Comparison of bronchoscopic diagnostic techniques with histological findings in brain dead organ donors without suspected pneumonia

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Abstract

***Background* – The techniques for recognising pneumonia in mechanically ventilated patients were evaluated as no "gold standard" is available to establish the diagnosis in these patients.**

***Methods* – A prospective study was performed on nine brain dead organ donors not suspected of having pneumonia to assess the specificity of bacteriological results from different samples by comparing them with the histological findings from an open pulmonary biopsy specimen taken immediately after death through a mini-thoracotomy.**

***Results* – Seven of the nine organ donors without clinical evidence of pulmonary infection and not on antibiotic therapy showed histological features of bronchopneumonia. There was no association between the histological findings and quantitative cultures of the lung biopsy specimen.**

***Conclusions* – Histological evidence of pneumonia was common in this group of ventilated patients who had no clinical signs of the disease.**

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Keywords: protected specimen brush biopsy, bronchoalveolar lavage, intracellular organisms, pulmonary biopsy, brain dead organ donors.

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We have shown that up to 18% of protected specimen brush biopsies and bronchoalveolar lavage specimens yield significant bacterial growth in ventilated patients without evidence of pulmonary infections[1] and have suggested that these findings may be a feature common to most patients who undergo prolonged mechanical ventilation. This prompted us to perform a prospective study to assess the significance of these results by comparing them with the findings obtained in a pulmonary biopsy specimen taken immediately after death in ventilated brain dead organ donors not suspected of having pneumonia.

Methods

PATIENTS

Nine brain dead organ donors in the intensive care unit (ICU) who were not suspected of having pneumonia participated in a prospective study. None had fever, leucocytosis, evidence of pulmonary infiltrates on chest radiographs, or had received antibiotics. All patients had had an endotracheal tube in place for at least 24 hours. At the outset 10 ml of sterile 0.9% saline was aspirated through the suction channel of the bronchoscope for bacteriological examination.

SPECIMEN COLLECTION

Both protected specimen brush biopsy and bronchoalveolar lavage were performed in the superior segment of the lower right lobe through a fibreoptic bronchoscope as previously described.[1 2] A large specimen (approximately 3 cm^3) was then cut from the superior segment of the lower right lobe through a mini-thoracotomy. This biopsy sample was sectioned into two fragments, one for bacteriological examination and the other for pathological processing.

The study was approved by the local research ethics committee and informed consent was obtained in all cases.

MICROBIOLOGICAL PROCESSING OF SPECIMENS

Specimens were transported immediately to the laboratory and processed for quantitative bacterial and fungal culture using standard methods as described in previous studies.[1 2] Biopsy samples were weighed, covered with 1 ml of sterile saline, and homogenised. An aliquot of 0.1 ml was inoculated onto the same plates as those used for the protected specimen brush biopsy and bronchoalveolar lavage. Bacteriological counts for the biopsy specimens were expressed as colony forming units per gram of tissue (cfu/g) with counts of $\geqslant 10^3$ cfu/g being considered significant.

CYTOPATHOLOGICAL STUDY

Two 0.5 ml samples of resuspended original bronchoalveolar lavage fluid were cytocentrifuged and stained for cell identification, differential counting, and estimation of the percentage of cells with intracellular organisms as described in previous studies.[2] Tissue blocks were embedded in paraffin and cut into sections of 4 μm. At least 10 sections were obtained per sample. The presence or absence of bronchopneumonia was determined according to the criteria described by Rouby *et al.*[3] Two different pathologists evaluated all histological specimens without knowing the study protocol.

Results

The mean (SD) age of the nine donors (six men) was 37.6 (16.2) years (range 20–63

Table 1 Histological and bacteriological findings of nine brain dead organ donors without suspected pneumonia

Diagnosis	Age (yr)	Sex	MV(h)	FB/LB(h)	PSB (cfu/ml)	BAL (cfu/ml)	ICO	LC (cfu/ml)	Histology
Cerebral haemorrhage*	49	M	33	6	Sterile	4×10^4 *S pneumoniae*	4%	—	Focal bronchopneumonia
Subarachnoid haemorrhage	36	F	88	0	Sterile	10^5 *S viridans*	0%	Sterile	Confluent bronchopneumonia
Cranial trauma*	63	F	72	0	10^2 *S aureus*	8×10^5 *H influenzae* 5×10^5 *S viridans* 9×10^5 *S aureus*	0%	10^3 *H influenzae* 10^3 *K oxytoca* 10^2 *S viridans*	Focal bronchopneumonia
Cranial trauma	20	M	168	0	Sterile	Sterile	3%	Sterile	Normal
Cranial trauma	31	M	240	1.5	Sterile	10^4 *Citrobacter diversus* 5×10^3 *S viridans*	0%	Sterile	Normal
Cranial trauma	61	F	89	0	Sterile	2×10^4 *P aeruginosa* 2×10^4 *S aureus*	3.4%	Sterile	Focal bronchopneumonia
Cranial trauma	23	M	72	9	10^5 *P aeruginosa* 10^5 *S aureus* 5×10^4 *S viridans*	10^5 *P aeruginosa* 10^5 *S aureus* 5×10^4 *S viridans*	36%	10^3 *S aureus*	Confluent bronchopneumonia
Cranial trauma	32	M	42	7.5	Sterile	10^5 *H influenzae*	80%	Sterile	Confluent bronchopneumonia
Cardiac arrest	24	M	84	0	4×10^3 *S maltophila*	Sterile	30%	Sterile	Confluent bronchopneumonia

M = male; F = female; MV = period of mechanical ventilation; FB/LB = time between fibreoptic bronchoscopy and lung biopsy; cfu = colony forming units; PSB = protected specimen brush; BAL = bronchoalveolar lavage; ICO = intracellular microorganism; LC = lung culture.
* Patients with purulent tracheobronchial secretions.

years). The cause of brain death was head injury in six cases, cerebrovascular disease in two, and cardiac arrest in one (table 1). The mean duration for which patients were mechanically ventilated was 93.1 (68.4) hours (range 33–240) and the mean time lapse from fibreoptic bronchoscopy to thoracotomy was 2.66 (3.73) hours. Arterial blood gas analysis showed a $Paco_2$ of 5 (1.6) kPa, pH of 7.37 (0.03), and Pao_2 of 47.3 (14.6) kPa with an Fio_2 of 100%. Fibreoptic bronchoscopy was considered normal in seven cases and purulent bronchial secretions were noted in the remaining two patients. None had received antibiotics. The mean axillary temperature was 36.5 (0.75)°C and the mean white blood cell count was 8.5 (2.0) $\times 10^9$/l.

The histological and bacteriological results are shown in table 1. The average percentage of bronchoalveolar fluid retrieved was 30% (range 15–45%). Contamination by squamous epithelial cells was less than 1% of the total number of cells recovered by lavage in all cases. The percentage of neutrophils recovered by lavage was 70.6 (31.1)% and the percentage containing intracellular organisms was 20.7 (27.1)%. Only in three patients were infected cells not observed.

Discussion

The main finding of this study is that seven out of nine donors with no clinical evidence of pulmonary infection who were not receiving antibiotic therapy showed characteristic lesions of bronchopneumonia (fig 1). To our knowledge, these findings have not previously been reported in patients not suspected of having pneumonia.

We have previously studied the results of protected specimen brush and bronchoalveolar lavage cultures in ventilated patients without clinical suspicion of pneumonia[1] and found a significant percentage of patients with a moderate or high bacterial growth in specimens obtained from the distal airways. It was not clear whether these findings represented a limitation of the diagnostic techniques or were a feature present in many patients who undergo prolonged mechanical ventilation. From the present results the latter hypothesis seems to be the most probable. As stated by Carlet,[4] two types of pneumonia are found in ventilated patients – one localised but extending rapidly which has a poor prognosis and the other a diffuse bronchopneumonia which is often subacute and may resolve without antibiotic therapy. An alternative explanation would be that, since it may take several days for

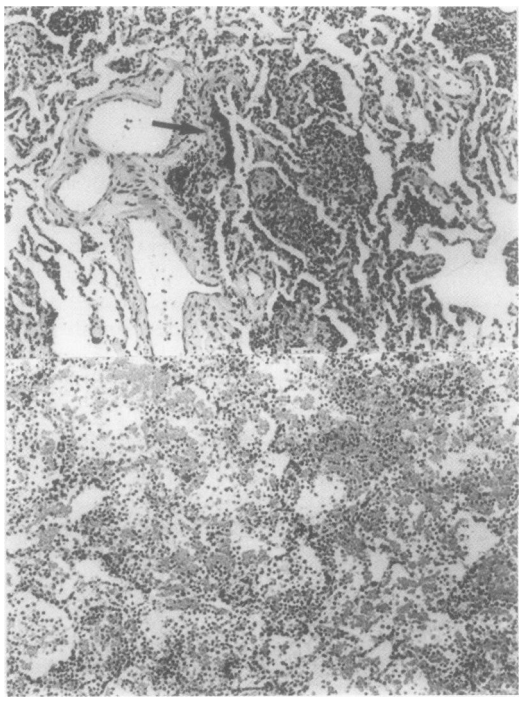

Figure 1 Top: Focal bronchopneumonia. An acute inflammatory infiltrate can be seen beneath a residual layer of bronchiolar epithelium (arrow) limited to a few alveoli. Stain: haematoxylin and eosin; original magnification ×100. Bottom: Confluent bronchopneumonia. The alveolar spaces show haemorrhage and moderate polymorphonuclear leucocyte accumulation within a large pulmonary area. Stain: haematoxylin and eosin; original magnification ×100.

pneumonia to become clinically evident, these findings may simply represent the early identification of pneumonia. In fact, in our previous study we found that four of six patients with a significant growth in both protected specimen brush biopsy and bronchoalveolar lavage specimens subsequently developed pneumonia. Others[5 6] have found a high and constant rate of acquisition of nosocomial pneumonia in the first 8–10 days of intubation with a low rate thereafter. The pathogenetic explanation for this high initial risk is not known. It is possible that the initial period in the ICU involves the interaction of several factors, particularly the prior risk of aspiration which may occur at the start of intensive therapy, just before or during tracheal intubation. The high incidence of inhalation of gastric contents and/or blood in brain dead organ donors should also be emphasised.[7]

We observed a poorer yield of positive results by protected specimen brush biopsy than with bronchoalveolar lavage which may provide a better reflection of the lung's bacterial burden. Moreover, we did not find any association between the histological findings and quantitative cultures from lung biopsy specimens (table 1). This has also been observed by Rouby *et al*[3] and Torres *et al*[8] and may be due to the effect of antibiotics and the non-homogeneous distribution of bacteria infecting the lung parenchyma. As the bacterial burden can vary considerably from one zone to another, it is possible that lung culture, bronchoalveolar lavage, and protected specimen brush biopsy may be sampling different areas of the lung from that sampled during the pneumonectomy immediately after death and may explain our findings.

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