**Case Reports**

**Distribution of human neutrophil elastase in diffuse alveolar damage and pneumonia in a case of neonatal sepsis**

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**Introduction**

Sepsis in newborn babies is dangerous because of their immature immune systems. Human neutrophil polymorphonuclear leucocytes provide host defence against bacterial and fungal infection, but they also cause tissue destruction which is mediated by certain proteolytic enzymes secreted from their own granule fractions. In addition, evidence indicates that neutrophils play a contributory and perhaps primary role in many cases of diffuse alveolar damage (DAD) (1). We performed an autopsy on a newborn baby who showed pneumonia and DAD in the same lung section. Distinct differences were shown in the neutrophil distribution patterns.

**Case Report**

A newborn baby (male, 39 week gestation, body weight 3278 g, premature rupture of the membrane 12 h before birth, induction and vacuum delivery, Apgar score 9 at 1 min, the pregnancy and the antenatal care of his mother was not particular) was treated for respiratory failure. Upon physical examination, cyanosis was observed. Blood gas analysis showed severe hypoxia and the baby died of respiratory failure 20 h after birth. Streptococcus agalactae (Group B) was cultured from blood, faeces, laryngeal swab and cerebrospinal fluid. The clinical diagnosis was pneumonia, sepsis and respiratory distress syndrome. An autopsy was performed. The lungs were congested and weighed 28 g, (left) and 36.5 g, (right).

The lungs showed changes due to pneumonia with haemorrhage in sharply or vaguely demarcated segmental areas in all lobes of the lungs. Bloody pleural effusion was noted bilaterally (left, 18 ml; right, 36.5 ml). Histological examination revealed changes of pneumonia and DAD. Pneumonia was associated with intraalveolar haemorrhage and was more severe in the left lung. A greater or lesser degree of DAD was observed in other areas of the lungs. Alveolar exudate contained bacterial proliferation. A thick hyaline membrane, stained by PAS reaction, was partly formed. In some specimens, both pneumonia and DAD could be observed to be well demarcated and mutually exclusive (Plate 1a). At the DAD site, the formation of a hyaline membrane was observed. Distribution patterns of neutrophils were clearly demonstrated by immunohistochemistry using antibodies to neutrophil elastase (Serotec). In this case, neutrophil distribution was quite different between pneumonia areas and those of DAD. In the pneumonia areas, neutrophils aggregated in alveolar cavities and very few were retained in alveolar septa (Plate 1b); but in DAD areas, neutrophils were located in the alveolar septa with few infiltrating the alveolar cavities (Plate 1c).

**Discussion**

Neutrophil elastase, a neutral serine protease, is localized in the azurophilic or primary granules in neutrophils, and plays an important role in host defence (2). It is used as a neutrophil marker, targeting only those neutrophils in complicated lesions. It is especially useful in some cases when many of the infiltrating neutrophils are premature, having a non-segmented nucleus. In cases of newborn fatal pneumonia, a higher than expected number of cells were...
Plate 1 (a) Haematoxylin-eosin stain of the autopsied lung, showing a site of bronchopneumonia (left) and a site of DAD (right); (b) Immunostain for human neutrophil elastase of the autopsied lung. At the site of bronchopneumonia, the distribution of neutrophils was mainly intraalveolar; (c) Immunostain for human neutrophil elastase of the autopsied lung. At the site of DAD, neutrophils showed septal distribution.
revealed to be neutrophils in a section stained by haematoxylin-eosin.

It has been suggested that the contribution of neutrophils in the lung in adult respiratory distress syndrome (ARDS) is not the same as that in a simple infection, such as pneumonia (3). In pneumonia, neutrophils attracted to combat infection by chemotactic factors are not activated until they arrive at the site of infection (alveoli). In ARDS, aggregated neutrophils damage the endothelium of the pulmonary microvasculature and the alveoli, presumably by releasing enzymes such as elastase or collagenase, or generating toxic oxygen radicals (1,4–8). Neutrophils may also damage the endothelium directly by neutrophil-mediated cytotoxicity.

However, in many adult materials, several factors modified the conditions so that the distribution pattern of neutrophils was not typical even in cases of pneumonia. However, in the present case, DAD, which was caused by neonatal sepsis and pneumonia, was observed in the same autopsy section and the distribution of neutrophils and possibly the sites of neutrophil elastase activity were quite different. In areas of diffuse alveolar damage, neutrophils were localized in the alveolar septa. In contrast, in areas of pneumonia, neutrophils were localized in alveolar spaces. These findings might suggest different modes of contribution of neutrophils in pneumonia and DAD.

References