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Source: Journal of Wildlife Diseases, 8(4) : 321-324

Published By: Wildlife Disease Association

URL: <https://doi.org/10.7589/0090-3558-8.4.321>

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## NATURALLY OCCURRING SQUIRREL FIBROMA WITH INVOLVEMENT OF INTERNAL ORGANS

JOHN M. KING<sup>1</sup>, ALAN WOOLF<sup>2</sup>, and JAMES N. SHIVELY<sup>1</sup>

**Abstract:** One of two gray squirrels (*Sciurus carolinensis*) with typical skin lesions attributable to the squirrel fibroma virus also had generalized disease involving fibromatous reactions in the lung, liver, kidney, lymph node; and focal adenomatoid changes in the lung.

### INTRODUCTION

Multiple skin tumors on gray squirrels have been described previously.<sup>1,2,3,6</sup> The etiologic agent is squirrel fibroma virus, a pox virus. Experimental transmissions of the virus have produced pulmonary, hepatic, and renal lesions in addition to the characteristic skin lesions.<sup>3,4</sup> To our knowledge, naturally occurring involvement of internal organs with fibromatous reaction or adenomatoid lung lesions have not been reported.

This report describes squirrel fibroma virus lesions in two cases, one having extensive involvement of viscera. Both animals were juveniles found in Ithaca, New York in October and November 1971.

### GROSS LESIONS

Squirrel 1 had numerous lesions irregularly distributed over the body including the face, lips, and footpads. They were soft, elevated, plaque-like nodules, 2-10 mm in diameter. Some nodules were hairless, but others were partially covered with hair. The largest fibromas were located on the hind legs and perianal region. Lesions were clearly delineated on the undersurface of the skin as pale, gray areas infiltrating the skin itself, but not mass-producing. A firm, white nodule 2x4 mm was located on the surface of the internal intercostal muscles. A similar nodule 1x2 mm was on the coccygeal

vertebrae near the tail tip. The lung was about 50 percent involved with whitish, gray, focal, firm masses (Figure 1). The liver had multiple pale, blotchy areas on both peritoneal and cut surfaces. The spleen was slightly enlarged and had prominent germinal centers.

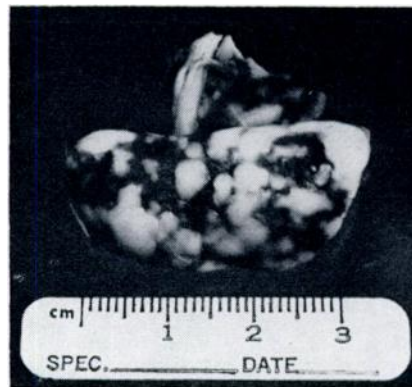


FIGURE 1. Focal masses in lung of squirrel with fibroma.

The second squirrel had more numerous but smaller lesions than the first. Lesions were most conspicuous in the perianal region. The spleen was slightly enlarged and a single grayish-white lesion about 3 mm in diameter was visible in the parenchyma just below the capsule. No other gross lesions were noted in squirrel 2.

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### HISTOPATHOLOGY

Histologic changes associated with skin lesions were similar to those reported by other workers.<sup>2,3,5</sup> The epithelium was proliferated, with acanthosis and a thin keratin layer. Many ballooned epithelial cells contained hyaline bodies. A small amount of scattered surface necrotic debris was present. The epithelium was elevated and the basal border appeared very irregular with elongated rete pegs. The dermis was characterized by massive loose connective tissue proliferation. Both epithelial and connective tissue cells contained acidophilic intracytoplasmic inclusion bodies. Skin lesions were similar in both animals, but were less pronounced in squirrel 2.

The lungs of squirrel 1 had multiple discrete areas of adenomatoid proliferation of alveolar lining cells (Figure 2).

Several areas of loose connective tissue proliferation were present around bronchioles in addition to the adenomatoid reaction. Intracytoplasmic inclusions indistinguishable from those observed in skin lesions were present both in the adenomatoid and fibromatous areas (Figure 3).

The liver in squirrel 1 had scattered large areas of centrilobular necrosis and fatty vacuolization. Many sinusoids were partially filled with chronic inflammatory cells. Concentric proliferations of loose connective tissue around some triad areas were similar to that observed around bronchioles and in the dermis. Scattered acidophilic intracytoplasmic inclusions were in the connective tissue.

Sections of lymph node had small areas of loose connective tissue nodules in the parenchyma and raised areas in the capsule. Inclusions were present in the con-

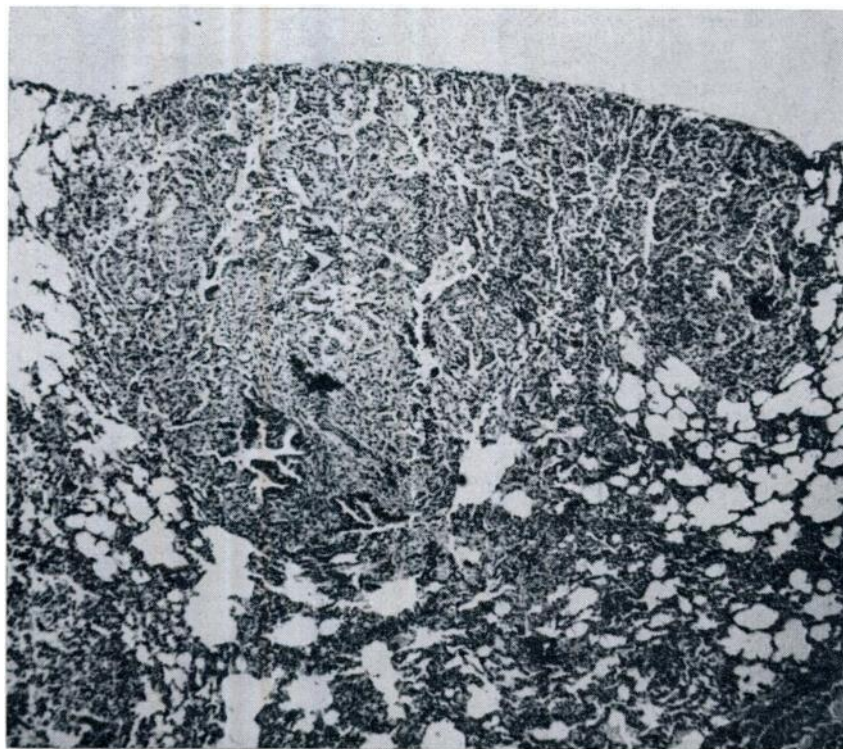


FIGURE 2. Section of lung showing adenomatoid proliferation of alveolar lining cells. H&E x 55.

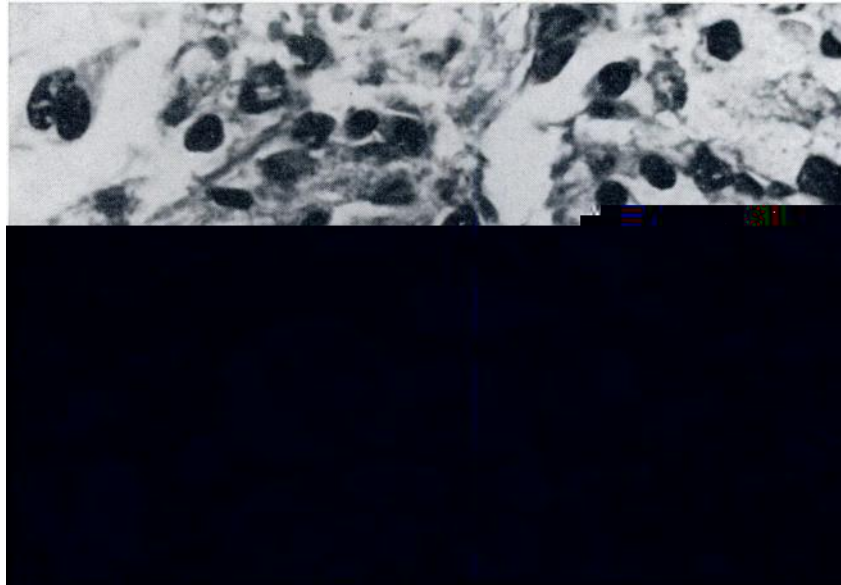


FIGURE 3. Intracytoplasmic inclusions (arrows) in lung section. H&E x 540.

nective tissue cells. The kidney had focal connective tissue proliferation, again with scattered inclusions present.

Internal organs of squirrel 2 did not have the fibromatous reactions observed in squirrel 1. The liver had scattered areas of necrosis with chronic inflammatory cells near triads, but no inclusion bodies were observed. The spleen had a single large infarct. No lesions were found in other organs and tissues.

#### ELECTRON MICROSCOPY

Cubes of tissue from lesions in the skin and lung of squirrel 1 were fixed in 6% glutaraldehyde in phosphate buffer, post-fixed in 1% osmium tetroxide and processed for electron microscopy. Sections were stained with uranyl acetate and lead citrate.

Almost every cell contained large numbers of typical poxvirus virions in many areas of the skin lesions. The viral particles measured approximately  $230 \times 280$  mu. Many of these loci also contained immature poxvirus. Mature viral particles identical in size and morphologic characteristics to those in the skin lesions, im-

mature virions, and viral matrices were in many cells in the masses in the lungs (Figure 4). Unequivocal demonstration of poxvirus has not been achieved in liver fixed for several weeks in formaldehyde. Other tissues were not examined.

#### DISCUSSION

The association of epithelial and visceral lesions with the squirrel fibroma virus was demonstrated experimentally by other investigators.<sup>3,4,5</sup> The presence of similar acidophilic intracytoplasmic inclusions in the skin, lung, liver, kidney, and lymph node lesions observed in squirrel 1 suggested a common viral etiology for the lesions observed. Although no viral isolations were attempted from affected viscera, morphologically characteristic pox virus particles were demonstrated by electron microscopy. Attempts to culture bacteria were unsuccessful in both cases.

The liver necrosis and splenic infarct observed in squirrel 2 did not appear to be related to the pox virus etiology of the cutaneous lesions or the visceral lesions observed. We could not find inclusion bodies or diagnostic histologic changes.



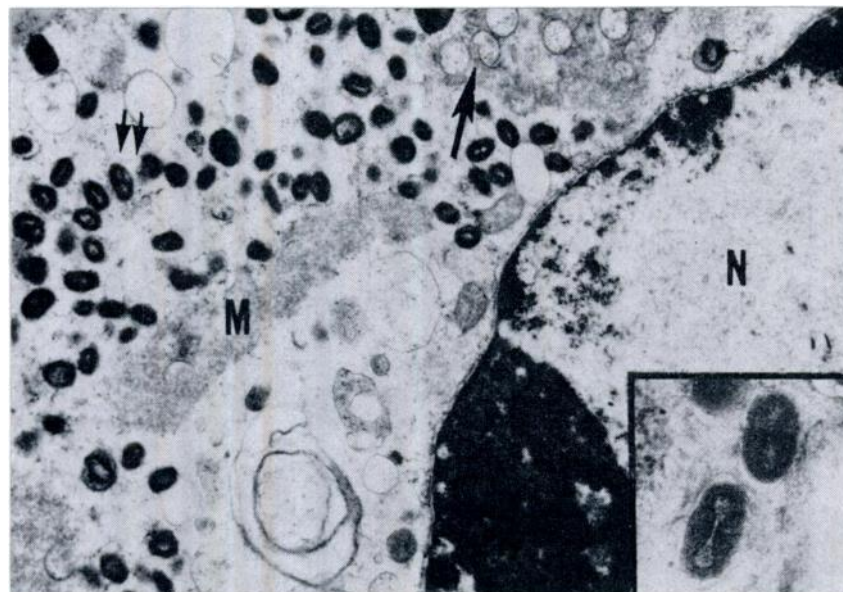


FIGURE 4. Mature poxvirus (double arrow), immature virus (arrow) and virus matrix (m) in the cytoplasm of a cell from a lung mass. Chromatin is clumped at the margin of the nucleus (n). X13,500. Inset: Mature poxvirus. X38,000.

We consider these lesions as incidental findings.

The one squirrel having generalized disease associated with the fibroma virus demonstrated that involvement of internal organs can occur in natural infections.

Future studies of squirrel fibroma cases should include examination of viscera, both grossly and microscopically to determine the prevalence and relationships of cutaneous and visceral lesions.

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Received for Publication March 9, 1972