SOME PULMONARY LESIONS OF CALVES AND THEIR SIGNIFICANCE

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ABSTRACT

Although the traditional systems for classifying pulmonary lesions in calves have been useful, they should be reviewed taking into consideration new information about the cell populations that exist in the lungs and current concepts of inflammation.

Amidst the profusion of changes that can be seen in the lungs of calves with pulmonary disease, some can be recognised as landmarks. These may be helpful in assessing the disease process and may be used for classification purposes. The following identifiable lesions are described and their usefulness reviewed

1) cuffing pneumonia

2) viral pneumonia associated with inclusion bodies

3) exudative interstitial or fibrinous pneumonia

4) exudative pneumonia with or without suppuration

5) atypical interstitial pneumonia or the respiratory distress syndrome

6) fungal granulomas

7) plasma cell bronchitis and bronchiolitis

8) bronchiolitis obliterans

9) bronchiectasis

10) interstitial eymphysema and

11) pulmonary oedema.

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INTRODUCTION

In this paper some of the pulmonary lesions found in bovine animals, up to approximately six months of age, will be discussed. Although most of the material to be described refers to pneumonia occurring in calves indoors the abnormalities have been found in calves outside, particularly single-suckled calves. In this connection it should be remembered that pulmonary lesions in calves outside must always be differentiated from those caused by *Dictyocaulus viviparus;* these have been described earlier.

The pathological changes in calf pneumonia are diverse making this one of the most difficult groups of diseases to classify satisfactorily and usefully on a histopathological basis. Current classification and nomenclature are controversial and it is easy to find fault with them. Indeed it might be asked whether or not any classification will serve a useful purpose. However most clinically significant problems are associated with definite vascular, exudative and cellular changes in the lungs and by studying these we should be able ultimately to understand more about these reactions even if a universally acceptable classification based on them is not immediately obvious. Other criteria for classifying calf pulmonary diseases are no better. The aetiological agents that initiate these changes are not known in many cases nor are the mechanisms which mediate inflammatory and immunological reactions in the bovine lung as well understood as those in some other species.

In spite of the difficulties, several distinct lesions can be recognised which can be used as guidelines when trying to unravel the complexities of the problem and it is these which will be considered here. It should be remembered that in any given case of pulmonary disease more than one of these lesions can be seen, for example, bronchiolitis obliterans may exist with cuffing pneumonia and the lesions characteristic of the respiratory distress syndrome may be found with exudative

pneumonias. One fundamental aspect of the calf pneumonia problem is to resolve whether or not, in these cases, we are dealing with independent or interrelated processes.

Cuffing pneumonia

Cuffing pneumonia is a lesion that, in its fully developed form, is usually seen in calves three months of age or older. The changes occur in the anterior parts of the lungs and, although clinically significant, are not usually extensive enough to be responsible for death. Peribronchiolar lesions that almost certainly represent an earlier phase of cuffing pneumonia are seen in calves from two months of age.

The reaction was initially described by Jarrett et al. (1953) and further details were given later (Jarrett 1954, 1956). Essentially the term applies to a lesion recognised by the large number of lymphocytes which have accumulated in and around bronchioles forming a cuff. At its maximum development the lesion encloses the affected bronchiole in a sheath of lymphocytes which narrows its lumen and compresses surrounding alveoli. The cuff eventually becomes follicular with germinal centre-like areas. Plasma cells can be seen in the lamina propria of the bronchi and bronchioles along with the lymphocytes. In affected lobules the alveoli are either collapsed or there is an alveolitis. The alveolitis results in collections of neutrophils and macrophages in the alveolar air spaces sometimes accompanied by oedema fluid; multinucleate macrophage giant cells are found in some animals. Complicating lesions may also be found but they do not affect the basic diagnosis.

Cuffing pneumonia is considered to be strongly suggestive of mycoplasma infection. Peribronchiolar lymphoid hyperplasia was found in 75% of a series of 45 three month old calves from which mycoplasmas including *Mycoplasma dispar* and *Ureaplasma spp.* were isolated (Gourlay et al., 1970). A significant association between fully developed cuffing lesions and infection with *M. dispar* and *Ureaplasma spp.* was shown in a group of calves by

Pirie and Allan (1975). *Mycoplasma dispar* has also been shown to be present in other groups of calves with naturally occurring cuffing pneumonia from two months of age upwards and mycoplasmas have been demonstrated on the surface of affected bronchial epithelium in these animals by electron microscopy (Allan and Pirie 1977, Allan et al., 1976).

Small peribronchiolar accumulations of lymphocytes can be found in non-pneumonic calves (Pirie and Allan 1975) and even in pneumonic animals a major problem when identifying this lesion is deciding when the accumulations are large enough and numerous enough to warrant the diagnosis cuffing pneumonia. Nevertheless at one end of the spectrum this is a readily recognised change in calf lungs. It has been suggested that agents other than mycoplasma will produce marked peribronchiolar lymphocytic accumulations but there is as yet no good evidence that all the features implied by the term cuffing pneumonia can be found in lesions produced by other organisms. Conversely severe pneumonic reactions not characterised by peribronchiolar lymphocytic accumulations can be produced in mice by infection with a high dose of *Mycoplasma pulmonis* (Lindsey and Cassell 1973) who demonstrated that the severity, duration and pathological character of the pulmonary disease was dependent on the dose of infecting organisms.

Virus Pneumonia with Inclusion Bodies

Although pulmonary changes suggestive of virus infection can be found in calf lungs one cannot be sure that they are associated with virus infection when using microscopy, unless inclusion bodies are seen or viral antigen can be detected by immunofluorescence. Another consideration is the fact that, in our experience, viruses such as parainfluenza (PI3) virus can be isolated from calf lungs when inclusion bodies can not be detected and specific lesions are absent.

Lesions of virus pneumonia may be found in calves one week old which contrasts with the age of animals in which cuffing

lesions are seen. Usually in natural or experimental infections with viral agents the lesions produced are comparatively localised and extensive pulmonary consolidation, when it occurs, is attributed to secondary bacterial infection initiating a widespread inflammatory response. Therefore in animals dying with extensive pneumonic lesions it is often considered that the original viral lesion might be difficult to find. Nevertheless in one investigation (Omar 1966) 16% and 17.6% of 125 outbreaks of pneumonia in calves in East Anglia were thought to be associated with PI3 virus and adenovirus respectively on the basis of finding typical lesions in lungs from the farms studied.

Lesions which are useful diagnostic markers are found in infections with PI3 virus, bovine adenovirus, infectious bovine rhinotracheitis (IBR) virus and bovine respiratory syncytial virus (BRS).

Experimental infection of calves with PI3 virus (Betts et al., 1964, Dawson et al., 1965, Omar et al., 1966) results in a reaction that is mainly proliferative and involves the bronchiolar and the alveolar epithelium. Hyperplasia of the alveolar epithelium (epithelialisation) is a well recognised feature of this infection and epithelial syncytial giant cells can be found. Eosinophilic intracytoplasmic inclusion bodies are also seen; they are found mainly at five days post infection and persist for only two days. Giant cells have also been reported in bronchial lymph glands (Omar 1966). During our own investigations calves infected with PI3 virus were found to have a bronchiolitis characterised by focal degeneration of the epithelial cells and infiltration by neutrophils; along with this there was either alveolar collapse or a neutrophilic alveolitis. In these animals, although intracytoplasmic inclusion bodies were found in the bronchial and bronchiolar epithelium, there was no alveolar epithelial hyperplasia or giant cell formation.

The pneumonic lesion characteristic of adenovirus infection

in calves (Darbyshire et al., 1966, 1969) is a bronchiolitis with necrosis of bronchial epithelium, occlusion of bronchioles and alveolar collapse; eosinophilic or basophilic intranuclear inclusion bodies are seen in the bronchial epithelial cells and cells of the alveolar walls. The inclusions are most numerous seven days after infection. Cells containing intranuclear inclusion bodies may also be seen in the bronchial lymphnodes.

The virus of infectious bovine rhinotracheitis (IBR) will also produce intranuclear inclusion bodies in the epithelial cells of the respiratory tract particularly those of the trachea and bronchi (Crandell et al., 1959). This disease is usually associated with marked changes in the upper respiratory tract and pneumonia in the absence of these is uncommon.

Another virus induced pulmonary lesion of calves is that of BRS virus. Microscopically it is characterised by large multinucleated giant cells, syncytial cells, which are larger and have many more nuclei than those usually seen in PI3 virus infections. These have been described in the lungs of experimentally infected calves (Mohanty et al., 1975) although eosinophilic cytoplasmic inclusion bodies, which occur in tissue culture cells infected with this virus, were not seen. The syncytia were found 14 and 21 days after infection.

Jolly and Ditchfield (1965) and Wellemans (1976) demonstrated PI3 virus infection and BRS virus infection in field cases using fluorescent antibody methods.

Interstitial emphysema has been found in animals with viral pneumonias; this is referred to later.

Exudative Interstitial Pneumonia or Fibrinous Pneumonia

Exudative interstitial pneumonia was the term used by Jarrett (1956) to describe a pneumonia of calves which is also referred to as fibrinous pneumonia (Omar 1966, Jubb and Kennedy 1970). This is an easily recognised lesion characterised by an acute inflammatory reaction in the lung with marked

exudation of fluid, in which fibrin formation is a prominent feature into the alveolar air spaces and the interstitial tissue of the interlobular septa and pleura; the latter is seen as fibrinous pleurisy. Additionally there is severe pulmonary congestion, thrombosis of small blood vessels, necrosis of alveolar walls and bands of inflammatory cells outlining connective tissue structure such as bronchiolar walls, blood vessels and interlobular septa. The overall effect leads to the lung having a marbled appearance as has been mentioned earlier when the pneumonias of adult cattle were discussed.

In most instances in Britain this lesion is considered to be due to *Pasteurella multocida* or *Pasteurella haemolytica* infection and in our experience these organisms can be isolated in large numbers from lungs with exudative interstitial pneumonia. However cases do occur when the *Pasteurella spp.* are not found. *Pasteurella spp* are often found in lungs which do not have the changes described above but in these instances they are usually present in small numbers.

Fibrinous pneumonia can be fatal and has been seen in calves indoors and calves outdoors (Wiseman et al., 1976). There may or may not be a history of recent movement and it is not always possible to show that PI3 virus has been involved in the development of the lesion.

Exudative Pneumonia with or without Suppuration

Exudative pneumonias are those in which the foundation of the lesion is the acute inflammatory response without marked proliferative changes in the cell populations of either the lung tissue itself or the immune-inflammatory infiltrate. Traditionally these are considered to be caused by bacterial colonisation of the lung and mostly have been called broncho-pneumonias. Depending on the character and distribution of the reaction it is sometimes possible to classify them further into interstitial or suppurative or necrotising. This in turn

may be related to the nature of the infecting organism. This momenclature can be used for pneumonias with a wide variety of exudative or cellular reactions and the variation is usually ascribed to the fact that the inflammatory process is seen at different stages. In some animals neutrophils are the main cell types present, in others the cells of the mononuclear phagocytic system predominate. Often the cellular infiltrate appears to be more significant than the fluid exudation. In all cases there is fluid or cells or both within the alveolar and bronchiolar air spaces.

Exudative pneumonias can spread to involve as much as 75% of an animal's lung tissue. When this degree of damage is produced they can be fatal without the development of complicating lesions such as those associated with the acute respiratory distress syndrome (ARDS). Although exudative pneumonias are generally attributed to primary or secondary bacterial infection in fact the aetiology is not often identified nor is their development adequately explained.

Atypical Interstitial Pneumonia or the Acute Respiratory Distress Syndrome

Some calves indoors develop respiratory distress and die due to any combination of the following pulmonary lesions

1) congestion and oedema
2) hyaline membranes
3) alveolar epithelial hyperplasia
4) interstitial emphysema.

This group of lesions is characteristic of the bovine acute respiratory distress syndrome (ARDS) (Breeze et al., 1976). Earlier descriptions of this type of pulmonary change in indoor calves in Britain used the term atypical interstitial pneumonia (AIP) (Omar and Kinch 1966) and one type of atypical pneumonia described by Jarrett (1954) was also in this category.

This syndrome has not been investigated in Britain in any detail and only a few cases have been reported although the condition may not be uncommon. Most animals with ARDS are between four and five months old although younger animals can be affected and it has been found in single-suckled calves in a straw yard (Omar and Kinch 1966) or an open court (Wiseman et al., 1975). What could be termed a standard death rate from calf pneumonia was assessed, on one farm with a problem, as 4% of the animals at risk (Thomas and Swann 1973). When AIP is involved it has been stated that mortality can be as high as 38% within a group (Omar and Kinch 1966); the total number of calves at risk in the latter investigation was not given. The pulmonary changes characteristic of this condition can occur on their own but there may be areas in the lung with other acute or chronic bronchopulmonary damage such as cuffing pneumonia (Omar and Kinch 1966) or exudative interstitial pneumonia (Wiseman et al., 1976). Many lungs with ARDS are bacteriologically sterile although some have been found to contain *P. haemolytica* or *M. dispar* or *Ureaplasma spp.* The aetiology of this reaction in calves is not known and any association between it and the other pulmonary lesions of calves is unproven. The term ARDS is preferable to AIP since the latter has been used for other pathologically distinct conditions such as bovine farmer's lung and diffuse fibrosing alveolitis.

Fungal Granulomas

Granulomas containing fungi, usually similar to *Aspergillus spp.*, are seen in calf lungs. In our experience the animals have not been less than two months old but Jarrett (1956) described one case one month old. Usually the granulomas are few and when they are the only lesion present they are probably of no consequence. Their significance when they are accompanied by other lesions is not known. It is commonly supposed that acute respiratory damage may develop in calves as a result of hypersensitivity to fungal or actinomycetal organisms in mouldy hay or mouldy bedding but there are no unequivocally confirmed cases in the literature.

Plasma Cell Bronchitis and Bronchiolitis

A lesion affecting the anterior parts of the lungs and recognised by marked accumulations of plasma cells in peribronchiolar tissues and the lamina propria of bronchioles and bronchi has been found in calves three to four months of age. The calves with this lesion have been in groups whose other members have had cuffing pneumonia. The distribution of cells is similar to that seen in cuffing pneumonia but plasma cells are by far the most numerous cell type present; the peribronchiolar lesions are diffuse in nature and not follicular.

Bronchiolitis Obliterans

Bronchiolitis obliterans can be a major component of pneumonic reactions in calves two months of age and older. The lesion is seen in animals with cuffing pneumonia but also occurs in exudative pneumonias. It is not an uncommon abnormality and apart from its intrinsic effect in disturbing lung functions it may be important in delaying resolution of any accompanying alveolar reaction. Why it should develop in some animals is not clear but it is interesting that some of the microbiological agents that infect calves can damage bronchiolar epithelium for example *M. dispar*, PI3 virus, bovine adenovirus and RSV. Bronchiolitis obliterans is seen in adult cattle with farmer's lung and in young animals in the later stages of parasitic bronchitis.

Bronchiectasis

Although bronchiectasis is usually found in older cattle it has been seen in calves only four months old. In calves the dilated bronchi may be full of viscid clear or grey mucus instead of purulent exudate. The lesions are usually in the anterior part of the lungs. This type of abnormality produces permanent lung damage and if bronchiectasis is extensive the animal will not thrive.

Interstitial Emphysema

Interstitial emphysema is found in calves in the following circumstances

1) as part of the bovine ARDS

2) with severe pneumonias and

3) less frequently as the only abnormality.

When it is severe it will cause considerable interference with normal ventilation and afflicted animals usually have marked clinical signs. Although interstitial emphysema can affect a localised area of lung and in some incidents has been described as predominantly affecting the anterior lobes only (Omar and Kinch 1966) it is more frequently found in the diaphragmatic lobes and is usually most severe in this situation. Interstitial emphysema is probably produced following mechanical damage to the respiratory acini as a result of increased resistance in the conducting airways, particularly on expiration, brought about by either contraction of smooth muscles of the bronchi and bronchioles or exudate in the lumen of these structures or thickening of their lamina propria by inflammation. The possible role of uninhibited proteolytic enzymes in weakening the respiratory acini is not known.

Severe interstitial emphysema has been recorded in calves naturally infected with PI3 virus (Jolly and Ditchfield) and with BRS virus (Wellemans 1976). The latter cases were usually seen in autumn.

Pulmonary Oedema

Massive pulmonary oedema is included in this discussion since it may be found as the only lesion to explain sudden death in calves which may or may not have had clinical signs of respiratory embarrassment. In some instances the pulmonary oedema is obviously secondary to a cardiac lesion such as a ventricular septal defect. However morphologically detectable cardiac lesions are not always present and it is then very difficult to ascertain whether the pulmonary oedema is secondary to acute left heart failure or just a primary change in the haemodynamics of the pulmonary circulation such as that

brought about during bovine anaphylaxis. These calves do not have the combination of lesions of the bovine ARDS.

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