Clinical Reports

Adult respiratory distress syndrome after radical neck dissection

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The clinical management of an unusual case of postoperative ARDS is reported. A few hours following neck surgery and septic insult, the patient developed unexpected ARDS. Aetiologic and supportive treatment were successfully instituted and after 72 hours of intensive therapy, the patient's clinical status improved. The very short time lapse between the septic insult and appearance of ARDS is emphasized. A brief literature review on aetiology, diagnosis and therapy of sepsis, as well as some pertinent aspects concerning the pathogenesis of ARDS and its linkage to sepsis are presented.

La prise en charge clinique d'un cas inhabituel d'ARDS postopératoire est décrit. Quelques heures après une chirurgie du cou et une plaie septique, le patient a développé un ARDS imprévu. Une thérapeutique étiologique et curative fut mise en oeuvre et après 72 heures de soins intensifs, l'état du patient s'améliora. Il faut insister sur le délai très bref entre la plaie septique et l'apparition de l'ARDS. Une brève revue de la littérature sur l'étiologie, le diagnostic et le traitement du sepsis, ainsi que quelques points pertinents concernant la pathogénie de l'ARDS et ses rapports à un sepsis sont présentés.

Hypoxaemia is a common postoperative occurrence,[1] caused among others by ARDS[2] which in turn may be secondary to sepsis, aspiration pneumonitis and trauma.[3] We present an uncommon case of a patient, who without any apparent preoperative signs of local or systemic infection, developed ARDS a few hours after surgery, probably due to sepsis.

Key words
LUNG: respiratory distress syndrome.

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Accepted for publication 28th April, 1993.

Case report

A 72-yr-old patient was scheduled for radical neck dissection to excise a metastatic neck tumour. Two months earlier, he underwent total laryngectomy for a squamous cell carcinoma of the larynx. He had a history of heavy smoking and alcoholism. At the preanaesthetic examination, the patient, fitted with a permanent metallic tracheostomy cannula, appeared to be in good condition. The physical examination was normal, his rectal temperature was 36.5°C and the laboratory data were within normal limits. A chest *x*-ray revealed emphysema.

On arrival at the operating room, he felt well and with vital signs within normal limits. A catheter (AL) was introduced into the left radial artery and a central venous line into the left basilic vein.

After substituting the permanent tracheostomy cannula with a flexible Ruschlit tracheostomy tube (Rush, Germany), anaesthesia was induced with midazolam (3 mg), fentanyl (0.01 $mg \cdot kg^{-1}$), followed by boluses (0.002–0.003 $mg \cdot kg^{-1}$) as needed, and pancuronium (0.1 $mg \cdot kg^{-1}$), and maintained with N_2O:O_2 (65%:35%). Monitoring included ECG, direct and indirect blood pressure, rectal temperature, central venous pressure, pulse oximetry, capnography and urinary output.

The operation lasted seven hours. Throughout surgery, temperature, haemodynamic and laboratory data were within normal limits (Table I). During surgery, the patient received 3000 ml of lactated Ringer's solution. No blood was given, since the estimated blood loss was less than 200 ml. Surgery involved right neck dissection and excision of a necrotic neck tumour. Biopsies were obtained for pathological examination and bacterial cultures. At termination of surgery, a Portex tracheostomy tube (9 mm id) was left in place and the patient was transported to the Post Anaesthetic Care Unit (PACU).

In the PACU the patient was haemodynamically stable, temperature, arterial blood gas (ABG) analysis (Table I), electrolytes and CBC were all within normal limits. Ar-

TABLE I Arterial blood gases

Time of sampling	*pH*	*$PaCO_2$ mmHg*	*HCO_3 mEq · L^{-1}*	*BE mEq · L^{-1}*	*PaO_2 mmHg*	*SaO_2 %*	*FiO_2*	*Mode of ventilation*
Before surgery	7.38	40	25	0.3	77	95	0.21	Spontaneous
During anaesthesia	7.39	40	24	0.1	106	98	0.35	IPPV
At the arrival to PACU	7.40	40	24	0.1	126	99	0.4	IPPV
Four hours after surgery	7.27	38	17	−7	47	72	0.4	SIMV
Five hours after surgery	7.30	40	19	−5	58	89	1	CMV
24 hours after surgery	7.40	38	24	1	78	93	0.8	IPPV PEEP 10 cm H_2O
48 hours after surgery	7.38	39	22	−2	76	92	0.5	IPPV PEEP 5 cm H_2O
72 hours after surgery	7.42	35	23	−2	71	92	0.4	IPPV PEEP 5 cm H_2O
96 hours after surgery	7.40	37	25	0.3	69	91	0.5	Spontaneous

TABLE II Haemodynamic variables

Time	*BP mmHg*	*HR BPM*	*CVP mmHg*	*PAP mmHg*	*PCWP mmHg*	*CO L · min^{-1}*	*SVR dyn · sec · cm^{-5}*
Before surgery	130/80	84	8	–	–	–	–
Six hours after surgery	95/45	126	5	20/10	5	7	650
24 hours after surgery	140/75	100	12	25/15	13	6.7	1099
48 hours after surgery	140/85	96	10	–	–	–	–
72 hours after surgery	160/90	98	–	–	–	–	–

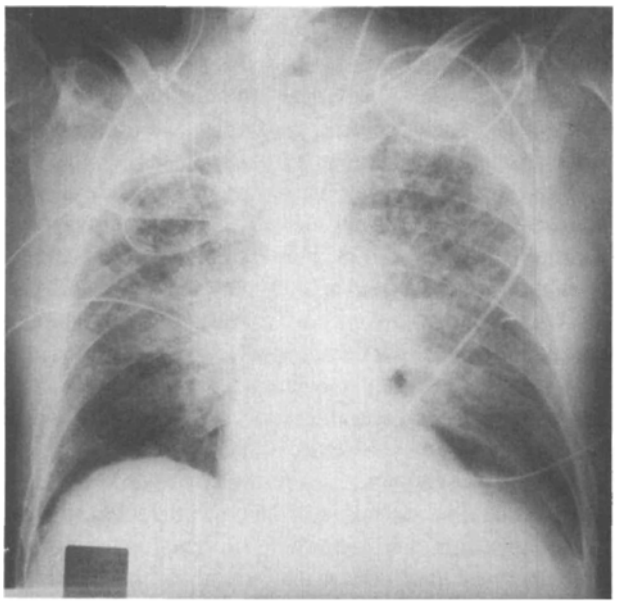

FIGURE 1 Bilateral diffuse, patchy interstitial infiltrates.

terial oxyhaemoglobin saturation (SpO_2) and end-tidal CO_2 ($PETCO_2$) were within the normal range (99–100% and 34–36 mmHg, respectively). The patient was allowed to wake up gradually, while muscle relaxation was reversed with neostigmine (0.04 mg · kg^{-1}) and atropine (0.02 mg · kg^{-1}). The lungs were ventilated with a Bennett MA2 respirator, set in SIMV mode ($FiO_2 = 0.4$).

Four hours after surgery, the patient became restless and struggled against the ventilator. The SpO_2 and $PETCO_2$ gradually decreased, reaching 90 min thereafter levels of 72% and 30 mmHg, respectively. Successive ABG samples showed the development of severe hypoxaemia and mild metabolic acidosis (Table I), and a $PaCO_2$:$PETCO_2$ gradient at the upper normal limit (4–6 mmHg). At the same time blood pressure and CVP also decreased gradually (Table II). The patient became tachypnoeic (40 rpm), tachycardic (120 bpm) and body temperature was 36.8° C. At this stage FiO_2 was increased to 1 and the respirator was set to the CMV mode. All other laboratory data were normal.

Physical examination of the lungs was normal; however, chest *x*-ray showed bilateral patchy interstitial infiltrates, suggesting pulmonary oedema (Figure 1). The ECG was normal and pH of gastric fluid and lung secretions was >5. In spite of inducing massive diuresis, administration of furosemide did not improve the patient's oxygenation.

After insertion of a pulmonary artery catheter (PAC), the central venous pressure (CVP), pulmonary artery pressure (PAP) and pulmonary capillary wedge pressure (PCWP) were all low (Table II). Cardiac output (CO), measured by thermodilution, was increased (7 L · min^{-1}), while systemic vascular resistance (SVR) was low (650 dyn · sec · cm^{-5}). Based on these findings, cardiogenic pulmonary oedema and pulmonary embolism were excluded as possible causes for the severe hypoxaemia.

Neither massive atelectasis, nor pneumonia or pneumothorax were detected. Subsequent administration of aminophylline (5 $mg \cdot kg^{-1}$ given over 30 min), dopamine (5–6 $\mu g \cdot kg^{-1} \cdot min^{-1}$) and midazolam (2 mg) produced no improvement in the patient's condition. Blood was sent to the laboratory for culture and coverage with broad spectrum antibiotics was started with *iv* cefalexin 1000 mg, metronidazole 500 mg and gentamycin 80 mg. Fluid replacement, including crystalloids and blood along with dopamine infusion (5–6 $\mu g \cdot kg^{-1} \cdot min^{-1}$), resulted in stabilizing blood pressure at normal levels. At this stage rectal temperature rose to 37.8°C, while cardiac output was 6.7 $L \cdot min^{-1}$ and both PCWP and SVR (Table II) returned to normal. The lungs were ventilated with O_2 and a positive end expiratory pressure (PEEP) of 10–15 cm H_2O. Hypoxaemia persisted for the next 48 hr and thereafter oxygenation improved, allowing the patient to be gradually weaned from ventilation, high F_IO_2, and finally PEEP. By the fourth postoperative day the patient was breathing spontaneously, feeling well and the chest *x*-ray was almost normal (Figure 2). All blood and neck lymph node cultures were positive for S. aureus. The biopsy taken from the tumour revealed metastatic squamous cell carcinoma, probably secondary to the previously detected and excised laryngeal tumour.

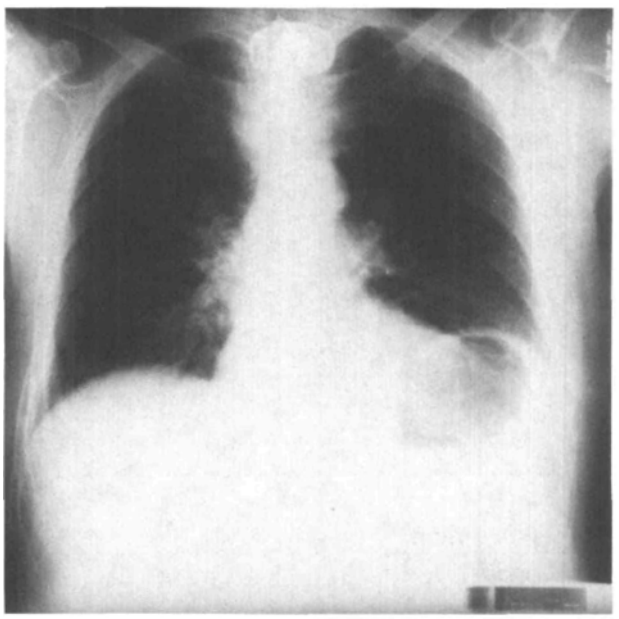

FIGURE 2 Hyperinflated lungs.

Discussion

A case of rapidly progressing severe postoperative hypoxaemia, lacking any initial clues or apparent reason, is presented. For the purpose of establishing a differential diagnosis, information based on physical examination, chest *x*-ray, ABG analysis and invasive monitoring, such as CVP catheter and PAC was used. Massive atelectasis and/or pneumothorax and pneumonia, as well as malposition of the tracheostomy cannula, were excluded on the basis of a chest *x*-ray, taken at the onset of hypoxaemia. No signs of airway obstruction or hypoventilation were detected. Likewise, there was no evidence for pulmonary air embolism (AE), which may occur due to surgical manipulations of large veins under conditions of neck operations, especially in the head-up position.[4] Furthermore, AE occurs during surgery and not postoperatively, and as neither the $P_{ET}CO_2$ was decreased nor the PAP increased, that excluded this diagnostic possibility.

Consequently, pulmonary oedema (PE) either cardiogenic or due to ARDS, remained the only possible diagnosis to be considered. A chest *x*-ray, obtained 30 min after the onset of hypoxaemia, suggested frank PE while the heart shadow was not enlarged (Figure 1). Analysis of the ECG excluded myocardial ischaemia or infarction. Likewise, the low PCWP argued against cardiogenic PE, all of which led to suggest ARDS.

Further support for the diagnosis of ARDS in the reported case was based on the severe persistent hypoxaemia in spite of 100% O_2 (large shunt) administration, bilateral diffuse patchy lung infiltrates revealed by chest *x*-ray, low left side heart filling pressures (PCWP) and stiff lungs. The latter was suggested by the 40 cmH_2O airway pressure and decreased lung compliance without any change in tidal volume, peak flow, airway resistance and chest wall compliance.

Both the clinical evolution and haemodynamic profiles pointed to sepsis and ensuing septic shock as the most plausible cause for ARDS. This assumption was strengthened by the hyperdynamic state with high CO and low SVR, presence of an infected cervical tumour possibly serving as the primary source of infection and subsequent isolation of the same pathogenic agent (S. aureus) from the biopsy sample, neck and blood. It may be postulated that manipulation of the neck throughout the surgical procedure caused gross bacteraemia with the resultant sepsis. The initial lack of fever may be attributed to both an impaired immune response in this carcinomatous patient and heat loss during anaesthesia. Later, however, the patient's rectal temperature increased to 37.8°C.

Based on the evidence presented, it seems reasonable to conclude that the primary underlying cause of the severe hypoxaemia seen in this case was sepsis-related ARDS. Admittedly, this is rather unusual in view of the short time lapse between surgery and appearance of ARDS in addition to the absence of any preoperative indications of sepsis.

Postoperatively mild hypoxaemia has been attributed to analgesic-induced alterations in bronchomotor and vas-

cular tone.[1] Other known factors include atelectasis,[3] abnormality in control of breathing,[1] diffusion hypoxia, decreased FRC due to pain, especially after abdominal surgery,[3] and decreased cardiac output.[5] Occasionally, hypoxia has been found to result from conditions such as cardiogenic and noncardiogenic PE,[3,6,7] pneumothorax, pulmonary embolism, etc.[2,3]

Shock (haemorrhagic, anaphylactic or septic), trauma, aspiration pneumonitis, massive transfusion, DIC and others have been cited as the main causes for postoperative ARDS.[3,8]

Sepsis is regarded as a systemic response to infection by microorganisms or their products and as such constitutes the most common cause of death among surgical patients in noncoronary intensive care.[9]

Sepsis is manifested by two or more of the following conditions:[9]

1 Body temperature $>38°C$ or $<36°C$.
2 Heart rate >90 beats $\cdot$ min^{-1}.
3 Respiratory rate >20 breaths $\cdot$ min^{-1} and $PaCO_2 < 32$ mmHg.
4 White blood count $>12{,}000$ or $<4{,}000/mm^3$.
5 In severe cases: organ dysfunction and in the absence of other hypotensive causes, decreased systolic blood pressure to <90 mmHg or reduction of $>40\%$ from baseline.

In the case reported here, the patient fulfilled three of the above criteria, tachycardia, tachypnoea and hypotension. With respect to aetiology, the causative agents of sepsis include the following:[10]

1 Gram-positive infections by dissemination of exotoxin and without evidence of bacteraemia (i.e., clostridium perfringens) or most often fulminating staphylococcal or streptococcal infections. Infection with S. aureus can lead to septic shock and ARDS, particularly in older patients concomitantly suffering from serious illnesses (i.e., carcinomatosis as in the reported case) and with ARDS serving as the first sign of sepsis.[8]
2 Gram-negative infections. Among these, the most frequent are coliform, anaerobic bacilli, klebsiella and serratia infections of the urogenital, respiratory and alimentary systems.[10] ARDS is most frequently associated with gram negative septicaemia.[8]
3 Other infective agents which may lead to sepsis and septic shock include viruses, parasites and fungi.[10]

Haemodynamic changes observed in gram-positive septic shock are milder than those encountered in gram-negative septic shock. Thus, in the former, cardiac output is not reduced, urinary flow is normal and serum lactic acid is not increased.[10] Such was the case in our patient who suffered from staphylococcal septic shock and exhibited an elevated cardiac output.

Apart from the aetiologic (antibiotics and surgery) and supportive (fluids, vasoactive drugs, steroids, etc.) therapy, treatment of severe sepsis includes the so-called "innovative therapies,"[9] i.e., those aimed at mediators of inflammation.

Use of immunotherapy as a therapeutic means for gram-negative sepsis, involves administration of serotype-specific antibodies, core LPS (lypopolysacharide also called endotoxin), immunization with E. coli antiserum and purified intravenous immunoglobulins to E. coli (for septic shock).[11] Most of these are still in the experimental stage.

In a retrospective study by Fein *et al.*[12] an incidence of 18% was reported for sepsis-induced ARDS. According to these authors this rate depended on whether bacteraemia was complicated with shock or not.

Kaplan[13] estimated that the incidence of ARDS in septic patients reaches 20%. Likewise shock may considerably enhance the risk for ARDS, from 5.8% to 64.8%.[14] Bachoften[15] found lesions of ARDS 24 hr after the onset of respiratory symptoms due to septicaemia and referred to sepsis-associated ARDS as "septic lung disease." At this early stage, pathology of the lungs revealed widespread interstitial and alveolar oedema. Rapid proliferation of type II epithelial cells was also noted.[15] Niederman *et al.*[16] described the initiation of ARDS indirectly by activation of a systemic inflammatory response to bacteria, viruses, fungi or traumatized tissue. This in turn triggers a systemic response, characterized by hypermetabolism and subsequent organ failure due to tumour necrosis factor (TNF) and interleukin-1 which modulate the response to sepsis. Other potential mediators are activated neutrophils, complement and components of the thrombotic system.

Fein[12] found that sepsis-induced ARDS is usually preceded by shock and thrombocytopenia. It has also been reported that in sepsis-related ARDS, survival rate was reduced to 19% as compared with 65% for non-ARDS septic patients.[8] In this respect the data was similar to survival rates of 10 and 17%, reported by Kaplan[13] and Lee.[17]

As already mentioned, the reported case is unusual on account of the brief time between the suspected initial septic insult and onset of ARDS. In this connection, mention should be made of Matthay[18] who stated that in many patients the time lag between the onset of the inciting event and development of acute respiratory failure is as brief as six hours.

Criteria for diagnosing ARDS include:[19]

1 Clinical setting (catastrophic event, exclusion of other lung diseases), respiratory distress.
2 Diffuse pulmonary infiltrates on chest *x*-ray.
3 Physiological ($PaO_2 < 50$ mmHg with $FiO_2 > 0.6$, compliance 0.05 L $\cdot$ cm H_2O^{-1}, increased shunt and

dead space ventilation), or pathological (heavy lungs, congestive atelectasis, hyaline membranes,[22] fibrosis) criteria.

Murray[20] has defined ARDS on the basis of a lung injury score, comprising the following variables: chest *x*-ray, hypoxaemia, PEEP and compliance. Each variable is scored from 0 to 4 and the final value is obtained by dividing the aggregate sum of scores by the number of variables. Thus, a score of 0 = no lung injury, 0.1–2.5 = mild to moderate lung injury and >2.5 = severe lung injury (ARDS). The scores obtained in our patient were as follows: chest *x*-ray = 4 (alveolar consolidation in all four quadrants); hypoxaemia = 3 ($PaO_2 \div FiO_2$ (47 ÷ 0.4 = 102)), PEEP = 2 (PEEP 10 cmH_2O); lung compliance (static) = 3 (static compliance 0.035 $L \cdot cmH_2O^{-1}$). This brought the aggregate to 12 and the consequent lung injury score to 3, indicating severe lung injury (ARDS).

Apart from the above criteria and in order to differentiate between cardiogenic and noncardiogenic PE verification of ARDS diagnosis should also take into account left heart filling pressure as reflected by PCWP.

Murray and Petty[20,21] considered the measurement of haemodynamic variables using a PAC as a guide to therapy rather than diagnostic criteria, whereas Simmons[22] suggested that a PCWP value of less than 12–18 mmHg was required for a diagnosis of ARDS.

The pathogenesis of ARDS is complex, multifactorial, and, as yet, not fully understood. Recent studies have emphasized the role played by oxygen-free radicals, proteolytic enzymes and arachidonic acid in the pathogenesis of ARDS.[23] Neutrophils induce permeability PE through secretion of elastase.[24]

Activated complement 5 (C5a) and leukotriene B4 as well as thromboxane A2 were implicated in neutrophil migration and their chemotactic activity in the pulmonary vasculature.[24] Activated platelets may also be involved in the pathogenesis of acute lung injury due to release of free radicals and so the increase of lung vascular permeability through thromboxane E A2.[24] Cytokines, especially tumour necrosing factor (TNF) were detected in the serum of ARDS patients.[25] Both the coagulation and fibrinolytic system have also been implicated on account of increased procoagulation activity and depressed fibrinolysis, favouring fibrin deposition.[24]

In spite of advances made with respect to diagnosis and management, the mortality in ARDS is still very high, and ranges between 40–80%.[19]

To the best of our knowledge, a case of ARDS such as the one described here (i.e., ARDS shortly following ENT surgery), has not been reported in the literature.

In conclusion, an uncommon case is presented of early postoperative, unexpected and most likely sepsis-induced ARDS, occurring in a patient without any apparent preoperative indications of sepsis. In order to deal effectively with such a case, rapid, thorough diagnostic and therapeutic procedures, are required which present a challenge to the anaesthetist.

Acknowledgement

The authors thank Dr. Yona Greenfield for his help in the preparation of this manuscript.

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