N., Tomozawa, H., Tagawa, Y. (2000). Hematological characteristics of rats spontaneously developing eosinophila. Exp. Anim. 49:211-215.

Li, Y., Bae, H., Kim, H., Kang, M., Jung, W., Kim, K., Song, Si., Kang, B. (2014). The spectrum of eosinophilic infiltration of the cecum and its relationship to other disorders of multiple granulomas and arteritis in Sprague-Dawley rat. J. Toxicol. Sci. 39(2) 243-249.

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