FIBROSING mediastinitis is a rare disease characterized by an abnormal proliferation of fibrous tissue and acellular collagen within the mediastinum. Most cases of fibrosing mediastinitis in the United States are caused by an exaggerated granulomatous immunologic response to Histoplasma capsulatum infection.\(^2,^7\) However, other possible etiologic conditions include tuberculosis, mediastinal malignancy, and autoimmune diseases.\(^8\) In advanced stages of the disease, these patients may have signs and symptoms of extrinsic compression of airways, intrathoracic vessels, or the esophagus.\(^1,^2\) We describe a patient with fibrosing mediastinitis who, after sedation, awake tracheal intubation, and being positioned supine, experienced acute cardiovascular collapse due to occlusions of the pulmonary veins. It is well known that patients with anterior mediastinal mass can experience posture-dependent compression of airways, vascular structures, or both.\(^9,^10\) However, our case is the first report of position-dependent occlusion of pulmonary venous outflow associated with a disease that is primarily distributed throughout the middle mediastinal compartment.

**Case Report**

A 27-year-old woman was admitted for evaluation of severe progressive dyspnea on exertion and a nonproductive cough. Soon after development of these symptoms, 5 months before admission to the Mayo Clinic (Rochester, Minnesota), her chest radiogram revealed a right lower lobe infiltrate, which worsened despite therapy with levofloxacin, and hemothysis developed. A repeat chest radiogram and computed tomography scan of the chest, 3 months after initial presentation, demonstrated bilateral ground glass infiltrates with diffuse mediastinal lymphadenopathy. All infectious and rheumatologic tests were negative, whereas pulmonary function tests revealed a restrictive pattern. Transthoracic echocardiography indicated pulmonary hypertension with significantly reduced right ventricular function (cor pulmonale). The patient underwent a mediastinoscopy, but pathology was unrevealing. Mediastinoscopy was complicated by sudden "oxyhemoglobin desaturation and cardiovascular collapse" requiring mechanical ventilation and inotropic support. The patient was stabilized in the intensive care unit, and in the absence of explanation for cardiovascular collapse, she was transferred to the Mayo Clinic for further evaluation.

At admission, the patient was stable, requiring no additional oxygen, and showed no signs of respiratory distress. Immediate bronchoscopy was scheduled. She arrived to the bronchoscopy suite sitting comfortably in her stretcher. After standard American Society of Anesthesiologists monitors were applied and after blood pressure (100/70 mmHg), heart rate (90 beats/min), and oxyhemoglobin saturation (SpO2 91% on room air) were recorded, the pulmonologist used lidocaine to anesthetize the upper airway with the patient in the semisitting position. The patient tolerated awake tracheal intubation with 1 mg midazolam. After her trachea was intubated, she was positioned supine for flexible bronchoscopy. After initiation of bronchoscopy, the patient became "uncooperative"; her oxyhemoglobin saturation decreased to the low 80s, and her blood pressure decreased to 65/35 mmHg. Bronchoscopy was aborted, and pure oxygen was administered via the endotracheal tube. At this time, the consultant anesthesiologist was urgently summoned. In addition to fluid boluses, several 100-µg doses of phenylephrine were given, and with each bolus, the patient’s arterial blood pressure increased and respiratory distress lessened. While the anesthesiologist was resuscitating the patient, the pulmonologist informed him of this patient’s underlying mediastinal pathology as well that there was no bronchial compression visualized during bronchoscopy. Because no resistance was encountered during bag ventilation, an assumption was made that the patient’s problem was arising from some type of mechanical compression on pulmonary vasculature. Therefore, to facilitate pulmonary blood flow, we did not administer muscle relaxants, and we maintained the patient breathing spontaneously. In addition, we positioned the patient in steep reverse-Trendelenburg posture with the back further elevated to near sitting position. With this maneuvering, hemodynamics and oxyhemoglobin saturation normalized. An infusion of propofol at 40 µg · kg\(^{-1} \cdot \text{min}^{-1}\) was initiated. At that point, we inserted a brachial arterial catheter; arterial blood pressure was 85/50 mmHg. An infusion of phenylephrine was initiated to keep the systolic blood pressure above 90 mmHg for transfer to the intensive care unit. During transport, the patient’s oxyhemoglobin saturation was in low 90s, while spontaneous breathing was assisted with bag ventilation. At arrival to the intensive care unit, a pulmonary artery catheter was inserted; cardiac index was 2.5 l · min\(^{-1} \cdot \text{m}^{-2}\), pulmonary artery occlusion pressure was 38 mmHg, and pulmonary artery pressure was 86/47 mmHg (at systemic arterial blood pressure of 110/85 mmHg). Epoprostenol (970 ng/min) as well as nitric oxide was added, with minimal effects on pulmonary artery pressure (68/41 mmHg). Soon after, the patient’s arterial blood pressure decreased to 59/31 mmHg, and her oxyhemoglobin saturation decreased to 75%. At that time, we initiated controlled ventilation with 100% oxygen. To maintain systolic arterial blood pressure above 100 mmHg, high-dose norepinephrine and dobutamine were infused together with additional fluid boluses. A transthoracic echocardiogram showed right ventricular enlargement with a moderate decrease in function and estimated right ventricular systolic pressure of 69 mmHg. The left atrium was of normal size, the left ventricular ejection fraction was 65%, and the patient had no valvular (mitral) disease. High pulmonary artery occlusion pressure in context of normal left ventricular...
function and anatomy (no mitral stenosis) suggested the possibility of pulmonary vein occlusion as a cause for pulmonary hypertension (postcapillary pulmonary hypertension). The transthoracic echocardiogram confirmed high-flow velocity in the single pulmonary vein that was able to be visualized, consistent with a narrowed vein lumen. A computed tomography scan (fig. 1) and computed tomography angiogram confirmed near-total occlusion of the right inferior and left superior pulmonary veins along with moderate occlusion of the right superior pulmonary vein; only the left inferior pulmonary vein was patent. The patient’s condition continued to deteriorate rapidly, and she was unable to maintain blood pressure and oxyhemoglobin saturation while supine, even with vasopressors. It was repeatedly noted that the patient’s oxyhemoglobin saturation and hemodynamics fared much better when she was turned on her side, suggesting position-dependent occlusion of her pulmonary vessels. An interventional cardiologist was consulted, and the patient was emergently brought to the catheterization laboratory, where successful angioplasty of the right superior pulmonary vein via transseptal puncture was performed. Given her high fever (41.6 °C) suggestive of infection, the stents were not used. After single-vessel angioplasty, the patient’s hemodynamics improved, and at that point, it was believed that the patient’s “state of infection” should be brought under control before performing more extensive procedures, including stenting. All blood cultures test results remained negative, but fever persisted despite wide-spectrum empiric antibiotic coverage. Serology test results were positive for previous exposure to histoplasmosis. While the patient was in the intensive care unit, her clinical status continued to deteriorate rapidly, and she died 3 days after angioplasty.

Autopsy confirmed the diagnosis of sclerosing mediastinitis producing bilateral pulmonary hilar encasement, extrinsic pulmonary vein compression, and severe pulmonary congestion. A fibrous mediastinal mass with necrosis in the middle (explaining the fever) was partially encasing the left and right pulmonary hilar regions constricting the vasculature. Fungal stains showed rare organisms consistent with Histoplasma species.

Discussion

Large anterior mediastinal masses can cause compression of mediastinal structures, causing airway obstruction or cardiovascular compromise.10 The additive effects of anesthesia, paralysis, and supine positioning can lead to acute airway or vessel occlusion and death.10,11 These respiratory and hemodynamic problems may resolve in the sitting, prone, semiprone, or lateral decubitus position.9,10 Contrary to anterior mediastinal pathology, it is generally considered that diseases in the middle mediastinal compartment do not have significant implications for anesthetic management. However, our case illustrates that fibrosing mediastinitis, a disease distributed mostly throughout the middle mediastinal compartment, can cause equally severe hemodynamic and oxygenation compromise, resembling the clinical picture of an anterior mediastinal mass. The fibrotic process in patients with advanced fibrosing mediastinitis may affect mediastinal structures to produce airway or vessel occlusion, most frequently causing superior vena cava syndrome.12,13 Pulmonary artery or vein compressions are less frequently described.1,7,14 To the best of our knowledge, position-dependent pulmonary vein compression, as present in our patient, has never been reported.

Pulmonary hypertension and cor pulmonale associated with fibrosing mediastinitis are caused by critical obstruction of pulmonary venous outflow.15,16 This is potentially a reversible cause of pulmonary hypertension, because relieving the obstruction with angioplasty normalizes venous inflow into the left atrium. Pulmonary artery catheter pressure measurements may provide a significant clue in elucidating the mechanism of pulmonary hypertension, and when combined with an echocardiogram, the mechanism of pulmonary hypertension may be even further pinpointed. In fact, high pulmonary artery end-diastolic pressure (47 mmHg in our patient) which is 5–15 mmHg higher than pulmonary artery occlusion pressure (38 mm in our patient) strongly suggested postcapillary pulmonary hypertension in our patient, i.e., pulmonary venoocclusive disease.17 Postcapillary pulmonary hypertension is caused by either left heart–related factors (failure, mitral stenosis, atrial myxoma) or pulmonary venous factors (pulmonary vein stenosis or other type of pulmonary venoocclusive disease). Because our patient’s echocardiography demonstrated normal left ventricular function and anatomy (no valvular disease, thrombus, etc.), the most plausible etiology of postcapillary pulmonary hypertension was venous obstruction, associated with mediastinal disease. This hypertension may be subject to correction with stenting; therefore, it is important to make an early diagnosis before the disease advances and irreversible parenchymal changes occur.1,16 Furthermore, sudden onset of pulmonary hypertension in conjunction with mediastinal pathology, in a previously healthy young patient, should have raised a high suspicion of mechanical cause, such as venous outflow obstruction, much earlier in the course of her disease.

Fig. 1. Computed tomography scan using intravenous contrast depicts the main branches of the left and right pulmonary veins draining into the left atrium and displays the significant mediastinal fibrosis. This radiodens depicts total occlusion of the right inferior pulmonary vein as it enters the left atrium. The left inferior pulmonary vein is patent. No significant calcifications were noted in the subcarinal, hilar, or mediastinal locations.
Radiographic abnormalities in patients with fibrosing mediastinitis consist of diffuse lesions, atelectasis, and infiltrates. Chest radiographs may occasionally be deceptively unremarkable, even in the presence of major central airway or vascular occlusion, especially when the lesion is subcarinal. Our patient had pathology in the middle mediastinum, which radiologically, from an anesthetic (mechanical) standpoint, seemed benign, but at the same time, total occlusion of three pulmonary veins was present. Furthermore, our case is unique in the sense that the pulmonary vein occlusion was posture dependent, the same as in patients with anterior mediastinal masses. Unfortunately, an episode of “cardiovascular collapse” during mediastinoscopy at an outside institution was only retroactively related to this patient’s pulmonary vein pathology.

In conclusion, we describe a patient with mediastinal fibrosis and position-dependent occlusion of pulmonary veins. Her presenting chest radiogram was deceiving, and providers in two institutions were puzzled with hemodynamic and oxygenation problems they encountered after tracheal intubation with the patient in supine posture. Our case illustrates that if intractable hypotension after induction of anesthesia occurs, even in patients with midmediastinal pathology, a possibility of vascular compression should be considered. Finally, acute development of pulmonary hypertension in previously healthy young individuals, associated with radiologic changes in the mediastinum, should alert physicians to search for venoocclusive etiology of pulmonary hypertension. Information obtained from pulmonary catheter measurements in conjunction with transthoracic echocardiographic findings can give us important clues regarding the mechanism of pulmonary hypertension.

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Low-dose Propofol Infusion for Controlling Acute Hyperspasticity after Withdrawal of Intrathecal Baclofen Therapy

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BACLOFEN, a potent γ-aminobutyric acid (GABA) type B receptor agonist, has been used widely as an antispasticity drug since the 1970s. Baclofen decreases synaptic transmission by binding to the presynaptic GABA type B receptor at the primary sensory afferent terminal through a second-messenger pathway, thereby decreasing calcium influx and neurotransmitter release. Binding of baclofen to the presynaptic GABA type B receptor also decreases neurotransmitter release by activating potassium channels, contributing to its presynaptic inhibitory effect. Baclofen may also act at supraspinal sites, including enhancement of vagal tone and inhibition of mesolimbic and nigrostriatal neurons. Although baclofen has major postsynaptic effects on motoneurons and interneurons, experimental models of chronic spinal cord injury do not support a postsynaptic action contributing to its antispasticity effect.

Intrathecal baclofen has benefited patients with a

References

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Case Reports

Case 1

A 65-yr-old man was admitted to the hospital with suspected baclofen pump failure. The pump had been sited 6 yr previously for severe spasms after a complete C5 injury, necessitating ambulatory noninvasive ventilation. The patient had felt increasingly unwell over the previous 24 h, with increasing spasticity and pyrexia (38.1°C). Laboratory investigations did not indicate an infective component. Five hours after admission, the hyperspasticity became more marked, with bilateral clonus and increased abdominal and respiratory muscle tone despite oral loading with baclofen. At admission to the critical care unit, arterial blood gas analysis revealed a metabolic acidosis (base deficit = 3.2). Plasma creatinine kinase was and remained within normal limits. Propofol was infused intravenously at 5–15 mg/h. Within 2 h, the base deficit had normalized, and both the spasms and clonus were markedly reduced. Abdominal and respiratory muscle tone decreased, with the patient feeling settled. Low-dose propofol had no effect on cardiorespiratory parameters or sedation status. The propofol infusion (target-controlled plasma concentration 0.6 μg/ml) was then continued, preventing the return of hyperspasticity, and stopped 2 days later, during which time a new baclofen pump was resited surgically.

Case 2

Three separate episodes of acute hyperspasticity were treated in a 34-yr-old man who required intrathecal baclofen therapy after a complete C4 spinal cord lesion.

Admission 1 After an elective change of intrathecal baclofen pump, severe hyperspasticity developed within 24 h, accompanied by hyperpyrexia (40.1°C), tachycardia (160 beats/min), hypertension, and a respiratory rate of 33 breaths/min. Propofol was infused intravenously at 20–150 mg/h, in addition to 20 mg sublingual nifedipine and 100 mg dantrolene. Within 1.5 h after commencing the propofol, the spasms ceased. Within 5 h, heart rate and respiratory rate had decreased to 110 beats/min and 22 breaths/min, respectively, with normal core temperature and conscious level throughout the admission. The plasma creatinine kinase concentration was also normal throughout. During the first 5 h of admission, the patient also received 100 μg intrathecal baclofen via a newly introduced intrathecal catheter. Surgical relocalization of the catheter was undertaken the next day. Propofol was infused for optimal control of spasms for a further 24 h while intrathecal baclofen was reintroduced via a newly inserted pump.

Admission 2 Two years after admission 1, the patient was admitted with new onset spasms, pyrexia (38.6°C), and respiratory discomfort (respiratory rate 24 breaths/min, no metabolic acidosis). Propofol was administered solely, with two boluses of 50 mg plus a 20-mg/h background infusion resulting in complete resolution of hyperspasticity, pyrexia, and respiratory rate within 2 h. The spasms returned after 7 h, during which time the propofol infusion had been reduced. The spasms resolved after increasing the propofol background infusion (50–150 mg/h). No changes in gas exchange or sedation levels were observed throughout the admission.

Admission 3 Three yr after admission 2, pyrexia (37.6°C) and increasingly severe spasms were noted 4 days after the scheduled reimplantation of a new baclofen pump. Propofol was commenced solely (10 mg/h), with resolution of tachycardia, pyrexia, and spasms within 1.5 h. Propofol was continued for 20 h, over which time pump-delivered baclofen administration was established. Again, no changes in gas exchange or sedation levels were observed throughout the admission.

Discussion

Oral baclofen administration is usually inadequate to treat or prevent intrathecal baclofen withdrawal.20 The
clinical data presented support the hypothesis that propofol is the agent of choice for acute control of acute hypertonicity. Although the neuropharmacologic actions of propofol and baclofen are incompletely understood, they share many similarities (fig. 1). Propofol enhances GABA-mediated synaptic inhibition in a number of neuronal systems.23 Propofol enhances presynaptic inhibition at primary afferent terminals in human spinal cord24 and dose-dependently decreases the firing rate and burst activity of nigral dopaminergic neurons, an effect reversed by a selective GABA type B antagonist.25 Interestingly, propofol administered via both intrathecal and intraperitoneal routes produces antinociception in rats by acting on spinal cord δ-opioid receptors, whereas only intrathecally administered midazolam produces the same effect.26 This may mirror our clinical experience of low-dose propofol infusions being effective in contrast to several previous case reports requiring high-doses of benzodiazepines for control of hypertonicity. Furthermore, the antiinflammatory27 and antinociceptive28,29 effects of propofol may also confer some protective effect during baclofen withdrawal.

These clinical data lend support to the idea that propofol is the agent of choice for treatment of this and perhaps other hypertonicity syndromes. Propofol possesses important neurophysiologic, neuropharmacologic, and pharmacokinetic properties to ameliorate the symptoms and prevent the pathophysiologic progression of acute baclofen withdrawal. In clinical practice, titration of propofol therapy using a target-controlled intravenous infusion against an objective score of spasticity (such as the Ashworth scale score30 or Penn Spasm Scale score31) offers a new therapeutic approach to this potentially life-threatening syndrome.

References