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Pathology of pulmonary masses in rabbits: A retrospective study of 608 rabbit necropsy cases

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Abstract

The prevalence of both neoplastic and non-neoplastic pulmonary masses in rabbits is considered low. Gross examination alone is insufficient to reliably differentiate between these lesions. This study evaluated necropsy cases presented to the Department of Veterinary Pathology, College of Veterinary and Animal Sciences, Mannuthy, from May 2019 to December 2025. Among a total of 608 cases examined during this period, twelve cases showed pulmonary mass. Most of the affected rabbits were older than three years. Among these twelve cases, two were males and ten were females. Based on histopathological examination, six cases were non-neoplastic and six were neoplastic. The non-neoplastic pulmonary masses consisted of abscesses, granulomatous inflammation, and bronchopneumonia. The overall prevalence of neoplastic lung masses in rabbits was 0.98 % (6/608). Among the six neoplastic cases, five were uterine adenocarcinomas, metastasised to lungs and one was a primary lung tumour. These findings emphasise that gross examination alone is inadequate for definitive diagnosis. Histopathology, supplemented by special staining techniques and immunohistochemistry, is essential in differentiating neoplastic from non-neoplastic pulmonary masses in rabbits.

Keywords: *Abscesses, granulomatous inflammation, uterine adenocarcinoma, primary lung tumour*

Pulmonary masses, both neoplastic and non-neoplastic, are considered rare in pet rabbits (Cooper et al., 2017). Although several reports described rabbit neoplasms, especially tumours involving the female genital tract, mammary gland, skin and oral cavity, studies addressing non-neoplastic pulmonary masses are rare (Bertram et al., 2021). The neoplasms of the female reproductive tract, especially uterine adenocarcinoma, represent the commonly reported neoplasms in rabbits (Baba and Von Haam, 1972). The prevalence rate of uterine adenocarcinoma in female laboratory rabbits ranges between 13.7 % and 24.4 % (Bertram et al., 2018).

Granulomas, abscesses, and consolidated nodules in pneumonia are examples of non-neoplastic diseases that can be mistaken for pulmonary neoplasms during necropsy. Granulomatous lesions may arise from bacterial, fungal or parasitic infections (Percy and Barthold, 2013). Infection with bacterial agents such as *Pasteurella multocida* and

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Staphylococcus aureus causes abscess formation in rabbit lungs (Yang et al., 2022). Fungal infections such as *Aspergillus fumigatus*, *Cryptococcus neoformans*, and *Histoplasma capsulatum* can cause granulomatous pneumonia or pulmonary nodular lesions in rabbits (Percy and Barthold, 2013). Because of their gross resemblance to the neoplastic pulmonary masses, these conditions are difficult to differentially diagnose under field conditions. The present study investigated pulmonary masses in rabbits retrospectively in post-mortem cases and indicated the importance of histopathological, special stain and immunohistochemical techniques for definitive diagnosis.

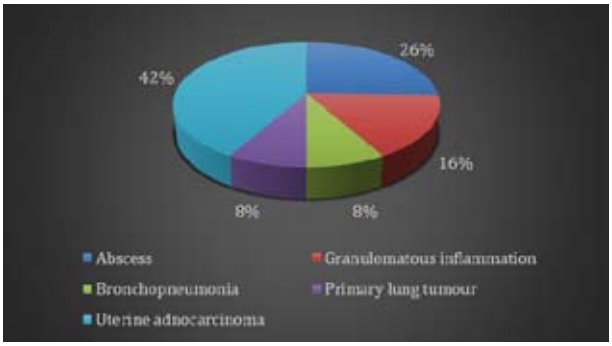


Fig. 1: Distribution of pulmonary lesions in rabbit necropsy cases

Materials and methods

A retrospective review of rabbit necropsy cases submitted between May 2019 and December 2025 was conducted. Cases exhibiting pulmonary masses were selected for further evaluation. The lung tissues collected in 10% neutral-buffered formalin (NBF) were subjected to routine histopathological processing; tissues were embedded in paraffin and sections were cut and stained according to the standard protocol (Suvarna et al., 2019). Masson's trichrome staining was performed for detecting collagen deposition and fibrosis. Suspected cases of pulmonary neoplasms were evaluated further by immunohistochemistry (IHC) using a pan-cytokeratin antibody to confirm their tissue origin. For IHC, tissues were taken in poly-L-lysine coated slides and antigen retrieval was done using citrate buffer (pH 6.0) in a pressure cooker for 20 minutes. Endogenous peroxidase activity was quenched using 3% hydrogen peroxide, and non-specific binding was minimised by applying 3% bovine serum albumin as a blocking agent. The sections were incubated overnight at 4°C with pan-cytokeratin antibody in 1:100 dilution (Abcam) followed by incubation with a secondary antibody (PolyQ stain 2 step detection kit, DSK-211-015, Quartett, Berlin, Germany) and the immunoreactivity was visualised using a DAB chromogen system.

Results and discussion

Of the 608 rabbit necropsy cases examined during the study period, 12 cases (1.97%) exhibited pulmonary masses. The pulmonary masses that mimicked neoplastic lesions included abscessation, bronchopneumonia and granulomatous pneumonia or inflammation which could be due to infectious or non-infectious causes. Most of the rabbits affected were older than three years of age, and which is consistent with the report of Weisbroth (1974), suggesting that rabbits older than 2 years of age are more susceptible to neoplastic changes than young ones. Based on histopathological examination, six cases were found to be non-neoplastic, and six cases were neoplastic. The females were affected with tumour masses more than males, with a high occurrence of uterine adenocarcinoma (Sovan et al., 2017). The distribution of different pulmonary lesions in rabbit necropsy cases is given in Fig. 1.



Fig. 2: Diffuse hemorrhage in the right lobe and pale left lung lobe. A dark coloured mass was found on the right cranial lobe (yellow circle)

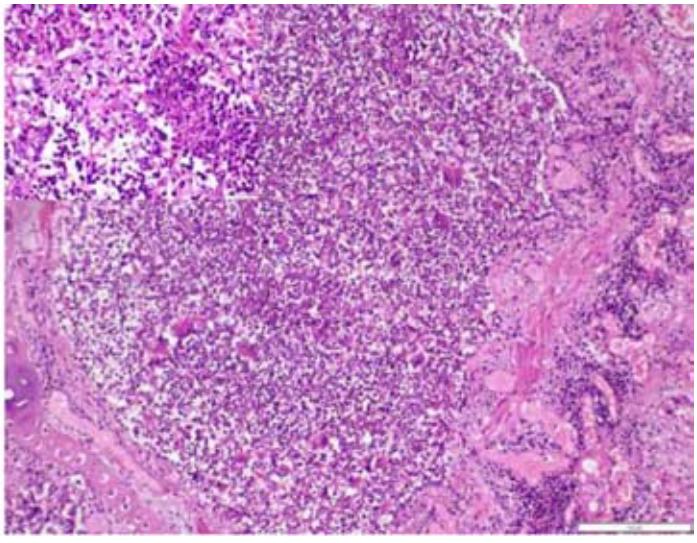


Fig. 3: Presence of inflammatory cells in bronchial lumen. Inset: Alveolar lumen contains predominantly neutrophils and macrophages (H&E, x100; inset: x400)

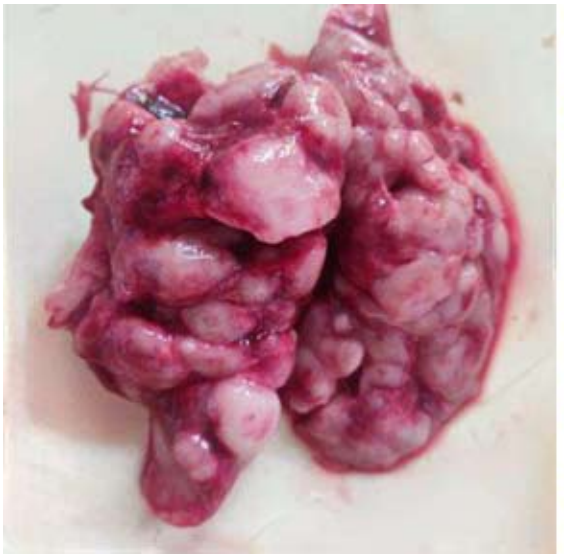


Fig. 4: Multiple nodules of varying size distorting the normal lung structure

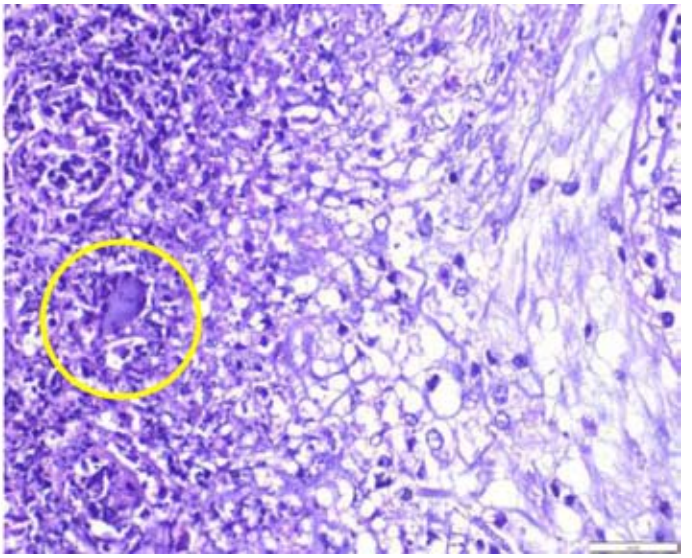


Fig. 5: Necrotic area surrounded by layer of inflammatory cells including multinucleated giant cells (yellow circle) (H&E, x400)

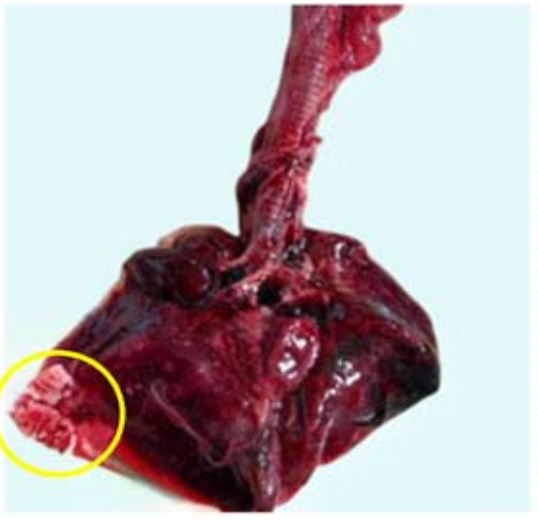


Fig. 6: Diffusely congested lungs with presence of a rigid mass at the base of middle lobe of left lung (yellow circle)

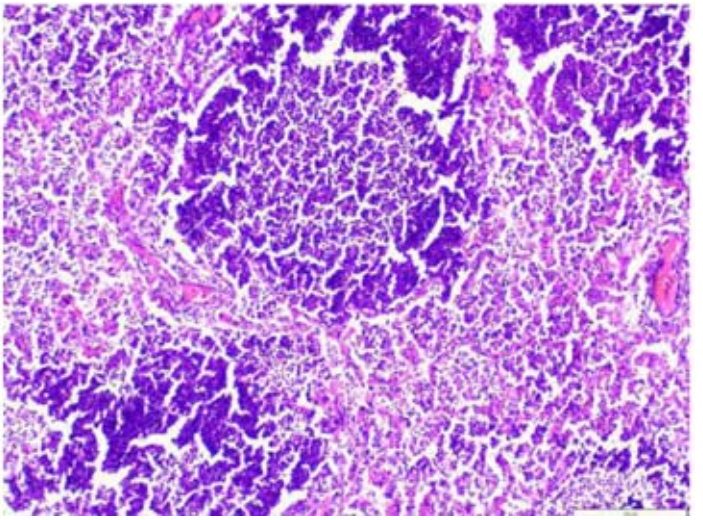


Fig. 7: Severe infiltration of inflammatory cells with collapsed alveolar lumen (H&E, x100)



Fig. 8: Multiple single to coalescing nodules on the surface of lung

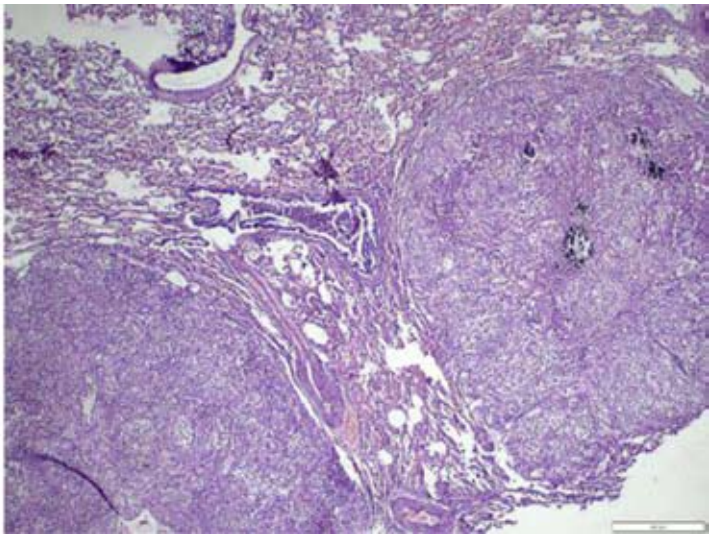


Fig. 9: Encapsulated tumour cells with extensive fibrosis and collapsed alveoli; (H&E, x40)

Non-neoplastic pulmonary masses

Among the six cases of non-neoplastic pulmonary masses in rabbits, the cut section of pulmonary mass in three rabbits showed exudation of pus. Grossly, the right lung lobe appeared haemorrhagic, while the left lung lobe was pale (Fig. 2). A dark grey to black nodular mass was seen on the right cranial lung lobe protruding from the lung parenchyma, and the cut section showed pus oozing out. Histopathological examination revealed distortion of normal lung architecture with marked infiltration of inflammatory cells; the bronchiolar lumen was filled with inflammatory cells, and the predominant cells seen were neutrophils and macrophages (Fig. 3). Histopathological examination revealed a chronic active inflammatory process. *Pasteurella multocida* is one of the major respiratory pathogens that produces pulmonary abscesses (Deeb, 2009). *Staphylococcus aureus* is another cause of systemic abscessation in rabbits (Corpa et al., 2009). *Streptococcus intermedius* was identified as the causative agent for pulmonary abscess formation in a five-month-old male rabbit (Iorgoni et al., 2025).

In two cases, lung nodules of varying size were the only lesions noted. Grossly, the lung consisted of multiple coalescing nodules of moderately firm consistency in all lobes (Fig. 4). Microscopically, the lung architecture was obliterated with severe infiltration of inflammatory cells. The lung showed several granulomatous inflammations with a central zone of necrosis surrounded by inflammatory cells, including giant cells (Fig. 5). The histological examination was suggestive of granulomatous inflammation, rather than neoplasia. Similar lesions were reported in a juvenile dwarf rabbit infected with *Mycobacterium genavense* (Ludwig et al., 2009). Lesions comparable to granulomatous inflammation were seen in rabbits affected with adiaspiromycosis caused by dimorphic fungi like *Emmonsia parva* and *Emmonsia crescens* (Hughes and Borman, 2018).

In the remaining one case among the six non-neoplastic pulmonary masses, in a white giant female rabbit, the lungs were diffusely congested with consolidation of the cranioventral lobes. A white nodule was seen in the middle lobe of the left lung (Fig. 6). The uterus was gravid with four foetuses. Histopathological examination revealed the loss of normal lung architecture and collapsed alveolar lumen (Fig. 7). Severe infiltration of inflammatory cells was evident, and blood vessels were engorged. The histopathological changes were suggestive of bronchopneumonia.

Neoplastic pulmonary masses

Among the six neoplastic pulmonary mass cases, lung in one case showed multiple, coalescing, white to pale nodular masses of varying size, raised above the surface, distorting the normal pulmonary architecture and extending deep into the parenchyma (Fig. 8). On histopathological examination, the lung architecture was obliterated with the formation of encapsulated neoplastic cells with extensive fibrosis confirmed using Masson's trichrome staining (Fig. 9). The bronchiolar lumen, as well as peribronchiolar and peribronchial regions, contained abundant inflammatory cells. The bronchiolar epithelium showed marked hyperplasia with the formation of papillary projections extending into the lumen and surrounding stroma. The tumour was confirmed to be of epithelial origin by IHC using a pan-cytokeratin antibody (Fig. 10). The tumour was diagnosed as a primary lung tumour, bronchogenic adenocarcinoma based on histopathology and immunohistochemistry. Primary lung tumours were

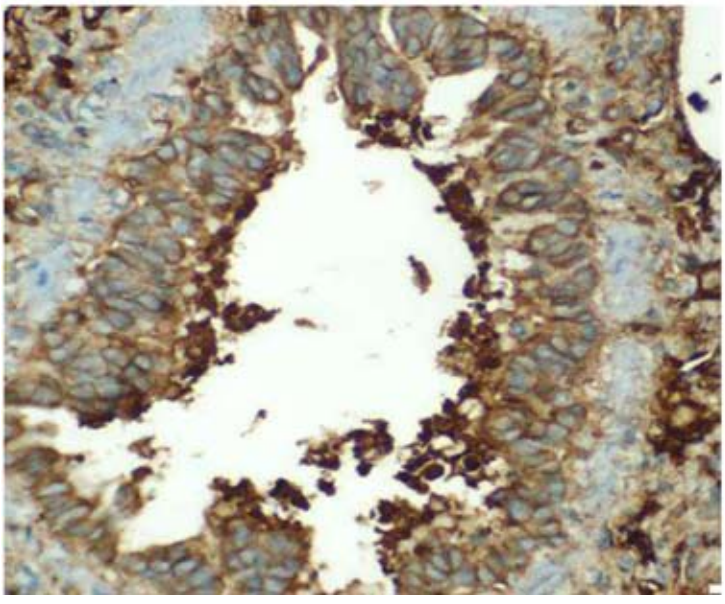


Fig. 10: Bronchiolar epithelial cells showing positivity for pan-cytokeratin (DAB, x1000)

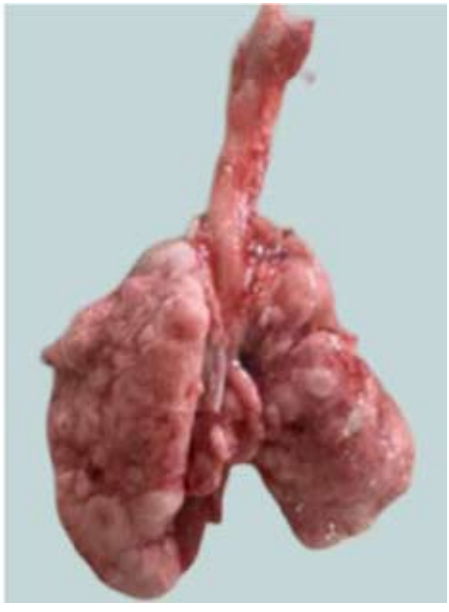


Fig. 11: Presence of variable sized nodules in all lung lobes

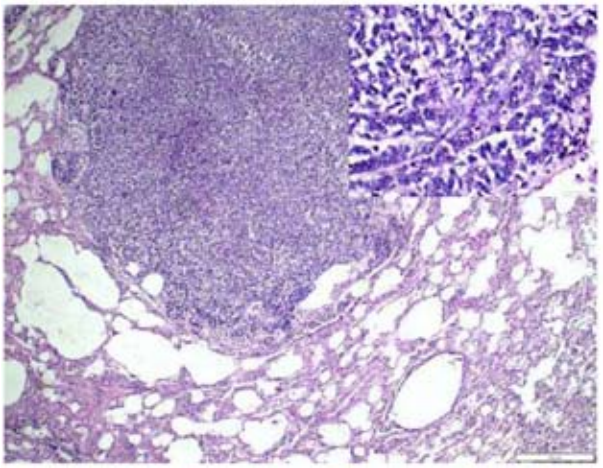


Fig. 12: Circumscribed foci of tumour cells in lungs. Inset: Pleomorphic epithelial cells (H&E, x40; Inset: x400)

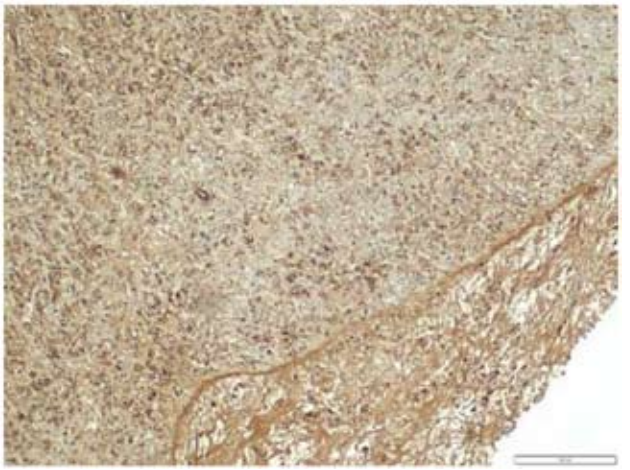


Fig. 13: Lung epithelial cells showing strong immunoreactivity with pan-cytokeratin (DAB, x100)

observed in five rabbits by Cooper et al. (2017). Sovan et al. (2017) reported bronchogenic adenocarcinoma in a two-year-old doe.

Five cases exhibited pulmonary nodules in association with marked uterine thickening and enlargement. Lungs showed numerous white nodules of 0.5 cm diameter (Fig. 11). The uterus appeared haemorrhagic and bulky, and the uterine wall was more than 3 cm in thickness. Histopathological examination of lungs revealed well-circumscribed foci composed of pleomorphic epithelial cells (Fig. 12). Alveolar areas near the tumour mass were compressed due to pressure atrophy. A few areas of glandular formation lined with cuboidal cells were observed, with cells showing variation in size with few mitotic figures. The endometrial region of the uterus was necrotic and infiltrated with inflammatory cells. Endometrial gland hyperplasia was evident. There were poorly circumscribed, invasive mass within the endometrium composed of epithelial cells showing anisocytosis and anisokaryosis, forming acinar structures supported by fibrous stroma. This was consistent with Kim et al. (2025). The case was confirmed to be of epithelial origin through IHC using pan-cytokeratin (Fig. 13).

Similar nodular growths involving the uterus and lungs were observed by Jasni et al. (1997) in a 5-year-old female rabbit and were diagnosed as metastatic uterine adenocarcinoma based on histopathology. According to Percy and Barthold (2013), there is a high probability of age-related predisposition to uterine adenocarcinoma with advanced age in female rabbits, with more than 80% incidence in female rabbits above five to six years of age. This is comparable to our present findings, where the occurrence of uterine adenocarcinoma was observed in rabbits above three years of age.

Both neoplastic and non-neoplastic lesions can lead to extensive distortion of the normal lung architecture, making it difficult to diagnose based on gross lesions alone. The findings of our study emphasise the role of histopathology in diagnosing and evaluating the pulmonary masses in rabbits. Histopathology, along with special stains and immunohistochemistry, enables the definite diagnosis and, thereby, identifies the exact origin of the tumour.

The retrospective study revealed that the most common cause of death was pasteurellosis (247 cases, 40.63%), followed by enteritis (107 cases, 17.59%). Concurrent haemorrhagic tracheitis and enteritis were observed in 73 cases, while 70 cases were positive for coccidiosis. Mixed infection with pasteurellosis and coccidiosis was recorded in 42 cases. Pneumonia was diagnosed in 15 cases, including one with a pulmonary mass. Reproductive disorders included metritis with abortion (14 cases), uterine prolapse (1 case), uterine torsion (1 case) and hydrosalpinx (1 case). A tumour in the mammary gland was seen in a single case. Two rabbits died following traumatic shock associated with a wound and fracture. No definitive diagnosis could be established in 22 cases.

Conclusion

The present retrospective pathological study of 608 necropsy examinations showed the prevalence of pulmonary masses in rabbits. Although rarely encountered, the rabbit pulmonary masses included both non-neoplastic and neoplastic masses. Lung masses due to secondary metastasis of uterine adenocarcinoma were observed more in rabbits than the primary lung tumours. Age-related increase in the risk of neoplastic development was observed, particularly in female rabbits. This highlights the importance of proper monitoring and accurate diagnosis of pulmonary lesions, especially in aged rabbits.

Conflicts of interest

The authors declare that they have no conflict of interest.

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