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Author: Brown, Corrie C.

Source: Journal of Wildlife Diseases, 24(2) : 214-219

Published By: Wildlife Disease Association

URL: https://doi.org/10.7589/0090-3558-24.2.214

Journal of Wildlife Diseases, 24(2), 1988, pp. 214–219

ENDOGENOUS LIPID PNEUMONIA IN OPOSSUMS FROM LOUISIANA

Corrie C. Brown
Department of Veterinary Pathology, School of Veterinary Medicine, Louisiana State University, Baton Rouge, Louisiana 70803, USA

ABSTRACT: Endogenous lipid pneumonia was present in 19 of 27 opossums (*Didelphis virginiana*) trapped in the vicinity of Baton Rouge, Louisiana. The severity of lesions varied from small pleural and subpleural aggregates of foamy macrophages with minimal disruption of pulmonary architecture to large nodular accumulations of foam cells with cholesterol clefts and localized emphysema. The cause of the lipid pneumonia may be related to pulmonary nematode parasite infections, which were evident in 13 of the affected animals.

Key words: Endogenous lipid pneumonia, foam cell pneumonia, opossum, *Didelphis virginiana*, *Didelphostrongylus hayesi*, *Capillaria* sp., *Besnoitia darlingi*, natural infections.

INTRODUCTION

Endogenous lipid pneumonia is an alveolar filling disorder reported frequently from rats (Beaver et al., 1963; Corrin and King, 1969; Flodh et al., 1974; Weller, 1985) and less frequently from other species such as mice (Emi and Konishi, 1985), cats (Dungworth, 1985), and humans (Kay et al., 1974). Grossly, it appears as multifocal to coalescing subpleural white stippling. Histologically, these foci consist of accumulations of foamy macrophages filling, and occasionally distending, the alveoli. In more severe cases, there is an associated foreign body reaction and formation of cholesterol clefts. The causes of endogenous lipid pneumonia are obscure but may be related to bronchial obstruction, inhalation of particulate dust, disturbance of lipid metabolism, or it may occur without apparent cause. This report describes endogenous lipid pneumonia in a group of opossums (*Didelphis virginiana*) from southern Louisiana.

MATERIALS AND METHODS

Twenty-seven (12 males, 15 females) adult opossums were trapped in the vicinity of Baton Rouge, Louisiana (USA; 30°30′N, 90°10′W) between January and May 1987. All were euthanized with an intraperitoneal injection of pentobarbital. Blood and various tissues were collected for culturing and histopathologic evaluation, respectively, to detect the presence of *Trypanosoma cruzi* and *T. cruzi*-induced disease. Those results will be reported elsewhere.

All lungs were examined grossly and placed in 10% neutral buffered formalin. From each animal, a section from the dorsocaudal area was embedded in paraffin, sectioned at 5 μm, and stained with hematoxylin and eosin. In cases where subpleural plaques were visible an effort was made to include the plaque within the section. One of the plaques (from animal Number 6) was later removed from formalin, minced into 1 mm cubes, placed in 3% glutaraldehyde, post-fixed in 1% osmium tetroxide, stained with 2% uranyl acetate, embedded in epoxy resin, sectioned, and examined with a Philips 410 electron microscope (N. V. Philips, Gloeilampenfabrieken, Eindoven, The Netherlands).

RESULTS

Gross examination

Subpleural plaques were present grossly in the lungs of 21 of 27 animals examined. These plaques measured 1–4 mm in diameter, were slightly raised, and soft (Fig. 1). They were most prominent in the dorsocaudal regions, and in the most severely affected animals they were coalescing. On cut section, the lungs in some of the animals showed peribronchiolar infiltrates and multifocal areas of consolidation scattered within the parenchyma.

Histopathology

Subpleural foam cell accumulation without apparent adjacent inciting cause was evident in 19 of 27 opossums (Table 1). In four of these, the foci were small and caused minimal disruption of pulmonary architecture (Fig. 2). In another 13, foci consisted of larger aggregates of

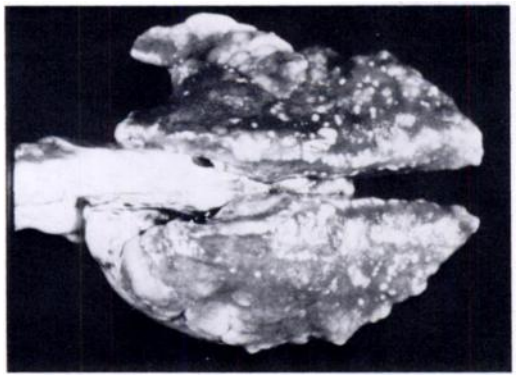

FIGURE 1. Subpleural plaques of endogenous lipid pneumonia in opossum lungs.

foamy macrophages with resulting nodular elevation of the pleural surface, mild localized emphysema, formation of lymphoid nodules, and type II pneumocyte hyperplasia at the periphery (Fig. 3). In two animals, cholesterol clefts had formed within large aggregates of pleural and subpleural foamy macrophages and hyperplastic type II pneumocytes (Fig. 4).

Parasites were present in 18 of 27 opossums and were identified according to morphologic appearance in tissue section (Flatt et al., 1971; Chitwood and Lichtenfels, 1972; Prestwood et al., 1977). These parasites included *Didelphostrongylus hayesi* (13 animals), *Capillaria* sp. (seven animals), and *Besnoita darlingi* (five animals) (Table 1). Six opossums had multiple parasite infections. Most of the animals with parasites had granulomatous reactions in the interstitium surrounding larvae of *D. hayesi* or degenerating cysts of *B. darlingi* and around disrupted bronchioles containing either *Capillaria* sp. adults or eggs. Small accumulations of foamy macrophages were often present around and within these parasitic granulomas.

Other histologic features included bronchial-associated lymphoid tissue (BALT) hyperplasia and hypertrophy of smooth muscle, especially that surrounding vessels. A pulmonary adenoma was present in one animal (Number 9).

TABLE 1. Microscopic features of the lungs of 27 adult opossums from Louisiana.

Opossum number	Severity of endogenous lipid pneumonia[a]	Parasites[b]	BALT[c] hyperplasia	Smooth muscle hyperplasia
1	++	–	–[d]	+
2	–	D	–	+
3	+	–	+	+
4	+	B	–	–
5	++	B	+	–
6	+++	B, C	–	+
7	++	C	–	–
8	++	D	–	+
9	–	D	–	+
10	++	D	–	–
11	++	D, C	+	–
12	++	C	–	+
13	–	D	+	+
14	++	D, B	+	–
15	–	D	–	+
16	–	D	–	+
17	++	D, C	+	+
18	++	D, C, B	–	+
19	+	D, C	–	+
20	++	–	+	–
21	++	D	+	+
22	–	–	+	–
23	–	–	+	–
24	++	–	+	+
25	–	–	–	–
26	+	–	–	–
27	+++	–	–	+

[a] –, Lesion not observed; +, small groups of foamy macrophages, with minimal disruption of pulmonary architecture; ++, larger accumulations of foamy macrophages with lymphoid aggregates, mild localized emphysema, and type II pneumocyte hyperplasia; +++, large accumulations of foamy macrophages with cholesterol clefts.

[b] D, *Didelphostrongylus hayesi*; C, *Capillaria* sp.; B, *Besnoitia darlingi*.

[c] BALT, bronchial associated lymphoid tissue.

[d] Absence (–) or presence (+).

Electron microscopy

Ultrastructurally, the plaque consisted of proliferated type II pneumocytes encroaching upon narrowed alveolar lumens containing large macrophages. These macrophages were covered with villous projections and the cytoplasms were filled with vacuoles, many of which contained osmiophilic laminated bodies similar to the specific inclusions of type II pneumocytes (Fig. 5).

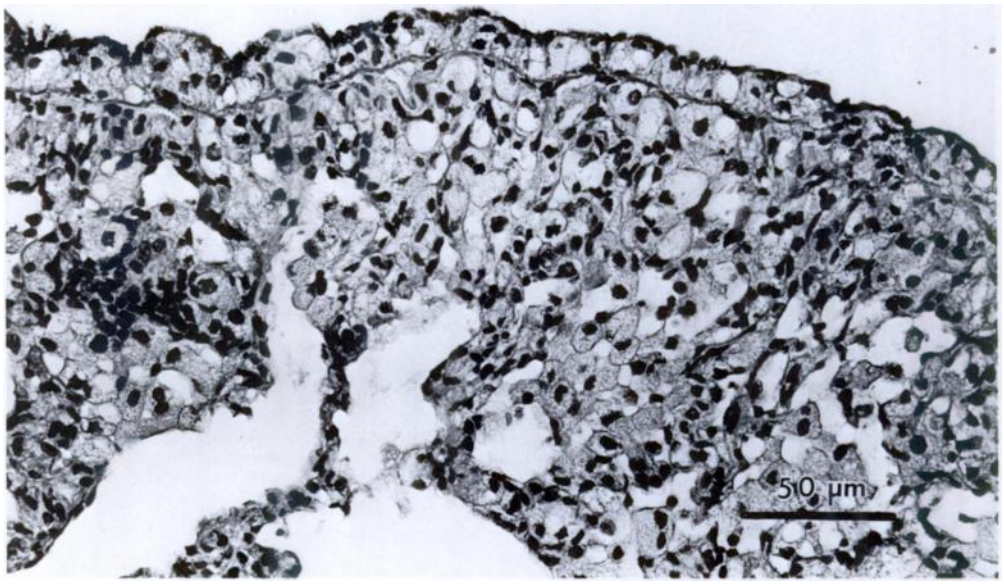

FIGURE 2. Small subpleural focus of foam cells causing minimal disruption of pulmonary architecture. H&E.

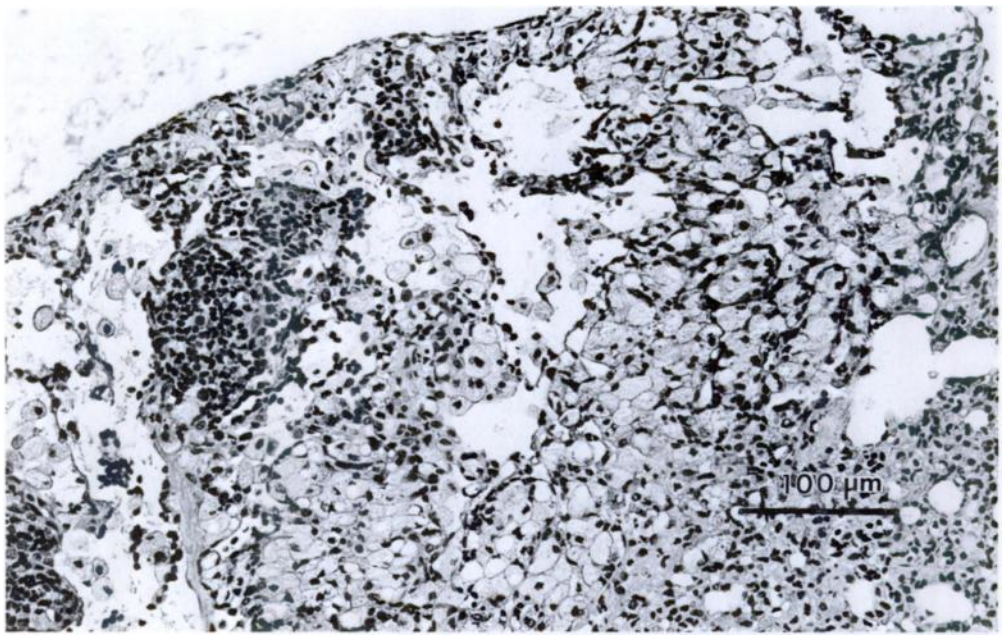

FIGURE 3. Large aggregate of foam cells with pleural elevation, formation of lymphoid nodule and mild emphysema. H&E.

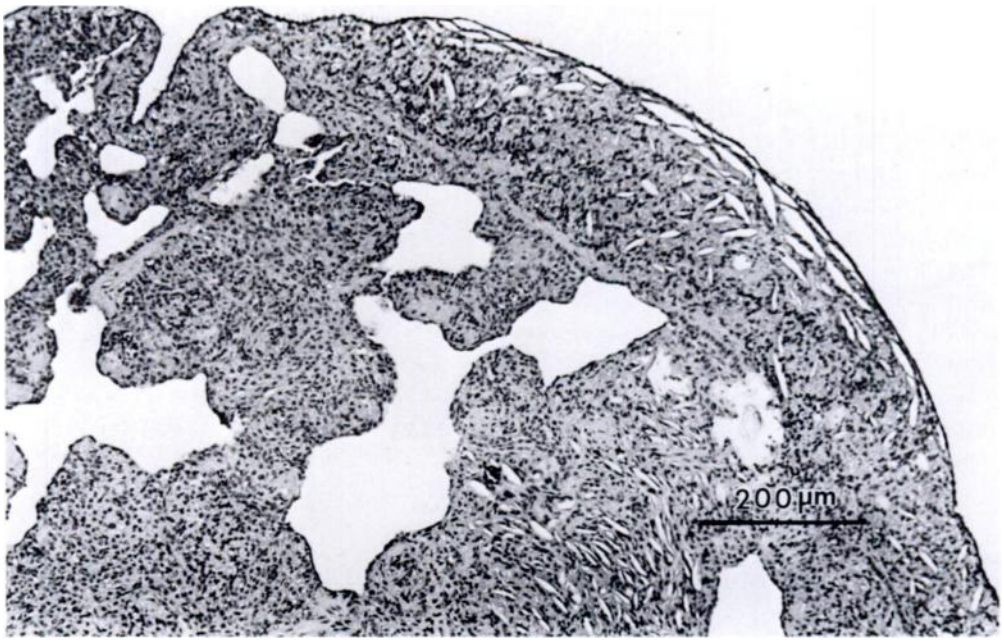

FIGURE 4. Large foam cell accumulation with cholesterol cleft formation and emphysema. H&E.

DISCUSSION

Endogenous lipid pneumonia has been reported most frequently in rats where it occurs spontaneously, with the frequency in normal rats varying between 0 and 55% (Weller, 1985). It is known also to occur secondary to a variety of causes including bronchial obstruction or irritation (Dungworth, 1985; Weller, 1985), long-term inhalation exposure to various dusts (Corrin and King, 1969; Lee et al., 1985), cirrhogenic and pantothenic acid deficient diets (Beaver et al., 1963), and hypophysectomy (Emi et al., 1985). The pathogenesis is proposed to be pulmonary injury causing hyperplasia of type II pneumocytes and resulting overproduction of surfactant (Lee et al., 1985). Another theory involves altered lipid metabolism, with pulmonary foam cells accumulating in an attempt to maintain a steady state of lipid metabolism (Flodh et al., 1974). Ultrastructurally, foam cells contain osmiophilic laminated bodies, similar to the specific inclusions of type II pneumocytes. Qualitative and quantitative lipid analysis of the lungs of mice with endogenous lipid pneumonia revealed six times greater concentrations of dipalmitoylglycerophosphocholine (DPPC) and phosphatidylglycerol than controls (Taki et al., 1986). Both DPPC

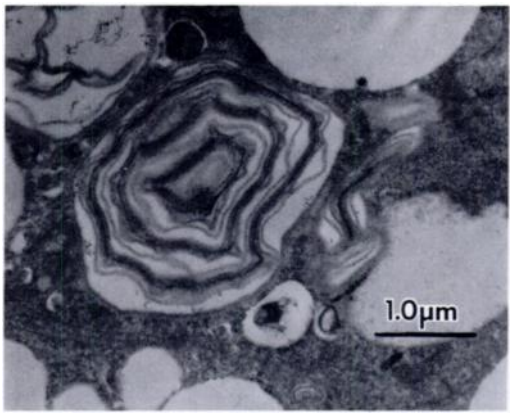

FIGURE 5. Osmiophilic laminated body present within foam cell. Transmission electron micrograph.

and phosphatidylglycerol are surfactants produced by type II pneumocytes.

The cause of endogenous lipid pneumonia in these opossums is possibly associated with parasitism. Of the 19 animals affected, 13 had *D. hayesi*, *Capillaria* sp., or *B. darlingi* apparent in the same histologic section. Of the remaining six animals without any parasites present in the tissue section examined, five had BALT hyperplasia or smooth muscle hypertrophy, both of which have been shown experimentally to be associated with *D. hayesi* infection (Prestwood et al., 1977). *Didelphostrongylus hayesi* and *Capillaria* sp. are common nematode parasites in the lungs of the opossum (Prestwood et al., 1977). *Besnoitia darlingi* is a protozoan found frequently in the lungs of the opossum (Flatt et al., 1971). Presumably, any of these three parasites could cause enough irritation to result in hyperplasia of type II pneumocytes, overproduction of surfactant and consequent accumulation of lipid-laden macrophages. However, it is interesting that most of the foci were subpleural and not usually in the vicinity of the parasite-induced granulomas.

The presence of endogenous lipid pneumonia in 19 of 27 wild-caught opossums indicates that this may be a common lesion in this species. Within the last two decades the opossum has become increasingly popular as a laboratory animal, proving useful in embryologic studies (Jurgelski, 1979), and as a model for bacterial endocarditis (Rowlands et al., 1970) and pulmonary adenomas (Vakilzadeh et al., 1971). Most animals used in the laboratory are wild-caught (Sherwood et al., 1969). Awareness of the prevalence of endogenous lipid pneumonia in the free-ranging population will be useful in the interpretation of pathologic findings in experimental animals.

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Received for publication 6 October 1987.

Journal of Wildlife Diseases, 24(2), 1988, p. 219

BOOK REVIEW . . .

Atlas of Zoo Animal Pathology, R. E. Schmidt and G. B. Hubbard. CRC Press Inc., 2000 Corporate Blvd., N.W., Boca Raton, Florida 33431, USA. 1987. Volume 1, 241 pp.; Volume 2, 192 pp. Set $215.00 U.S.

As stated by the authors in the Introduction "we prepared this atlas for individuals involved in zoo animal medicine. It is designed to give a pictorial reference to numerous lesions seen in zoo animals, and to include a number of pertinent references for in-depth study of the conditions." In addition, the authors have relied on morphologic diagnosis because of the difficulty in obtaining a specific etiology for many of the lesions. Both volumes consist of black and white photomicrographs of lesions arranged by systematic classification. These are supplemented by several photographs of gross lesions. Each photograph has a brief legend which includes the tissue stain used and magnification.

Volume 1 concentrates on mammals and includes lesions observed in 97 species, consisting of carnivores, herbivores, and primates. Each of the 14 chapters contains a brief text describing some of the major observations by the authors. The chapters are followed by an appendix of scientific and common names of animals used in the text. An extensive bibliography consisting of 268 references completes the volume. There are 383 photographs covering 47 bacterial diseases, four viral diseases, 46 neoplasms, 15 mycotic diseases, 26 parasitic diseases, 95 miscellaneous conditions and 151 diseases of unknown etiology. However, there are several photographs of the same lesion at different powers and there are several photographs of the same causative agent in different species. As a result the overall coverage of different diseases is not extensive.

Volume 2 includes data on 92 species of birds, 44 species of reptiles, three species of amphibians and five species of fish. As in Volume 1, lesions are classified by system and so each of the 14 chapters is devoted to a system. Each chapter includes members of the different animal groups having lesions in that system. The appendix of common and scientific names is followed by 190 references. The 298 photographs cover 31 bacterial diseases, seven viral diseases, 40 neoplasms, 30 mycotic diseases, 45 parasitic diseases, 50 miscellaneous conditions and 95 unknown etiologies. While there was a great deal of redundancy, as in Volume 1, the authors had better success at attributing more lesions to a specific cause in Volume 2.

Unfortunately, the quality of many photographs in both volumes is poor. Several are not in clear focus and many suffer from being taken at an inappropriate magnification. In such cases, it is difficult to appreciate what the legend is describing in the photograph. The legends could be more descriptive and the use of arrows would be beneficial. Many photographs are of conditions that are not special to zoo animals and so reduce the contribution of this work to zoo animal medicine. Consequently, the overall benefit of this work does not warrant the extreme cost.

Scott D. Wright, Department of Infectious Diseases, College of Veterinary Medicine, University of Florida, Gainesville, Florida 32610, USA.