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1 **Brief Research Reports**

2 **Endogenous lipid (cholesterol) pneumonia in three captive Siberian Tigers (*Panthera***
3 ***tigris altaica*)**

4
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1 **Abstract**

2 During 2009 to 2011 seven Siberian Tigers (*Panthera tigris altaica*) aged between two and
3 fourteen years from the Safaripark of Pombia were referred for necropsy to the Department
4 of Animal Pathology of the University of Turin (Italy) . Three tigers, aged ten (two animals)
5 and fourteen years, had multifocal, irregularly distributed, white, soft, subpleural, 3 mm
6 nodules scattered throughout the lungs. Histologically there were a marked infiltration of
7 macrophages, with foamy cytoplasm, and multinucleate giant cells interspersed with
8 numerous clusters of cholesterol clefts. A mild lymphocytic infiltration was localized
9 around the lesion. These findings were consistent with endogenous lipid pneumonia. It was
10 considered an incidental finding of no clinical significance.

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12 **Keywords:** cholesterol pneumonia, endogenous lipid pneumonia, *Panthera tigris altaica*,
13 Siberian Tiger

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1 Lipid pneumonia is a term used to describe the presence of lipid in the lungs¹⁷. Synonyms
2 for this condition include cholesterol pneumonia, lipoid pneumonia, paraffinoma¹¹ and
3 alveolar histiocytosis⁸.

4 Lipid pneumonia can be subdivided depending on the source of the lipids. Exogenous lipid
5 pneumonia occurs following aspiration or inhalation of mineral, vegetable, or animal oils
6 and has been reported in cattle and cats following forced administration of mineral oils⁵.

7 Endogenous lipid pneumonia occurs when pulmonary cell membranes degenerate causing
8 release of cholesterol and other lipids into the alveolar space³. The suspected pathogenesis
9 of endogenous lipid pneumonia is related to pulmonary injury which causes proliferation of
10 alveolar type II cells, resulting in overproduction of cholesterol-containing surfactant that
11 enters the alveoli and is phagocytosed by macrophages^{3, 4, 13}. These macrophages appear as
12 clusters of foamy macrophages associated with cholesterol clefts.

13 The primary cause may be proximal airway obstruction, inhalation of irritating dust
14 particles, pulmonary parasitism³ or disturbance of lipid metabolism^{3, 4}.

15 Experimentally, laboratory animals on protein-deficient cirrhogenic and pantothenic-acid-
16 deficient diets and those that have had hypophysectomy also have been shown to have an
17 increased prevalence of endogenous lipid pneumonia³.

18 The condition is reported frequently in rats¹⁶ and less frequently in other species such as
19 mice⁶, cats^{5, 10, 11}, human beings¹ and dogs^{3, 15}. It has also been described in wild animals
20 such as Raccoons (*Procyon lotor*)⁹, Opossums (*Didelphis virginiana*)³, Genet (*Gennetta*
21 *gennetta*)¹³, Foxes (*Vulpes vulpes*)⁷, Llama (*Llama glama*)⁹ and Shrews (*Tupaia belangeri*)².

22 Clinical signs, if present, are described as nonspecific, such as lethargy, anorexia, and
23 weight loss, or signs of respiratory tract disease^{12, 14}. No report is available in wild felids.

24 During the years 2009 to 2011 seven Siberian Tigers (*Panthera tigris altaica*) aged between
25 2 and 14 years were referred for necropsy examination to the Department of Animal

1 Pathology of the University of Turin (Italy) from the Safaripark of Pombia to ascertain the
2 causes of death.

3 Tissue samples for histological examination were fixed in 10% neutral buffered formalin
4 (pH7), wax-embedded sectioned at 4- μ m using a microtome^a, and stained with
5 haematoxylin and eosin. Other samples were frozen in OCT, 4- μ m section were cut using a
6 cryostat^b and stained with Sudan III. All tissues were examined by light microscopy^c.

7 At necropsy three out of seven tigers, whose cause of death was in two ten-year-old animals
8 renal failure, and in one fourteen-year-old animal a pyloric obstruction, showed multifocal,
9 irregularly distributed, white, soft, mainly subpleural, 3 mm nodules scattered throughout
10 the lungs (fig. 1). They were most prominent on the dorsal regions. On cut section the
11 plaques appeared to be solid and white, and located in the subpleural regions.

12 Histologically there was a marked infiltration of macrophages, with foamy cytoplasm, and
13 multinucleate giant cells interspersed with numerous clusters of cytoplasmic clefts that were
14 interpreted as outlines of cholesterol crystals (fig. 2). Localized around the lesions there was
15 a mild lymphocytic infiltration. The majority of the lesions were located under the pleural
16 surface. The same lesions were present to a lesser extension within the parenchyma, usually
17 in the peribronchial or periarteriolar regions. Sudan III staining revealed red-stained fat-
18 storing cells scattered in the lesions. The outlines and cholesterol crystals remained evident
19 and not dyed (fig. 3). These findings were consistent with a diagnosis of endogenous lipid
20 pneumonia as the necropsy of the animals included in the present study did not revealed any
21 pulmonary obstruction or parasitism. Furthermore, aspiration or inhalation of mineral,
22 vegetable, or animal oils due to oral administration of oil based drugs or substances were
23 excluded. No pulmonary clinical signs or other macroscopic or histological pulmonary
24 lesions were present. Moreover there were no cardiac changes compatible with a *cor*
25 *pulmonale*. While the cause of the endogenous lipid pneumonia in the tigers reported here is

1 not known, it seems reasonable to suggest that it could be associated with the inhalation of
2 irritating dust particles in the animal enclosures open to vehicular traffic of visitors,
3 however in our cases no additional histologic findings were detected to support this
4 hypothesis. A genetic predisposition, as described in humans, cannot be completely ruled
5 out in these tigers.

6 Endogenous lipid pneumonia is often an incidental and not life-threatening finding, in
7 absence of clinical signs or with non-specific symptoms, radiographic features, and
8 haematologic and serum biochemical findings¹⁰.

9 To the author's best knowledge this is the first report of endogenous lipid pneumonia in
10 tigers. The endogenous lipid pneumonia in these tigers was considered an incidental post-
11 mortem finding of no clinical significance.

12

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2 ^c Leica DM LS2, Leica Microsystems, Germany

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23 **Legend for Figures**

24 Fig. 1: lung, Siberian Tiger: multifocal, irregularly distributed, whitish, soft, subpleural
25 nodules.

- 1 Fig. 2: lung, Siberian Tiger: infiltration of macrophages with foamy cytoplasm, and
- 2 multinucleate giant cells, interspersed with numerous clusters of cytoplasmic cholesterol
- 3 clefts (HE stain; 200X) Bar = 50 μm .
- 4 Fig. 3: lung, Siberian Tiger: diffusely red-stained fat-storing cells with outlines of
- 5 cytoplasmic cholesterol crystals (Sudan III stain; 400X) Bar = 25 μm .