Acute pneumonia in a cat

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History:
A 4.5 year old neutered male domestic short-haired cat was presented to the referring practice for acute dyspnea, coughing, retching and anorexia. The coughing was productive of thick mucus. Initial treatment with broad spectrum antibiotics, carprofen and frusemide did not result in improvement. On radiography, there was a diffuse density in the lung field around the heart and a small amount of exudate with a predominance of neutrophils was present on thoracocentesis.

Clinical examination and imaging:
On referral to the University of Edinburgh one week later, the cat markedly dyspneic and was mouth-breathing. His body condition was good and no external lesions were seen. The heart rate was 140b/min and respiratory rate 24/min with increased inspiratory and expiratory effort. Increased lung sounds were audible bilaterally, mainly referred from the upper respiratory tract. There was increased soft tissue density throughout the left lung on radiography and evidence of consolidation of this lung and mild pleural effusion on the left on ultrasonography. A presumptive diagnosis of unilateral pneumonia, most likely of bacterial origin, was made.

Initial progress and treatment:
The cat was placed in an oxygen chamber and administered marbofloxacin, amoxicillin/clavulanate, clindamycin, dexamethasone and the bronchodilator, terbutaline. When the left thoracic wall was clipped, five, slightly raised, erythematous skin lesions were detected, each 3-4mm in diameter. Thoracocentesis and lung FNA were undertaken and a skin biopsy of a skin lesion performed. Direct smear preparations of pleural fluid were stained with May-Grünwald-Giemsa (MGG, Fig 1). MGG-stained lung FNA direct smears are shown in Figs. 2 and 3. The cat was too dyspneic for venepuncture or bronchoalveolar lavage.

What cytologic features are present?
What is your differential diagnosis and how would you investigate this case further?

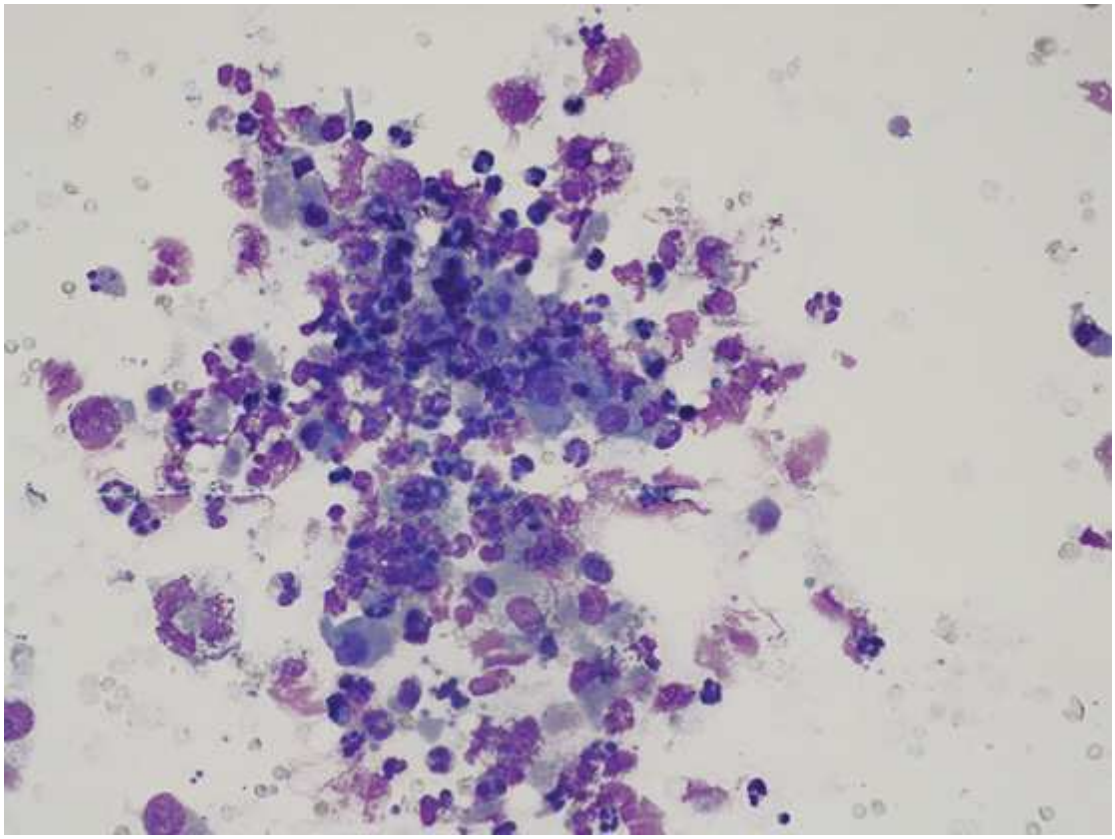

Fig. 1. Pleural fluid, direct smear. Degenerating neutrophils and macrophages are present. MGG x200.

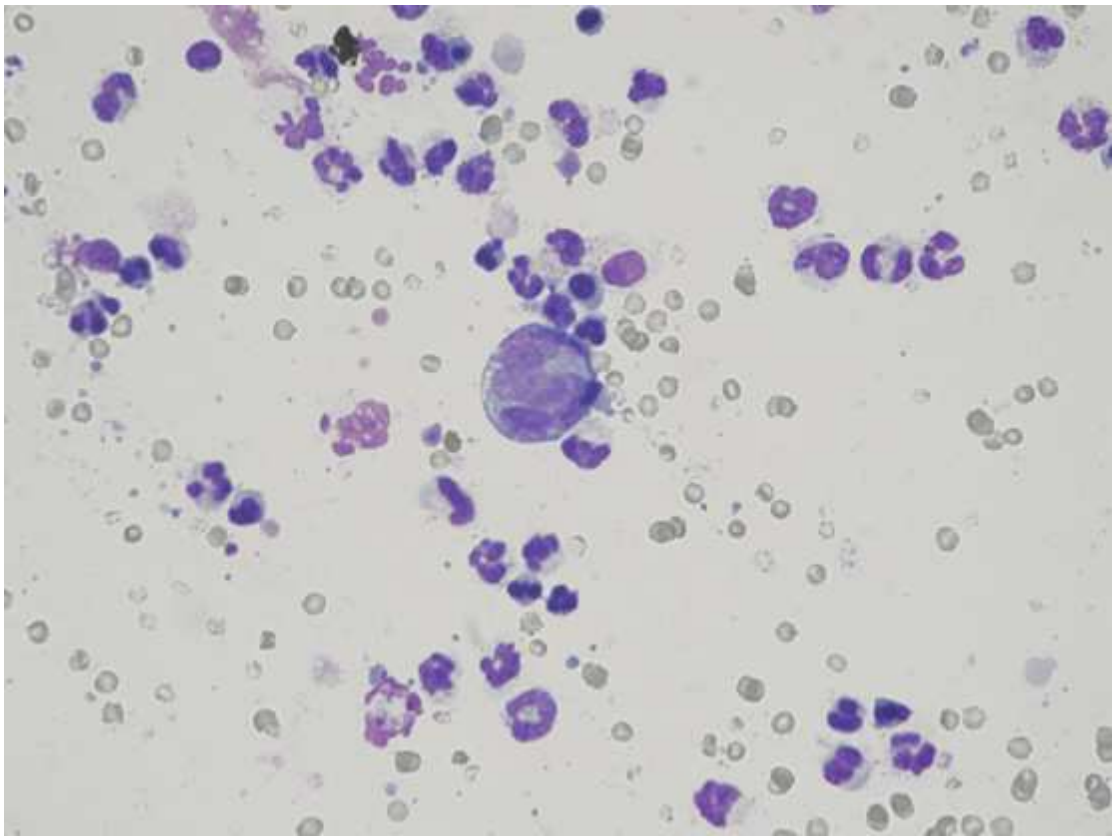

Fig. 2. Lung FNA, direct smear. Neutrophils and one giant cell are present. MGG x400.

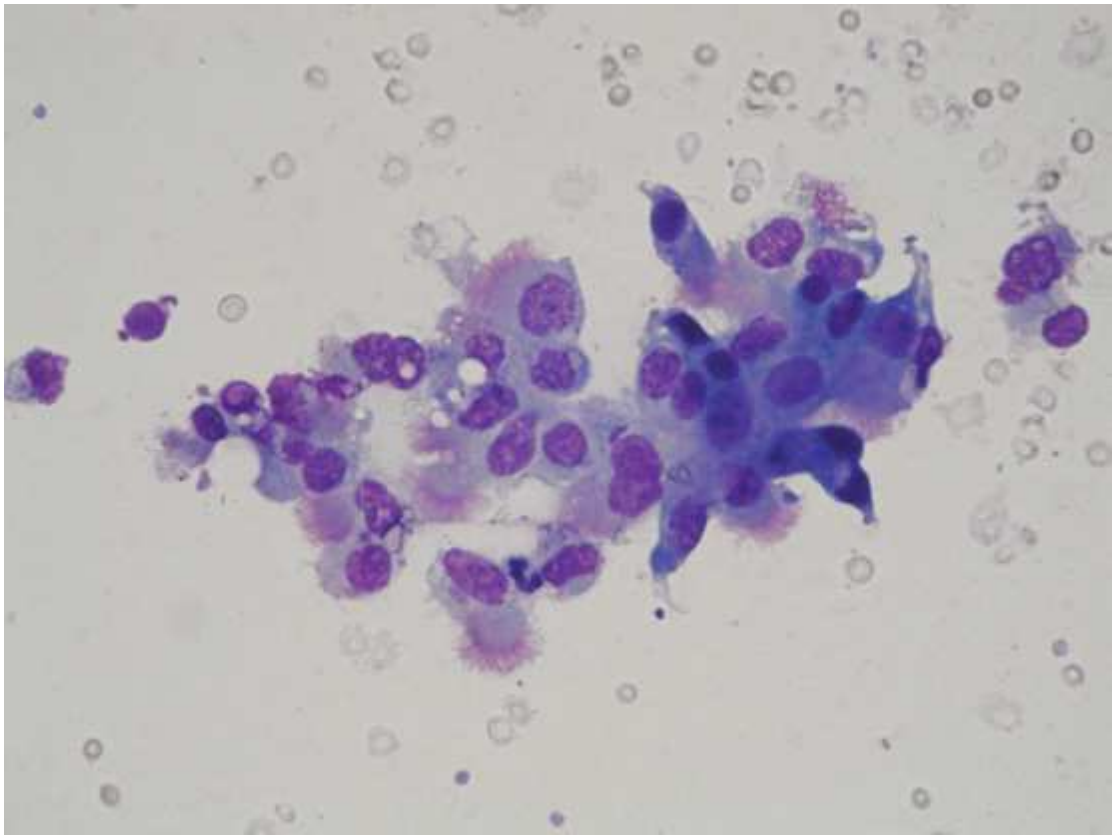

Fig. 3. Lung FNA, direct smear. A cluster of ciliated respiratory epithelial cells with dysplastic changes is present. MGG x400.

Cytologic findings:

Pleural fluid:

The smears were highly cellular with 86% non-degenerate and partially degenerate neutrophils, 8.5% vacuolated macrophages and 5.5% small to medium lymphocytes (Fig. 1) and occasional mesothelial cells, with a homogeneous, amphophilic, proteinaceous background, consistent with neutrophilic inflammation. Gram-stained smears were negative for bacteria.

Lung FNA:

The lung FNA was moderately cellular, comprising 93% non-degenerate and partially degenerate neutrophils, 4% small to medium lymphocytes and 3% macrophages (Fig. 2) with occasional giant cells. There were moderate numbers of small clusters of ciliated columnar, respiratory epithelial cells (Fig. 3) and goblet cells, and small clusters of alveolar epithelial cells. The respiratory epithelial cells showed moderate anisocytosis and anisokaryosis, and increased cytoplasmic basophilia (dysplastic change). No bacteria were evident. The findings were considered to be consistent with an acute suppurative pneumonia.

Main differential diagnoses:

Acute bacterial pneumonia
Mycoplasma sp. pneumonia
Aspiration pneumonia
Cowpox pneumonia

(Feline asthma)
(*Aleurostrongylus* infection)

On comprehensive re-examination of the smears (Fig. 4A and B), one large cell (likely ciliated respiratory epithelial cell) with 2-3 large, round, amphophilic, cytoplasmic type A inclusions was observed. This cell, and one other in the slide (Fig. 4B), also had elongated structures extending from the cell surface, resembling the actin tails seen in poxvirus infections. One ciliated respiratory epithelial cell had a circular cluster of small round amphophilic structures resembling a type B inclusion, or possibly *Mycoplasma* sp. organisms (Fig. 4A). In view of the skin lesions and the cytologic findings, a provisional diagnosis of cowpox was made.

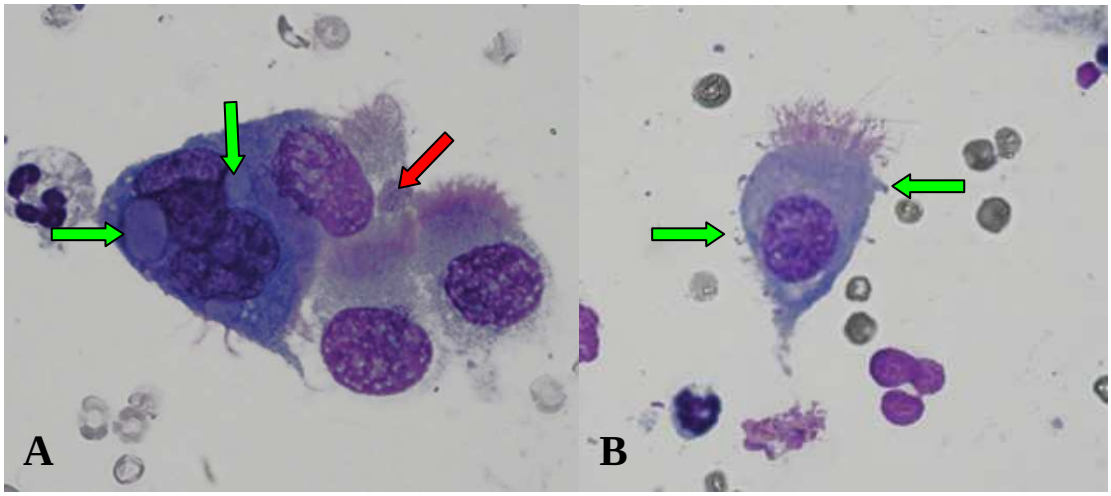

Fig 4. Lung FNA, direct smear. **A.** Two type A inclusions (green arrows) and a suspected type B inclusion (red arrow) are evident; **B.** Structures resembling actin tails are present (green arrows). MGG x1000.

Progress:
The cat was treated with recombinant feline interferon omega pending the results of the skin biopsy. The biopsy and pleural fluid were also submitted for virus isolation. *Mycoplasma* sp. was isolated on culture of pleural fluid.
However, the cat deteriorated rapidly and was euthanased and submitted for post mortem examination.

Skin biopsy histopathology:
The skin biopsy revealed extensive epidermal necrosis, crusting and ulceration, with separation from the underlying dermis. Many amorphous, brightly eosinophilic intracytoplasmic inclusions, 5-40µm in diameter, were present throughout the epidermis, follicular epithelium and sebaceous glands. Intact epidermis had areas of intracellular oedema (ballooning degeneration). Small numbers of scattered lymphocytes and plasma cells with rare mast cells and granulocytes were present throughout the superficial dermis. The findings were considered to be most consistent with cowpox infection.

Post mortem examination:
On post mortem examination, there were five slightly raised, multifocal, red lesions in the skin of clipped areas over the left hemithorax. The pleural cavity contained

approximately 150ml of watery, red fluid. There was mild thickening of the parietal pleura. The left lung lobe was markedly enlarged and diffusely firm and pale pink with red mottling and it failed to collapse upon opening the thoracic cavity. The visceral pleura was finely granular with strands of attached fibrin. The right lung lobes were darker red and softer but there was surface fibrin accumulation. No other significant macroscopic abnormalities were evident.

Post mortem histopathology:
Histopathology of the left lung revealed diffuse loss of normal alveolar, bronchial and bronchiolar architecture due to extensive, severe, acute necrosis. This was characterised by replacement of the interstitium by eosinophilic material and chromatin debris. The alveolar spaces were filled with necrotic neutrophils and foamy macrophages admixed with chromatin debris, strands of fibrin and granular eosinophilic necrotic cell debris. Some intact bronchiolar epithelial cells contained cytoplasmic viral inclusion bodies (Fig. 5). There was type II pneumocyte hypertrophy in the alveoli. The pleural surface was markedly thickened by necrotic cell debris and fibrin. The tracheal lumen was filled with necrotic cell debris and fibrin and the mucosa was lost and replaced by a meshwork of fibrin, neutrophils, lymphocytes and plasma cells. Some lining cells contained inclusion bodies similar to those described above. These findings were also considered consistent with pox viral pneumonia.

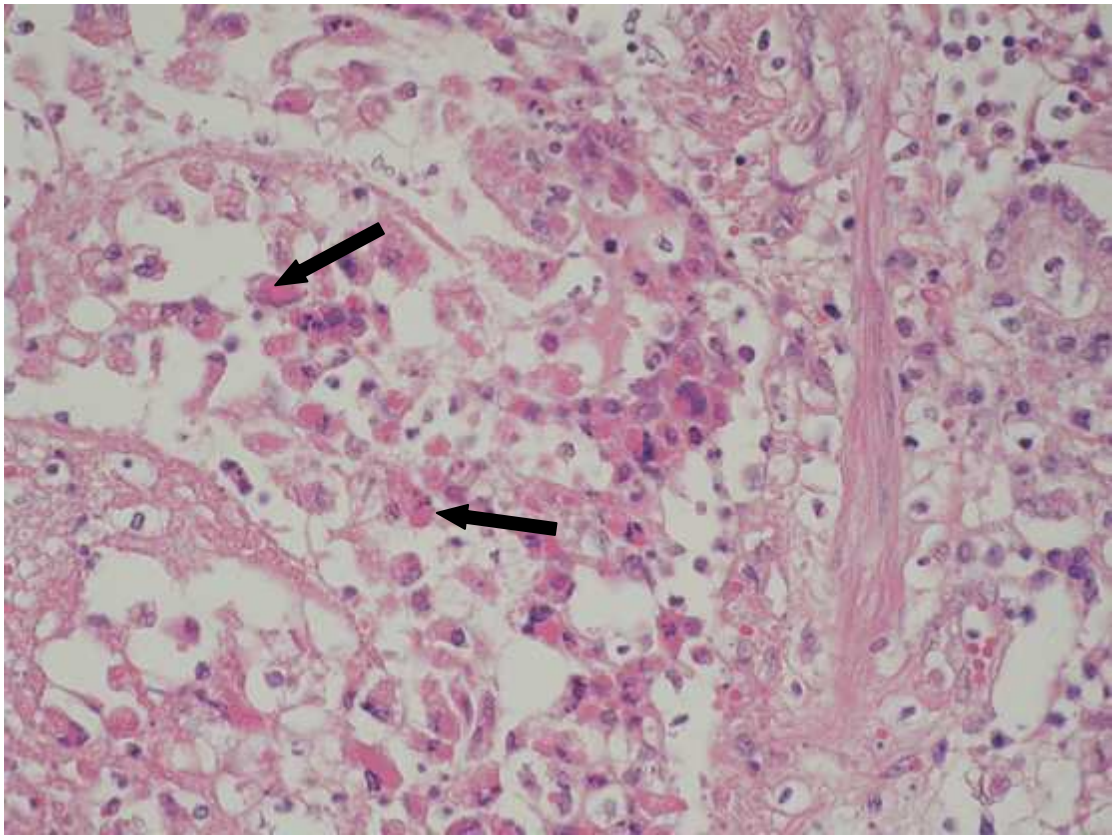

Fig. 5 Lung section with numerous inclusion bodies (arrows) in necrotic bronchial epithelial cells. H&E x400.

Diagnosis:
The final diagnosis of cowpox infection was made on the basis of virus isolation from the original skin biopsy and from pleural fluid.

Discussion:

Cowpox is a member of the *Orthopoxvirus* genus of the Poxviridae and is an uncommon viral disease in cats, although the incidence appears to be increasing in the UK. Despite the name, it is rarely isolated from cattle. It is also a zoonotic disease and can rarely be fatal in humans. Rodents are considered to be the natural reservoir and cats become infected by rodent bites. It is usually manifest as skin lesions at the site of bites; these lesions are raised, ulcerated papules with histopathological findings similar to those described in the present case and are often on the head and limbs. From there, more widespread secondary skin lesions may develop. Viremia is only transient with mild systemic signs usually followed by recovery.

Severe pneumonia is an unusual manifestation of cowpox infection in cats. Previous case reports have described a necrotizing proliferative bronchointerstitial pneumonia with segmental loss of respiratory epithelium, hypertrophy of type II pneumocytes and a marked infiltrate of neutrophils, macrophages, lymphocytes and plasma cells and fibrin accumulation in the airways. Eosinophilic to amphophilic intracytoplasmic type A inclusions are seen in airway epithelial cells, type II pneumocytes (Hinrichs *et al*., 1999; Shöniger *et al*., 2007). These findings are very similar to those in our case.

There appears to be only one previous case report describing cytologic findings; Johnson *et al.* (2009) described a moderate amount of mucus, many neutrophils and fewer activated macrophages, small lymphocytes and eosinophils and low numbers of ciliated epithelial cells on bronchoalveolar lavage cytology. Inclusion bodies do not appear to have been previously described in cytologic preparations from the lung of affected cats; in our case, there were very few which were only found after a considerable time spent examining the slides. However, it was of interest that there appeared to be both type A and possibly type B inclusions. Type A, most commonly seen in the disease, are protein-rich, with small numbers of virus particles at the periphery while type B are designated “virus factories”, with many virions present. It was also interesting that structures resembling actin tails, a means of transfer of virions between cells, and typical of poxvirus infection, were also seen on cytology.

Severe pneumonia may be more common in cases with immunosuppression including intercurrent disease such as feline herpesvirus (Johnson *et al*., 2009). In the present case, *Mycoplasma* sp. was isolated and it is possible that this acted as a predisposing factor in our case. Conversely, *Mycoplasma* sp. infection could have been secondary to the viral infection.

Confirmation of cowpox infection may be performed by virus isolation, immunohistochemistry, electron microscopy and/or PCR (Pfeffer *et al*., 2002; Godfrey *et al*., 2004), and a rising titre on serology may provide evidence of recent exposure.

This case shows that although unusual, cowpox infection should be considered in the differential diagnoses of acute pneumonia in cats. Cytology can be useful such cases, although the number of inclusion bodies may be low compared to those seen on histopathology and careful examination is required to detect them.

References:

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