thentic. The expected time for nerve regeneration has passed, suggesting that the injury is permanent.

The authors thank Dr. Daniel C. Moore for reviewing the manuscript and Lynn Adams for her expert editorial assistance.

REFERENCES


Anesthesiology
63:104–106, 1985

Respiratory Failure Secondary to Homologous Blood Transfusion

JOHN P. EBERT, D.O.,* BEN GRIMES, M.D.,† KURT M. W. NIEMANN, M.D.‡

The appearance of alveolar flooding in the perioperative period is often unheralded and usually unwelcome. Accurate diagnosis and prompt treatment are imperative. An example of a severe form of acute pulmonary edema with an uncommon etiology will be described, followed by a differential diagnosis and a review of the available information on this phenomenon.

REPORT OF A CASE

A 32-year-old man with progressive, juvenile rheumatoid arthritis was scheduled to undergo total hip arthroplasty. Preoperative evaluation also revealed a history of paroxysmal atrial tachycardia controlled with digoxin, inflammatory pericardial effusion—improved through the use of fluridone, pulmonal angiography, and iron deficiency anemia. Aspirin and steroid therapy had resulted in upper gastrointestinal bleeding several years earlier, necessitating a partial gastrectomy and vagotomy. Previous anesthetics were historically uncomplicated; the family anesthetic history was negative; and he neither smoked cigarettes nor used alcohol. Chronic medications included, in addition to those mentioned above, naproxen, aspirin, and prednisone, and he denied medication allergy. He was small in stature, at 167 cm tall, weighing 52 kg. In addition to the joint deformities associated with rheumatoid arthritis, the patient exhibited considerable restriction of temporomandibular and cervical motion, and anisocoria, with the diameter of the right pupil being approximately 3 mm larger than the left pupil. The preoperative chest roentgenogram showed evidence of early interstitial fibrous changes consistent with rheumatoid arthritis, and the EKG indicated digoxin effect. His hemoglobin concentration was 11.5 g·dl⁻¹ and the hematocrit was 35%; however, the remainder of laboratory data, including quantitative serum immunoglobulins and immunoelectrophoresis, were normal.

Anesthesia was induced with thiopental 300 mg iv, followed by succinylcholine chloride 70 mg iv to facilitate laryngoscopy. Using a conventional technique, only the tip of the epiglottis could be visualized; however, an 8-mm 1Duffed endotracheal tube was inserted successfully. Anesthesia was maintained with an initial fentanyl dose of 10 μg·kg⁻¹·hr⁻¹, along with isoflurane and oxygen. Following induction, radial arterial and central venous cannulae were inserted for monitoring. With an FiO₂ of 0.4, the pH was 7.47, PaO₂ 35 mmHg, and PaCO₂ 379 mmHg. His gas exchange and acid–base status did not change significantly during this 2-h operation. A central venous pressure of approximately 10 mmHg was maintained through an infusion of 1,800 ml lactated Ringer’s solution, two units of whole blood were transfused to replace blood loss, and nitroglycerin was administered to reduce the arterial blood pressure by 30% from his baseline. Paralysis was induced an atracurium infusion titrated to 90% train-of-four and electromyogram (EMG) depression; the effects later were antagonized with edrophonium and glycopyrrolate, and the trachea was extubated.

One hour after arrival in the recovery room, with an FiO₂ of 0.4, the pH was 7.42, PaO₂ 39 mmHg, and PaCO₂ 86 mmHg. His central venous pressure and arterial blood pressure were 8 and 136/74 mmHg, respectively. With a hematocrit of 28% and a heart rate of...
improvement. The weaning process was completed, and the trachea was extubated. On an FiO2 of 0.4, the pH was 7.43, PCO2 34 mmHg, and PaO2 83 mmHg. From this time onward, the recovery process was uncomplicated, and the patient was discharged from the hospital on the eighth postoperative day. Three months later, the same operative procedure was completed on the opposite side without complication. Washed red blood cells were transfused to replace the operative loss.

**DISCUSSION**

This case depicted a profound and apparently abrupt onset of acute pulmonary edema that was temporarily and erroneously associated with the transfusion of the third unit of blood, administered postoperatively in the recovery room. This life-threatening deterioration demanded immediate and effective therapy, supported by data that elucidated the physiologic disturbance, followed by determination of the precise cause through a process of elimination. The appearance of alveolar flooding with fluid of a high relative oncotic pressure in the presence of a high cardiac index and normal ventricular filling pressures indicated pulmonary edema of increased permeability, or noncardiac origin.\(^1\) The treatment centered around the improvement of oxygenation through expansion of the FRC with PEEP, increasing the FiO2 and aggressive lowering of the pulmonary vascular hydrostatic pressures with furosemide and vasoactive drugs.\(^2\)

Foremost on the list of potential causes was a pulmonary vascular insult associated with insertion of the hip prosthesis and a transfusion reaction; however, by necessity, shock, hypoxia, toxic inhalants, drug reactions, aspiration of gastric contents, neurogenic phenomena, and sepsis\(^3\) also were included. The diagnosis was made by exclusion.

Vigilance combined with online invasive monitoring modalities and timing made shock, hypoxia, and toxic inhalants remote possibilities. There was no history of penicillin allergy, so a drug reaction to nafcillin was unlikely. Allergic responses to thiopental and succinylcholine,\(^4,5\) have been described, however a delayed response of this magnitude would have been unusual. Aspiration as well as a neurogenic origin in a conscious and reflexive individual would have been paradoxic, while negative blood cultures eliminated sepsis. The only other possible causes were a pulmonary complication associated with the operation and an immunologically mediated transfusion reaction.

Pulmonary capillary leak associated with total hip arthroplasty has been reported; however, in this account, the phenomenon transpired intraoperatively; only right ventricular filling pressures were measured prior to treatment, pulmonary edema fluid oncotic pressure was not determined, and the pathologic signs dissipated rapidly. These problems make identification of the etiology of this occurrence obscure. The pulmonary and
circulatory reactions to total hip arthroplasty have been well described. Their etiology rests in the increased femoral intramedullary pressure and resulting pulmonary embolism of medullary contents during the insertion of the bone cement and prosthesis. These alterations vary in intensity and consist of increased venous admixture (Qv/Qa), dead space (Vd/Vt), PAa, pulmonary artery pressure and pulmonary vascular resistance, and decreased Pao2, thoracic compliance, and, occasionally, arterial blood pressure. Experimentally, these occur maximally within 5 min of the implantation of the prosthesis and return toward normal in the early postoperative period. If this embolization had contributed significantly to the pulmonary compromise in this patient, an earlier deterioration corresponding to prostatic impaction would have been expected.

Pulmonary edema associated with blood transfusion in the absence of hyperplenemia was first described in 1951, and since then several reports of leukocytosis-induced noncardiogenic pulmonary edema have appeared. While leukocytosis in the recipient's plasma directed against donor granulocytes can result in a reaction, it is commonly febrile and minor in nature. The pulmonary compromise in this patient was caused by the passive transfer from the donor to the recipient of agglutinating antibodies directed against human leukocyte antigens (HLA), granulocyte-specific antigens, or both. This transfer usually leads to prompt neutropenia—typical signs of a transfusion reaction including fever, chills, and pain—and, finally, overt pulmonary dysfunction and pulmonary edema.

The postulated pathophysiology of this pulmonary dysfunction is a complement C5a-mediated pulmonary leukocyte aggregation and leukostasis. While leukostasis by itself is not a trivial event, the pulmonary endothelial damage and subsequent alveolar flooding result from the increased adhesiveness of these complement-activated granulocytes and their production of oxygen radicles, which increase endothelial permeability. The addition of platelets to this reaction leads to further amplification of the endothelial damage wrought by the stimulated granulocytes.

The treatment of this type of pulmonary edema should include both supportive measures as well as inhibition of the ongoing pathophysiologic process. In this case, it consisted of previously mentioned measures that optimized gas exchange and ventilation—perfusion relationships and interventions that simultaneously reduced pulmonary intravascular hydrostatic pressure and thereby decreased the gradient influencing the movement of fluid into the alveoli. Additionally, large doses of corticosteroids were administered in hopes of interrupting this pathophysiologic process, for recent evidence indicates that pharmacologic doses of these drugs can prevent aggregation of granulocytes exposed to C5a in vitro and can also inhibit granulocyte production of superoxide.

This case of severe pulmonary edema and respiratory failure caused by a leukocyte agglutinin reaction associated with transfusion represents the most severe example of this phenomenon in a surviving patient. Early diagnosis, aided by availability of technical facilities and thoughtful treatment, resulted in a satisfactory outcome.

REFERENCES