REVIEW SERIES

The pulmonary physician in critical care • Illustrative case 8: Acute respiratory failure following lung resection

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Thorax 2003;**58**:820–822

The case history of a patient who developed acute respiratory failure following lung resection is described and the incidence, clinical course, pathophysiology, and outcome following acute lung injury/acute respiratory distress syndrome (ALI/ARDS) in surgical patients is reviewed.

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CASE HISTORY

A 75 year old male smoker of 60 pack-years presented with haemoptysis. Investigation revealed a bronchogenic carcinoma (non-small cell), apparently localised to the right upper lobe. The patient was otherwise well. Routine haematological and biochemical parameters were within normal limits. Spirometry was 2.4/3.01 litres (80%/76% predicted) and preoperative arterial blood gas tensions were satisfactory (Pa_{O_2} 10.7 kPa, Pa_{CO_2} 5.6 kPa on air).

Right thoracotomy revealed extensive malignancy filling the upper lobe and involving the middle lobe at the confluence of the fissures. Histological examination confirmed bronchoalveolar carcinoma and systematic nodal dissection demonstrated N1 disease at station 11. All mediastinal nodes were clear of disease. The patient underwent uncomplicated right pneumonectomy and was extubated shortly afterwards. The morning after surgery the chest radiograph was satisfactory and gas tensions were acceptable (Pa_{O_2} 13.5 kPa, Pa_{CO_2} 5.9 kPa using inspired oxygen concentration, Fi_{O_2} 0.4). However, a repeat chest radiograph the next day revealed alveolar infiltrates in the remaining lung and, by day 3, oxygen saturations had fallen to 85% despite oxygen supplements. The alveolar shadowing progressed despite the use of diuretic and antibiotic treatment and insertion of a mini-tracheostomy. By day 4 the blood gas tensions were Pa_{O_2} 6.5 kPa, Pa_{CO_2} 6.4 kPa (Fi_{O_2} 0.21). The patient was admitted to the intensive care unit and required sedation, endotracheal intubation, and mechanical ventilation the following day.

Fibreoptic bronchoscopy and bronchoalveolar lavage were negative for microbiological staining and culture. Electrocardiograms and troponin levels were normal. Pulmonary artery catheterisation showed no evidence of left atrial hypertension. A CT scan of the thorax revealed diffuse ground glass infiltrates throughout the left lung, coalescing into patches of consolidation in dependent areas.

The patient remained hypoxic and hypercarbic for 10 days before beginning to improve. He left the intensive care unit 26 days after admission with Pa_{O_2} 13.5 kPa, Pa_{CO_2} 5.2 kPa, Sa_{O_2} of 99% on 3 litres oxygen administered via nasal cannulae, and subsequently made a complete recovery.

DISCUSSION

The dominant clinical and radiological features of this case were refractory hypoxaemia developing in association with pulmonary infiltrates in the absence of raised left atrial pressure. These represent the defining criteria for acute lung injury (ALI) and acute respiratory distress syndrome (ARDS), depending on the severity of the impairment of gas exchange (Pa_{O_2}:Fi_{O_2} 300 mm Hg for ALI; <200 for ARDS)[1] and the presence of a known precipitating cause. The extent to which lung resection fulfils this requirement remains controversial in that pneumonectomy, by definition, precludes the development of bilateral pulmonary infiltrates. However, most authorities now accept that many patients with what has been termed "post-pneumonectomy pulmonary oedema (PPE)" display the physiological and radiological defining criteria for ALI/ARDS.[2]

Incidence of lung injury associated with lung resection

The reported incidence of lung injury associated with lung resection has varied widely partly due to the lack of an accepted definition of PPE.[3–6] However, a Consensus definition of ALI and ARDS was published in 1994[1] which is currently under revision. Before this date, the incidence of lung injury following pneumonectomy and lobectomy was estimated to be in the order of 4–7% and 1–7%, respectively.[4 6 7] Retrospective studies using the Consensus definitions were broadly in line with these figures, indicating the incidence of ALI and ARDS to be 2.2% and 5.2% after lobectomy, and 1.9% and 4.9% respectively after pneumonectomy, with an overall incidence of lung injury of 7%.[8] A second study reported an incidence of 6.0%, 3.7%, and 1.0% for ALI following pneumonectomy, lobectomy, and minor resections, respectively, and which caused 72% of all postoperative deaths.[9]

Clinical course

The onset of symptoms of ALI/ARDS may be delayed for up to 7 days after surgery.[7 10] The differential diagnosis includes lower respiratory tract infection and cardiogenic pulmonary oedema. Both can be excluded relatively simply in the intubated patient by bronchoscopy and (as was the case here) pulmonary arterial catheterisation. The syndrome tends to be progressive and is characterised by three overlapping stages. The acute or exudative stage is manifest by the onset

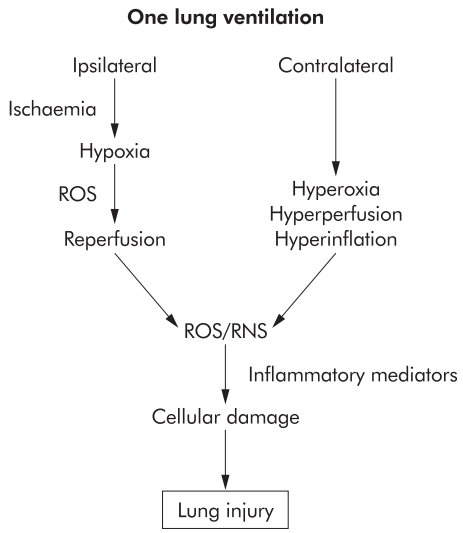

Figure 1 Possible role of one lung ventilation in the pathophysiology of acute lung injury (ALI) and acute respiratory distress syndrome (ARDS) following lung resection.

of dyspnoea, tachypnoea and respiratory failure. Arterial hypoxaemia refractory to oxygen therapy develops, with pulmonary infiltrates on the chest radiograph. Pleural effusions may also be a feature. CT scanning reveals dependent alveolar atelectasis and/or consolidation, or the classical "ground glass" appearance of alveolar inflammatory infiltrates. Histological examination of lung parenchyma shows diffuse alveolar damage with neutrophilia and proteinaceous oedema fluid.[11]

The acute phase may be followed by complete resolution or, more usually, by progression to the fibroproliferative stage. There is persistent refractory hypoxaemia and reduced pulmonary compliance. Radiological findings are those of bilateral opacities on the chest radiograph and pneumothorax may be present. The opacities may be seen more clearly, and bullae may be evident, on CT scanning.[12 13] Histological features are those of fibrosis and inflammatory cells, both acute and chronic. The final stage is resolution and recovery, which parallels resolution of hypoxaemia and increased pulmonary compliance.

Pathophysiology

Certain demographic features have been identified as risk factors for postoperative lung injury. In some series the incidence of ALI/ARDS after lung resection was thought to be higher in patients over 60 years of age, in men, and in those undergoing surgery for lung cancer. The extent of resection has been thought to be significant, although the side of resection has not.[4 14–16] Excessive perioperative administration of crystalloid has been thought to precipitate lung injury,[14 17–19] although the perceived role of fluid overload has recently diminished.[4 5 8 20]

It seems likely that a complex process with many contributing factors including altered redox balance, ischaemia-reperfusion, and altered capillary permeability may be responsible. Thus, one lung ventilation is required by all patients undergoing lung resection and entails exposure to high inspired oxygen concentrations, ischaemia-reperfusion, and other proinflammatory stimuli (fig 1). Hyperoxia may lead to oxidative stress through the generation of reactive oxygen (ROS) and reactive nitrogen (RNS) species.

By contrast, during the same periods the ipsilateral lung is hypoperfused. In a one lung rat model ROS were produced and further damage occurred following re-expansion and therefore re-oxygenation of the collapsed lung.[21] This was attributed to the production of ROS during reinflation.[21–23] There is already strong evidence for a role for ROS in the pathogenesis of tissue damage in ARDS.[24 25] Although most studies indicate that neutrophil activation plays no part in the initial phase of lung injury, they may cause ROS release and hence potentiate ischaemia-reperfusion injury.[26–28]

The pathophysiological end point of these disparate proinflammatory processes is increased endothelial permeability. Studies in rodents have looked at the effects of ischaemia-reperfusion on hypoxic pulmonary vasoconstriction using albumin escape as a marker of endothelial integrity.[21] The integrity of the endothelium was maintained for up to 30 minutes of ischaemia alone. If, however, a shorter period of ischaemia was followed by reperfusion, the tendency for oedema formation was dramatically increased. Ischaemia-reperfusion injury occurs following rapid re-expansion of a collapsed lung.[21 29–34] In a clinical investigation,[26] plasma thiols and protein-associated carbonyl groups were quantified as indicators of oxidative damage to proteins in patients undergoing single lung ventilation and lung resection. Gas transfer capacity fell perioperatively, while thiol levels decreased and protein-associated carbonyl levels rose and continued to rise for up to 24 hours postoperatively, suggesting that all patients undergoing lung resection suffer some degree of lung damage in association with a pro-oxidant insult.[35]

Outcome

Mortality attributable to ALI/ARDS following lung resection remains high[36] despite advances in supportive techniques and a possible fall in death rate in patients with lung injury from other causes.[37] Although not the most frequent postoperative complication in this patient population, lung injury produces the highest all cause mortality, usually through progression to multiple organ failure. Published figures for mortality after lung resection using the 1994 Consensus definition are 33.3% and 72.2% for ALI and ARDS, respectively, with an all cause mortality rate of 3.5%. ALI/ARDS contributed to death in 72.5% of these cases.[9]

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LUNG ALERT

Cinema smoking encourages the habit in adolescents

▲ Dalton MA, Sargent JD, Beach ML, *et al*. Viewing smoking in movies positively influences smoking initiation among adolescents. *Lancet* 2003;**362**:4999

Many studies have linked tobacco marketing with an increased uptake of smoking in adolescents. In this longitudinal study 3547 students aged 10–14 years who attended schools in Vermont and New Hampshire, USA and who had never smoked previously were assessed for exposure to smoking in cinemas. Fifty movies were randomly selected from popular contemporary cinema. Trained coders counted the number of smoking occurrences in each movie and exposure to movie smoking was classified in quartiles. At baseline, confounding variables such as grade in school, sex, friend smoking, sibling smoking, and parental smoking were measured. 2603 (73%) students were re-contacted 13–26 months later to ascertain smoking initiation in the interval period.

On average, the students had seen 16 of the 50 movies and were exposed to a mean (SD) of 98.5 (75.1) smoking occurrences; 259 (10%) had started smoking in the follow up period, 107 (17%) in the group with the highest quartile of smoking exposure and 22 (3%) in the group with the lowest quartile. This represents a relative risk of 2.71 (95% CI 1.73 to 4.25) between the two groups after correcting for other confounding variables. Although students with smoking parents had an overall higher risk of smoking initiation, the effect of smoking in cinemas was stronger in adolescents with non-smoking parents; 52.2% of smoking initiation was directly attributed to seeing smoking in movies.

This prospective study serves to establish a strong temporal and causal relationship between viewing smoking in movies and initiation of smoking among adolescents.

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