Early Human Development (2005) **81**, 455—460

ELSEVIER

Early Human Development

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Histopathological features of open lung biopsies in children treated with extracorporeal membrane oxygenation (ECMO)

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Accepted 4 November 2004

KEYWORDS
Extracorporeal membrane oxygenation (ECMO);
Alveolar capillary dysplasia;
Pulmonary hypertension

Abstract

Background: Extracorporeal membrane oxygenation (ECMO) has become an established treatment for severe respiratory distress in a range of pediatric conditions. This study describes the histopathological features in a series of 22 children receiving ECMO therapy in whom open lung biopsy was carried out.
Aims: To describe the histopathological features of open lung biopsies in children receiving ECMO therapy.
Study design: Retrospective review of clinical material.
Subjects: Children receiving ECMO therapy in whom open lung biopsy was carried out.
Results: In those investigated in infancy, open lung biopsy allowed a definite diagnosis to be made of the underlying condition in more than 90% of cases. In older children, the histopathological changes were more non-specific and, although providing useful clinical information, a definitive diagnosis could often not be made. In about a quarter of cases, there are additional pathological features, which may be related to ECMO treatment, such as significant intra-alveolar haemorrhage, but ECMO does not in itself impair the diagnostic usefulness of open lung biopsy in these selected patients.
Conclusion: Open lung biopsy provides clinically useful information in infants receiving ECMO therapy. The histopathological changes may be complex and represent both the effects of ECMO and progression of the underlying disease.

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doi:10.1016/j.earlhumdev.2004.11.004

1. Introduction

Extracorporeal membrane oxygenation (ECMO) is now an established treatment option for severe neonatal and infantile lung disease including congenital diaphragmatic hernia, pulmonary alveolar proteinosis, alveolar capillary dysplasia (ACD) and pertussis infection, potentially providing support while allowing recovery of the underlying condition if possible [1—5]. Diagnosis of the original pulmonary condition is usually based on clinical and imaging criteria. However, since some of the conditions which may result in severe neonatal respiratory failure are incompatible with unsupported life, a definitive diagnosis may be required to direct further management and histopathological examination of an open lung biopsy specimen has been reported for this purpose [6]. In one series of eight paediatric patients who underwent open lung biopsy while on ECMO, the biopsy confirmed the clinical diagnosis in five and three demonstrated other pathology. Significant haemorrhage complicated one case but did not result in morbidity or mortality [6]. However, the interpretation of such biopsies may be complicated because ECMO may prolong survival thus allowing progression of underlying lung disease to a state beyond that normally encountered in life, and ECMO itself may be associated with superimposed complications such as interstitial and alveolar haemorrhage and secondary epithelial alterations [7]. Several publications have described the pathological findings in various organ systems at autopsy in patients dying following ECMO therapy and have reported severe changes due to the underlying disease [8], interstitial and intra-alveolar hemorrhage, hyaline membrane formation, type II pneumocyte hyperplasia, squamous metaplasia, interstitial fibrosis and mucinous metaplasia of large airways [7], ischaemic neuronal lesions [9], sepsis [10] and myocardial ischaemic changes [10,11]. The aim of this study is to systematically examine the pathological features in a retrospective series of infant patients receiving ECMO therapy in whom open lung biopsy was carried out to determine whether the histopathological findings in life allow definitive diagnosis and whether direct ECMO-related changes are apparent.

2. Methods

Cases of open lung biopsy specimens from patients receiving ECMO therapy submitted for histopathological examination were identified from a pediatric histopathology database and anonymised. Histological sections, including special stains, were reviewed and abnormal features recorded. The clinical histories, as provided at the time of the open lung biopsy as part of patient management, were also reviewed. Departmental policy for the handling and assessment of open lung biopsy specimens includes use of the following special staining techniques in all cases: haematoxylin and eosin, reticulin, elastin Van Gieson, periodic acid Schiff and Perls stain. Immunohistochemical staining for cytokeratin (MNF116), endothelial cell markers (CD34/31), macrophages (CD68/MAC387) and other specific antigens was carried out as appropriate. The study was approved by the local research ethics committee.

3. Results

22 cases of open lung biopsies from children on ECMO therapy were identified during a 7-year period (1996—2003). A summary of the major histopathological findings and brief clinical information is provided in Table 1. The patient ages at the time of open lung biopsy ranged from 3 days to 6 years (median 3 weeks). The indications for biopsy were persistent pulmonary hypertension in eight of the 12 cases biopsied at less than 1 month of age. The remaining four patients in this group were biopsied because of respiratory insufficiency clinically suggestive of pulmonary hypoplasia. Four cases were biopsied at 6—10 weeks of age, one for assessment of pulmonary hypertension prior to open cardiac surgery for repair of complex congenital heart disease and three for severe respiratory distress with severely abnormal lung radiographs ('white-outs'). In all of the six cases biopsied at 3 months to 6 years of age, the indication was severe respiratory distress in association with markedly abnormal chest radiology suggestive of severe interstitial lung disease. Open lung biopsy provided adequate diagnostic material in all but 1 case (96%) and a definite pathological diagnosis in 12 cases overall (55%). However, in those investigated before 6 weeks of age, open lung biopsy provided definite diagnostic information in 11 of 12 cases (92%). Additional useful management information was provided by the biopsy in a further nine cases (45%) even though a definite specific diagnosis could not made on the basis of the biopsy findings.

In the group biopsied before 6 weeks of age, the underlying diagnosis was alveolar capillary dysplasia in three cases, lymphangiectasia in two (one in