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Paraplegia Immediately following Removal of a Cerebrospinal Fluid Drainage Catheter in a Patient after Thoracoabdominal Aortic Aneurysm Surgery

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SPINAL cord ischemia resulting in postoperative paraplegia is a devastating complication after thoracoabdominal aortic aneurysm (TAAA) surgery. Numerous strategies have been devised to protect the spinal cord from ischemia by maintaining spinal cord perfusion. Although controversial, one of the more popular clinical strategies, cerebrospinal fluid (CSF) drainage, theoretically increases spinal cord blood flow by decreasing CSF pressure.[1] This article describes a case report of a patient with a thoracic epidural catheter in place who developed paraplegia immediately after removal of a lumbar CSF drainage catheter during the postoperative period after TAAA surgery, suggesting that the technique may have been of benefit to this patient.

Case Report

The patient was a 74-yr-old man with an asymptomatic complex TAAA (Crawford classification III). The superior aspect of the aneurysm began in the midthoracic region (6.5 cm maximum diameter) and tapered to normal diameter at the superior mesenteric artery. A second aneurysm (5.0 cm maximum diameter) began at the renal arteries and extended into the left common iliac artery. Medical history was significant for hypertension. Medications taken included clonidine, amlodipine, and hydrochlorothiazide. On the evening before surgery, a thoracic epidural catheter was inserted atraumatically (first attempt) at T8. The catheter was advanced 5 cm into the epidural space.

On the morning of surgery, in the operating room, a lumbar intrathecal catheter was inserted atraumatically (first attempt) at L3 *via* a 14-gauge Tuohy needle. The catheter was advanced 5 cm into the intrathecal space. The CSF drainage catheter remained open throughout the intraoperative period and was adjusted to maintain the CSF pressure at 10 cm H_2O with a Becker® external drainage and monitoring system (Medtronic, Inc., Goleta, California). General anesthesia was then induced with intravenous midazolam, fentanyl, and pancuronium. Maintenance general anesthesia consisted of supplemental midazolam and fentanyl combined with inhaled isoflurane. The trachea was intubated with a left-sided double-lumen endotracheal tube and its proper position was verified *via* fiberoptic bronchoscopy. A central venous catheter was then inserted into the right internal jugular vein (through which a pulmonary artery catheter was eventually placed) followed by insertion of a right femoral artery catheter. Transesophageal echocardiography revealed mild hypokinesis of the left ventricular anterolateral wall, mild aortic insufficiency, and mild tricuspid insufficiency.

After adequate TAAA exposure *via* left thoracotomy and after 300 U/kg intravenous heparin, partial cardiopulmonary bypass (CPB) was initiated *via* femoral arterial and venous cannulae at approximately 1 $l \cdot min^{-1} \cdot m^{-2}$. Anticoagulation was assessed *via* activated clotting time (ACT) determinations (lowest 664 s, highest 855 s). Methylprednisolone (2 g intravenous) was administered before initiation of CPB and 12.5 g mannitol was added to the standard crystalloid CPB prime. Dopamine (3 $\mu g \cdot kg^{-1} \cdot min^{-1}$ intravenous) was administered throughout the intraoperative period. The proximal aortic cross-clamp was applied in the midthoracic region, and the distal aortic cross-clamp was applied just inferior to the renal arteries. A Dacron graft (28 cm) was inserted and the celiac trunk, superior mesenteric artery, and renal arteries were all reimplanted. No intercostal arteries were reimplanted. The patient's temperature was allowed to passively decrease (lowest esophageal temperature, 35.5°C). Following hemostasis, separation from CPB was accomplished without support of vasoactive medications. The ACT decreased to baseline (120 s) after protamine administration (250 mg). Total cross-clamp and CPB times were 38 and 48 min, respectively.

The patient was hemodynamically stable throughout the intraoperative period. Nitroglycerin was required for hypertension with initial application of the proximal cross-clamp. During cross-clamp application, proximal mean arterial pressure was maintained above 90 mmHg and distal mean arterial pressure was maintained above 60 mmHg. The CSF catheter drained 173 ml throughout the intraoperative period. During closure, an infusion of bupivacaine (1.0%) and fentanyl (5 μg/ml) was initiated at 10 ml/h *via* the thoracic epidural catheter. Total intraoperative intravenous fluids were 4,200 ml crystalloid, 1,500 ml colloid, 1,250 ml "cell-saver" blood, 2 units fresh frozen plasma, and 4 units packed erythrocytes. Estimated blood loss was 2,000 ml. Total intraoperative urine output was 710 ml.

Within a few hours of arrival to the intensive care unit (ICU), the patient was awake and neurologically intact. The CSF drainage catheter remained open and was adjusted to maintain the CSF pressure at 10 cm H_2O. Tracheal extubation occurred 6 h after ICU arrival. Soon thereafter, the patient complained of left leg weakness and inability to flex either knee. The epidural infusion was stopped and over the next hour, full motor strength and function of both lower extremities returned. Because of increased incisional pain during this same time period, the epidural infusion was reinitiated at 10 ml/h.

At 0900 on the first postoperative day, the CSF drainage catheter was removed. At this time the patient had full motor strength and function of both lower extremities and was ambulating without difficulty. During these initial ICU hours (ICU arrival to catheter removal), the patient was hemodynamically stable. The mean arterial blood pressure was never less than 70 mmHg and small amounts of intravenous nitroprusside were required to maintain the systolic blood pressure less than 130 mmHg. During these initial 16 ICU hours, the CSF catheter drained 64 ml to maintain the CSF pressure at 10 cm H_2O. Within 30 min of catheter removal, the patient reported bilateral lower extremity weakness during ambulation. One hour after catheter removal, he could not move his left lower extremity and soon thereafter(30 min) could not

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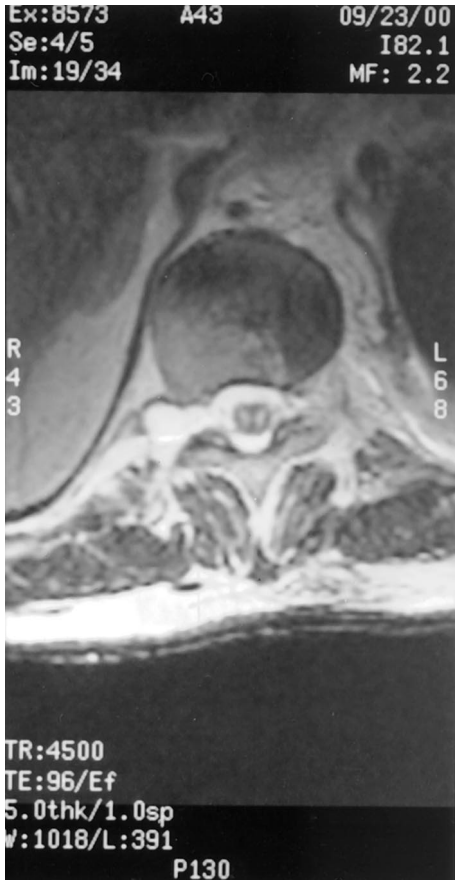

Fig. 1. Representative axial image of the spinal cord. The top of the image is anatomically anterior whereas the bottom of the image is anatomically posterior. The "snake eye"-shaped lesion demonstrated within the spinal cord is typical of cord ischemia and infarction.[2]

move either lower extremity at all. The epidural infusion was decreased to 7 ml/h. Seven hours after catheter removal, the patient was unable to move either lower extremity against gravity. The epidural catheter was repositioned (pulled back) and the infusion was decreased to 6 ml/h. Ten hours after catheter removal, the patient was unable to move either lower extremity. The epidural infusion was stopped. Twelve hours after catheter removal, bilateral paralysis persisted, prompting emergency magnetic resonance imaging, which revealed no signs of extradural mass or epidural hematoma yet demonstrated spinal cord infarction in the anterior spinal artery distribution. Observed on axial images were bilateral areas of abnormal signal within the spinal cord between the conus to the level of approximately T8, where axial images were no longer obtained. These "snake eye"-shaped lesions demonstrated in axial views (fig. 1) are typical of cord ischemia and infarction.[2] During the 12 h after CSF catheter removal, the patient was hemodynamically stable. Intensive therapy after emergent magnetic resonance imaging (reinsertion of CSF drainage catheter, intravenous dopamine, intravenous heparin, intravenous dexamethasone) failed to improve the neurologic deficit. By postoperative day 5, sensory level to pin prick had stabilized at T10 and the patient had no motor function in either leg. Posterior cord function (position sense and vibratory sensation) remained intact. On postoperative day 7, the patient experienced sudden cardiac arrest. Following emergent surgical exploration, the proximal and distal ends of the Dacron graft were found to be intact, yet large sections of the small and large intestine were infarcted. The patient died in the operating room. An autopsy was not performed.

Discussion

Autopsy studies indicate the prevalence of asymptomatic thoracic aneurysm is approximately 4–6 per 1,000 patients, with the incidence increasing with age.[3] TAAA is extremely rare and represents approximately 5% of all asymptomatic thoracic aneurysms.[3] Recent recommendations regarding TAAA management have emphasized individualized treatment based on balancing a patient's calculated risk of rupture with their anticipated risk of postoperative death or paraplegia.[4] With current techniques, elective TAAA resection can be accomplished with operative mortality rates of approximately 5–10%.[3,4] Major perioperative morbidity associated with TAAA resection includes myocardial infarction, respiratory failure, renal failure, stroke, and paraparesis or paraplegia. The incidence of postoperative permanent spinal cord injury remains high (10–30% depending on type of TAAA), likely a result of the remarkable variability among patients regarding spinal cord blood supply.[5] The tenuous collateral anastomosis of the anterior spinal artery in the midthoracic region places segments of the spinal cord in jeopardy during aortic occlusion or hypotension. Damage may result from either actual surgical dissection of the artery of Adamkiewicz (because the origin is unknown) or exclusion of the origin of the artery by the aortic cross-clamps.

Many techniques have been investigated in hopes of improving spinal cord protection during TAAA surgery, none of which have proven clinically reliable.[6,7] These various techniques include distal perfusion methods (arterial and venous), hypothermia (general and regional), monitoring spinal cord somatosensory and motor evoked potentials, pharmacologic agents (vasodilators, naloxone, *etc.*), intercostal artery reimplantation, profound hypothermic circulatory arrest, endovascular stents, and ischemic preconditioning. One of the most intensely investigated and clinically utilized techniques has been CSF drainage, which decreases CSF pressure and theoretically increases spinal cord blood flow by increasing spinal cord perfusion pressure. Animal studies[8] indicate that CSF drainage (to a CSF pressure of 10 mmHg) prevents paraplegia yet human studies[9] have been less successful. Following a recent systematic overview of evidence involving use of CSF drainage in TAAA surgery for prevention of paraplegia, Ling and Arellano conclude that the benefits, if any, are unsubstantiated.[1]

Almost half of all episodes of spinal cord injury related to TAAA resection occur during the postoperative period (for example, delayed neurologic deficits) and may occur anywhere from 12 h to 21 days after surgery.[10,11] Although many factors may play a role in delayed neurological deficit formation (underlying atherosclerotic vascular disease, spinal artery spasm, *etc.*), the two determinants of spinal cord perfusion pressure (CSF pressure and blood pressure) are thought to play pivotal

roles.[10,11] Postoperative episodes of increased CSF pressure (from an epidural injectate), and decreased blood pressure have been linked to development of delayed neurologic deficits in certain patients.[10,11] To the authors' knowledge, this case report represents the first description of delayed neurologic deficit possibly caused by cessation of CSF drainage. We theorize that with cessation of CSF drainage, CSF pressure may have increased to a point that initiated spinal cord ischemia/infarction (the patient's blood pressure did not change during this time). Although we cannot definitively conclude that the supposed increase in CSF pressure was the sole mechanism of the delayed neurologic deficit, the timing of the postoperative clinical events, along with the presence of hemodynamic stability during the same time period, suggest an etiologic role. We theorize that the second CSF catheter failed to improve the neurologic deficit because irreversible damage to the spinal cord had already occurred. On the other hand, the possibility exists that this patient suffered a coincidental embolic event that resulted in spinal cord damage, a possibility supported by the subsequent development of bowel ischemia. Thus, it remains possible that the neurologic deficit would have occurred despite removal of the CSF catheter or despite any CSF catheter at all.

The postoperative management of an epidural (lumbar or thoracic) catheter in a patient after TAAA surgery is certainly challenging and somewhat controversial. The goal is to attain adequate analgesia without detrimental effects (hypotension, respiratory depression, *etc.*). Furthermore, in this unique patient population, concern always exists regarding hematoma formation and masking a developing neurologic deficit. One could argue that in this patient, the thoracic epidural infusion should have been immediately discontinued when the neurologic deficit was first noted and that the MRI should have been performed earlier. In hindsight, these statements are probably true. Perhaps with earlier detection, prognosis would have been altered.

In conclusion, development of paraplegia after TAAA surgery remains a clinically important problem, the etiology of which is multifactorial. No one technique has been proven to substantially reduce incidence. Therefore, a multimodal approach to prevention of paraplegia should be adopted and tailored to each individual patient. CSF drainage may be of benefit to some patients, not only during aortic cross-clamp application intraoperatively, but also during the immediate postoperative period (the length of which remains to be determined).

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Reversal of Acute Paraplegia with Cerebrospinal Fluid Drainage After Endovascular Thoracic Aortic Aneurysm Repair

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EXCLUSION of a thoracic aortic aneurysm (TAA) by endoluminal deployment of a stent graft appears to be effective therapy.[1] Complications of endovascular graft placement include the technical problems associated with graft insertion, systemic effects of anesthesia and surgery, and specific problems related to the device reliability during follow-up.[1] Acute-onset paraplegia is an uncommon yet devastating complication of endovascular TAA repair.

Clinical Features

The patient was a 77-yr-old man with a descending thoracic aortic aneurysm (6 cm), infrarenal aortic aneurysm (3 cm), and left common iliac artery aneurysm (2.5 cm). He had a history of bilateral carotid artery stenosis, transient ischemic attacks, ischemic cardiomyopathy, mitral and aortic insufficiencies, hypertension, orthopnea, pulmonary emphysema resulting in dyspnea at rest, and gastroduodenal peptic ulcer. His poor physical status resulted in a decision to treat his TAA *via* an endoluminal approach.

The patient underwent transfemoral insertion of an endovascular stent-graft (Excluder 40 × 20; W.L. Gore & Associates, Inc., Flagstaff, AZ) that extended from a point just distal to the left subclavian artery to the level of the tenth thoracic vertebra. This was performed under general anesthesia with etomidate, fentanyl, vecuronium and O_2–air–isoflurane. The patient was hemodynamically stable throughout the procedure. There were no hypertensive or hypotensive episodes. He was extubated in the operating room, but showed acute onset of paraplegia, and was transported directly to the intensive care unit. The neurologist immediately evaluated the patient. She diagnosed flaccid paraplegia with total absence of sensation below the level of T4, accompanied by loss of movement, deep tendon reflexes, vibration, and joint-position sense in the lower limbs. Spinal cord ischemia was considered the most probable cause. No imaging of the spinal cord was performed. Conservative therapy was selected. The neurologist began anticoagulation with sodium heparin in order to limit neurologic deficit extension. Intravenous methylprednisolone (500 mg every 8 h), ranitidine (50 mg every 12 h) and N-acetyl-cysteine (2,000 mg every 8 h) were also given. The symptomatology did not improve in 1 h, so an urgent lumbar intrathecal catheter was inserted. Sodium heparin infusion was stopped at the moment of the catheter insertion. There were no difficulties during the placement of the intrathecal catheter despite of anticoagulation. The initial cerebrospinal fluid (CSF) pressure was greater than 25 mmHg. Immediate improvement was seen upon catheter insertion and commencement of drainage, which was continued in an effort to maintain CSF pressure of 12 mmHg. Immediate improvement was seen upon catheter insertion and commencement of drainage, which was continued in an effort to maintain CSF pressure lower than 12 mmHg. The patient began to recover sensitivity in 1 h and motor function in 3 h (in the left toes and foot at the beginning, extending afterwards to the rest of the lower limbs in 4 h).

The neurologic deficit resolved progressively. Recovery of sensory function was complete after 3 days, although motor function in the lower limbs continued to improve, extending to complete recovery after 13 days. CSF drainage was removed the third day due to fever, despite mild weakness of the right leg. Drug therapy was maintained 6 days. The patient was discharged with no neurologic deficit 15 days after surgery.

Discussion

The standard technique for the treatment of descending TAAs is elective open surgical repair with graft interposition.[1] Endoluminal approaches are becoming more common. Endoluminal therapy is restricted in our hospital to patients with aneurysms that contain proximal and distal stent graft landing zones whose coexisting diseases may preclude open surgical repair. This was believed to be most appropriate for the patient described.

Spinal cord ischemia may occur in 1–11% of operations involving open TAA repair. Acute-onset paraplegia after endoluminal TAA repair had not been reported previously. The etiology is multifactorial, involving a series of progressive interdependent events that include perioperative hypotension, increase in CSF pressure, inadequate perfusion to critical intercostal or lumbar vessels, oxygen radical–mediated lipid peroxidation and the extent of the aortic pathology.

The high cardiopulmonary risk of this patient resulted in a decision to treat his new deficit conservatively, so the therapy was focused on improving the etiologic factors. There was no perioperative hypotension, so cardiovascular drugs to maintain blood pressure were not needed. Second, oxygen radical–mediated lipid peroxidation has been suggested increasingly to be a therapeutic target for acute pharmacologic neuroprotection,[2] so N-acetyl-cysteine was administered to the patient (2,000 mg every 8 h). Methylprednisolone has been also shown to possess significant antioxidant efficacy.[2] This drug, in combination with CSF drainage, produces a synergistic benefit of extending the time interval of safe aortic cross-clamping[3] and improves neurologic outcome after normothermic spinal cord ischemia.[4] This patient received methylprednisolone (500 mg every

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8 h), although the utility of steroids with CSF drainage had not been reported yet in acute paraplegia after TAA repair. Greater doses of steroids (such as those used in spinal cord section) were avoided because of the patient's gastroduodenal peptic ulcer. Ranitidine (50 mg every 12 h) was also administered.

Third, prompt CSF decompression was performed to reduce the CSF pressure and improve spinal cord perfusion pressure.[3] Cerebrospinal fluid drainage was useful previously in treating three cases of delayed paraparesis at 13,[5] 12,[6] and 6 h[7] after aortic aneurysm repair, but this technique had not been employed before in acute-onset paraplegia. A CSF pressure of 12 mmHg was established as the critical point of drainage because this patient had acute paraplegia instead of delayed paraparesis (Khong *et al.*[5] reported 15 mmHg). We avoided CSF overdrainage, because it can cause complications that result in neurologic deterioration (such as acute pneumocephalus, brain collapse, Chiari II–like syndrome with vocal cord paralysis and life-threatening aspiration, or temporal downward herniation with kinking of the posterior cerebral artery and acute brain infarction) or even in the death of the patient.[8] Intermittent CSF drainage with a closed circuit (because of deficient flow throughout the catheter) and daily biochemical and microbiological CSF monitoring (to avoid infections) were established. Intrathecal catheter was removed the third day because of fever peak. CSF monitoring maintained negative all days. Neurologic recovery continued on after catheter removal, so we did not consider it necessary to insert a new one.

Finally, the extent of the aortic pathology is also important. Attachment of the endovascular stent graft to aortic wall could result in the stent crossing the ostia of critical intercostal vessels or even Adamkiewicz's artery (usually originated at T9–T12), leading to inadequate perfusion and spinal cord ischemia. The mechanisms involved in the improvement of the patient's neurologic deficit remain poor defined. Urgent CSF decompression could permit adequate spinal cord perfusion throughout collateral vessels, and pharmacologic therapy could have limited neurologic deterioration.

Conclusions

In conclusion, this case demonstrates the potential therapeutic role for prompt cerebrospinal fluid spinal decompression in combination with methyl-prednisolone and N-acetyl-cysteine administration to reduce the complications of acute paraplegia after endovascular thoracic aortic aneurysms repair.

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Cauda Equina Syndrome after Spinal Tetracaine: Electromyographic Evaluation—20 Years Follow-up

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CAUDA equina syndrome (CES) has long been recognized as a rare complication of spinal anesthesia.[1] CES has been described after administration of spinal anesthetics with lidocaine[2] and bupivacaine.[3] In 1991,[4] CES was reported after continuous spinal anesthesia with 1% tetracaine.

In 1980, at our university hospital, six adult female patients underwent perineal gynecologic surgery using a spinal anesthetic of 2 ml tetracaine, 1.2%, in 10% glucose. The concentration of the injected tetracaine was unknown by the anesthetists. In all cases, lumbar puncture was performed at the L3–L4 interspace with a disposable spinal needle while the patients were in the sitting position. CES was first diagnosed 72 h or later postoperatively; previous diagnosis was not possible because patients had an indwelling urethral catheter. The diagnosis of CES was confirmed in all patients.

During the past year, after institutional approval and informed consent, clinical, magnetic resonance imaging, electromyographic examinations, and conduction studies were performed in three of the above patients. Examinations were not possible on the other three patients because one had recently died, another could not be located, and the third refused to participate. T1 and T2 magnetic resonance image readings were obtained with Gadolinium contrast from a 0.5 Tesla General Electric apparatus (General Electric, Tokyo, Japan). Bilateral sensory and motor conduction studies of the sciatic nerve branches were obtained using a two-channel Nihon-Kohden Neuropack 2 (Nihom-Kohden Corporation, Tokyo, Japan). Electromyography was performed in accordance with conventional techniques.[5,6]

Case Reports

Case 1

A 29-yr-old woman underwent tubal ligation and perineoplasty. Intraoperative block level was T11 without complications. Soon after surgery she noted sensory abnormalities in the perineum, difficulties in micturition and defecation, and sexual disabilities, which have all continued to date. During the examination, bilateral perineal hypoesthesia in dermatomes S2, S3, S4, and S5 was noted, always with mild bilateral decrease in soleus muscle strength. Anal sphincter examination revealed hypotonia. The magnetic resonance imaging examination was normal. Bilateral sensory conduction studies on the sural nerve were normal. Bilateral motor conduction studies on the knee to ankle segment of the deep peroneal nerve were normal with abnormal F waves. Motor conduction studies on the tibialis posterior nerve (table 1) showed left side latency and bilateral decreased amplitude with abnormal F waves. Electromyography showed fasciculations in the soleus and the elevator anus muscles at rest and neurogenic motor units during mild voluntary muscle effort.

Case 2

A 65-yr-old woman underwent perineoplasty because of urinary stress incontinence. Her spinal anesthetic was unremarkable. However, after surgery her incontinence worsened. She noted perineal hypoesthesia and defecation disability. After a few weeks, she lost all perineal muscle strength. Her current examination revealed asymmetric bilateral hypoesthesia in dermatomes L5, S1, S2, S3, S4, and S5, which was more severe on the right and in most caudal dermatomes (S4 and S5). Muscle strength in myotomes S1 and S2 was decreased. Sphincter anal examination revealed atonia. Magnetic resonance imaging results were normal. Conduction studies and electromyography were similar to those in case 1.

Case 3

A 36-yr-old woman underwent surgical repair of the urethral–vaginal fistula. Soon after surgery, she noted perineal hypoesthesia, mainly perianal. Current examination revealed a decrease of cutaneous sensation in dermatomes S4 and S5. Sphincter anal examination revealed hypotonia. Magnetic resonance imaging results were normal. Conduction studies and electromyography were similar to cases 1 and 2.

Table 1. Case 1: Bilateral Motor Conduction Studies on the Tibialis Posterior Nerve

	Left	Right
Distal motor latency	4.9	6.42*
Amplitude	0.7†	3.7/2.6†
Velocity	41.0	40

* Abnormal value. † Slight temporal dispersion.

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Discussion

Tetracaine-related neurotoxicity has been seen in humans[7] and studied in animals.[8,9] These studies indicate that concentrations exceeding 1% may be accompanied by an increasing dose-related incidence of damage.[8–10]

Our experience with tetracaine started in February 1980. Initially, spinal anesthesia was performed in 29 patients with a 1:1 mixture of 1% tetracaine in distilled water (10–20 mg) and 10% glucose solution. Another protocol performed on 52 patients used 1% tetracaine in distilled water (5–10 mg) mixed 1:1 with a solution of 5% lidocaine (20–80 mg) diluted in 7.5% glucose. None of these patients showed neurologic complications.

In May of the same year, anesthesiology staff members requested a São Paulo laboratory to produce 60 vials of tetracaine containing 1% tetracaine diluted in 10% glucose (20 mg tetracaine and 200 mg glucose in each 2-ml vial), but the vials were produced with 24 mg tetracaine and 200 mg glucose. These vials were inadvertently used in the Obstetrics Center. In 16 patients with cesarian deliveries, spinal anesthesia was induced with tetracaine (7.2 mg = 0.6 ml in 10% glucose) and 5% lidocaine (30 mg = 0.6 ml in 7.5% glucose). Two cesarian deliveries were performed under spinal anesthesia with tetracaine (14.4 mg = 1.2 ml of 1.2%). None of these 18 patients showed neurologic complications. In nine patients, spinal anesthesia was induced with the 1.2% tetracaine vials (24 mg) in a single dose of 2 ml; there was just one male patient submitted to supra pubic prostatectomy. The remaining eight patients were women submitted to tube ligature, perineoplasty, or both. CES was postoperatively diagnosed in six of the female patients. This report clearly shows that neurotoxicity was dose related.

The importance of electromyography in the differential diagnosis of local anesthetic complications has been recognized for a long time, but electromyographic methods were not used in most of the recently published papers on human CES after spinal anesthesia. In a few cases, electromyography was incomplete; there was no available F-wave data.[2]

In our three patients, the electromyographic diagnosis criteria for CES were achieved. These criteria were normal sensory conduction studies, F-wave abnormalities, asymmetrical reduced amplitudes of the compound muscle action potential in the motor conduction studies, and neurogenic electromyographic abnormalities of the sacral root muscles. A 20-yr follow-up showed that tetracaine-induced cauda equine syndrome remained stable, stressing the irreversible character of this complication.

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Acute Hemodilution in a Chronic Polycythemic Patient May Be Deleterious

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ALTHOUGH data from animal studies of acute polycythemia show that this condition is associated with a decreased cardiac output and increased systemic vascular resistance (SVR) because of an increased blood viscosity,[1–3] this is not confirmed in man. In contrast to polycythemia, acute isovolemic hemodilution leads to an increase in cardiac output, a decrease in SVR, and an increase in the oxygen extraction. However, there is no report in the literature on the effects of acute isovolemic hemodilution in a polycythemic individual. We describe the treatment and the effects of acute hemodilution in a patient with chronic polycythemia undergoing surgery for an erythropoietin-producing renal tumor.

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Table 1. Systemic Hemodynamic and Oxygenation Parameters during Hemodilution

	Preanesthesia	Postanesthesia	−500	−1,000	−1,500	−2,000	−2,500	+500	Postoperative
Hct	59 (35–45)	57	49	41	39	34	30	37	42
MAP	121 (70–105)	102	84	100	114	86	77	101	87
HR	72 (60–90)	73	60	69	74	65	60	68	79
CVP	10 (4–8)	10	10	15	18	19	19	19	20
PAWP	16 (5–12)	16	12	19	25	23	23	24	12
CI	4.71 (2.5–4.0)	4.71	4.27	5.29	5.27	4.41	4.43	5.34	7.5
SVRI	1,883 (1,700–2,600)	1,561	1,384	1,286	1,457	1,215	1,046	1,228	906
PVRI	271 (70–180)	187	187	197	197	200	216	165	96
$P\bar{v}O_2$	44	56	56	55	53	51	51	46	46
$S\bar{v}O_2$	80 (60–80)	88	87	87	85	85	87	79	79
$\dot{D}O_2$	957 (550–650)	925	760	827	778	567	479	744	710
$\dot{V}O_2$	145 (115–165)	93	86	103	112	83	56	136	102
O_2ER	15 (24–28)	10	11	13	14	15	12	18	14

Before induction of anesthesia, after induction of anesthesia, during hemodilution, where − denotes withdrawal and + denotes administration of blood, and finally postoperative (normal values).

Hct = hematocrit (%); MAP = mean arterial pressure (mmHg); HR = heart rate (beats/min); CVP = central venous pressure (mmHg); PAWP = pulmonary artery wedge pressure (mmHg); CI = cardiac index ($l \cdot min^{-1} \cdot m^{-2}$); SVRI = systemic vascular resistance index ($dyn \cdot s \cdot cm^{-5} \cdot m^{-2}$); PVRI = pulmonary vascular resistance index ($dyn \cdot s \cdot cm^{-5} \cdot m^{-2}$); $P\bar{v}O_2$ = mixed venous partial pressure of oxygen (mmHg); $S\bar{v}O_2$ = mixed venous saturation (%); $\dot{D}O_2$ = systemic oxygen delivery ($ml \cdot min^{-1} \cdot m^{-2}$); $\dot{V}O_2$ = systemic oxygen consumption ($ml \cdot min^{-1} \cdot m^{-2}$); O_2ER = systemic oxygen extraction ratio (%).

Case Report

An 80-yr-old woman (height, 1.60 m; weight, 59 kg; body surface area, 1.64 m^2) was scheduled for surgery to remove an erythropoietin-producing renal tumor. Physical examination and laboratory tests on admission revealed an arterial blood pressure 160/75 mmHg, an erythropoietin concentration of 116 U/l (normal range, 1–10 U/l), and a hematocrit of 62%. The electrocardiograph showed signs of left ventricular hypertrophy. The patient was treated with a calcium-blocker (nifedipine) and a β blocker (atenolol) for chronic hypertension. It was decided to perform acute isovolemic hemodilution just before surgery, which would result in a quantity of autologous blood for transfusion during surgery if acute bleeding should occur.

After having obtained informed consent, and before anesthesia was induced, venous and arterial cannulae were inserted, including a pulmonary artery thermodilution catheter (Edwards 7-French; Baxter Healthcare Corp., Irvine, California) through the right internal jugular vein. Baseline measurements of the mean arterial blood pressure, pulmonary artery pressure, pulmonary artery wedge pressure, central venous pressure, and cardiac index were made before anesthesia. Arterial and mixed venous blood samples were obtained for the determination of hemoglobin, hemoglobin oxygen saturation (OSM 3; Radiometer, Copenhagen, Denmark), hematocrit, and partial pressure of oxygen (Po_2), partial pressure of carbon dioxide (Pco_2), pH, and base excess (ABL 505; Radiometer, Copenhagen, Denmark). From these data, systemic vascular resistance index, pulmonary vascular resistance index, left ventricle stroke work index, systemic oxygen delivery ($\dot{D}O_2$), oxygen consumption ($\dot{V}O_2$), and oxygen extraction ratio (O_2ER) were calculated, using the standard formulas. In addition, whole blood viscosity was measured using a Contraves LS 30 viscometer (Basel, Switzerland), measuring the blood viscosity at high (70 s^{-1}), medium (0.5 s^{-1}), and low (0.05 s^{-1}) shear rates. The microcirculation (sublingual mucosa) was visualized using orthogonal polarization spectral (OPS) imaging (Cytoscan; Cytometrics, Philadelphia, PA).[4] This device, which is commonly used in our hospital with approval of the Medical Ethical Committee, allows on-line microscopic observation of the microcirculation by use of a small endoscopic-like light guide placed on tissue surfaces. By placing this handheld light guide, which is attached to a video camera, on the sublingual mucosa of a patient, the human microcirculation can be visualized in a completely uninvasive way.

Preanesthetic medication consisted only of an oral dose of 50 mg atenolol, 6 h before baseline. Anesthesia was induced with 5 mg/kg thiopental, 2 μg/kg fentanyl, and 0.5 mg/kg rocuronium. After tracheal intubation, the lungs were ventilated with a mixture of oxygen in air (fractional inspired oxygen tension [FIO_2], 0.4), maintaining normocapnia. Anesthesia was maintained with isoflurane (end-tidal concentration, 0.7%) and fentanyl (100 μg/h); muscle relaxation was maintained with rocuronium. After induction of anesthesia, isovolemic hemodilution was performed by withdrawal of blood and simultaneous infusion of a 3.5% modified gelatin solution (Gelofusine®, molecular weight 35,000 Da; B.Braun Melsungen, Melsungen, Germany) in a ratio of 2:3. All measurements were repeated after exchange of 500, 1,000, 1,500, 2,000, and 2,500 ml, and after retransfusion of 500 ml autologous blood. Except for postoperative data, all measurements were performed before surgery was started, over a period of approximately 4 h. A selection of the parameters is given in table 1.

At baseline, a cardiac index above the normal range and a low systemic vascular resistance index were found. Exchange of up to 2,000 ml blood resulted in a decrease in hematocrit from 59% to 34%. Simultaneously the whole blood viscosity, which was 7.6, 64, and 121 mPa · s (at high, medium, and low shear rates, respectively) at baseline, decreased to 4.6, 18, and 41 mPa · s. During hemodilution, cardiac index increased only slightly despite a further decrease in systemic vascular resistance index. Pulmonary artery wedge pressure and central venous pressure increased, $\dot{D}O_2$ gradually decreased, and O_2ER increased from 10% at baseline to 15%.

On further hemodilution (to hematocrit 30%), $\dot{V}O_2$ suddenly decreased to a value of 40% of baseline, although the O_2ER remained at a low level (12%). At this last step of hemodilution, mean arterial blood pressure decreased to 77 mmHg, which was accompanied by acute ST depression and inverse T waves on the electrocardiograph. Simultaneously, the mixed venous base excess, which had been within the normal range of −3 to 3 mM, markedly decreased to −10.5 mM. Arterial base excess remained within the normal range. Because of these sudden changes, it was decided to retransfuse 500 ml autologous blood to a hematocrit of 37%. On retransfusion of this volume of autologous blood, the electrocardiographic abnormalities disappeared and $\dot{V}O_2$ increased above postanesthetic baseline values. Mixed venous base excess returned to baseline values. No additional blood was retransfused.

Orthogonal polarization spectral imaging showed an increased number of microcirculatory networks with significantly dilated venules as compared to normal (fig. 1). During the whole procedure, this image did not change.

After retransfusion, the surgical procedure was started. Because of metastases, surgery was discontinued after obtaining some tissue sam-

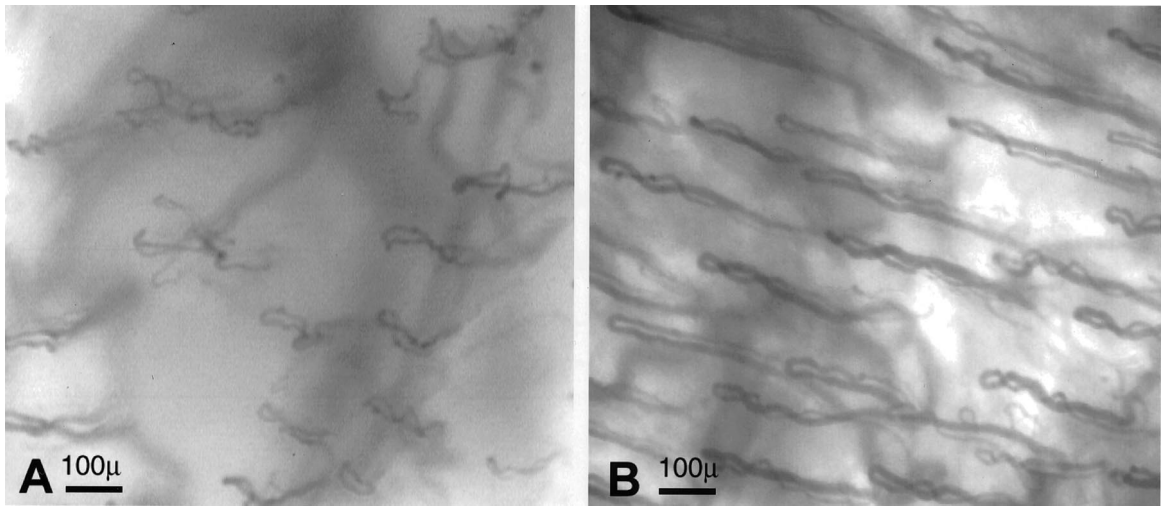

Fig. 1. Images of the sublingual microcirculation using orthogonal polarization spectral imaging (Cytoscan). (*A*) The microcirculation of a healthy, normocythemic volunteer and (*B*) the microcirculation of the presented polycythemic patient before induction of anesthesia. These images clearly show an increased number of microcirculatory networks with significantly dilated venules in the polycythemic patient as compared to normal. During the whole procedure this image did not change.

ples from the tumor. The postoperative course was uneventful, and treatment with chemotherapy was started.

Discussion

Alterations in hematocrit lead to corresponding changes in blood viscosity, which tend to cause blood flow to change in an inverse relation; isovolemic hemodilution is accompanied by an increase in carbon monoxide, whereas hemoconcentration (*e.g.*, chronic polycythemia) results in a decrease in carbon monoxide, due mostly to changes in systemic vascular resistance.[2,5] However, in the current chronically polycythemic patient, systemic baseline parameters were not as expected: the cardiac index was not decreased, but increased, and the systemic vascular resistance index was below normal levels. Together with the increased number of microcirculatory networks with dilated venules on the OPS images, these findings suggest shunting of blood at tissue level, which may explain the fixed low O_2ER, decreased systemic vascular resistance index despite high viscosity, and consequently the high cardiac index. Although to our knowledge OPS imaging has not been validated during polycythemic conditions, the OPS images, as well as the O_2ER, remained unchanged during hemodilution, suggesting that the possible shunting persisted. As blood is bypassing the capillary beds, more oxygen ends up at the venous side of the vascular bed without being utilized by the tissues, as is reflected in the current case by the mixed venous partial pressure of oxygen ($P\bar{v}o_2$) and mixed venous saturation ($S\bar{v}o_2$). Even when the $\dot{V}o_2$ started to decrease at hematocrit 34% (hemoglobin, 9.5 g/dl), suggesting that oxygen uptake was reaching a state of oxygen supply dependency, $P\bar{v}o_2$ and $S\bar{v}o_2$ showed little change.

The critical level of hemodilution at a hematocrit of 30–34% is in contrast with previous reports, where in anesthetized animals[1,3,6,7] and humans[8] a critical hematocrit of 9%–12% could be demonstrated, and in conscious humans no critical level of hemodilution could be determined.[9] At further hemodilution to a hematocrit of 30%, $\dot{V}o_2$ decreased severely, and cardiac ischemia became apparent on the electrocardiographic registration. This indicates that, in our patient at a hematocrit of 30% (hemoglobin, 8.0 g/dl), myocardial oxygenation was already compromised. Although this report encompasses only a single patient, such a severe decrease in $\dot{V}o_2$ is not likely to be caused by intermeasurement variations. In a recent study of hemodilution down to a hemoglobin concentration of 5.2 g/dl in awake volunteers, 3 of 55 subjects showed electrocardiographic changes, but not before a hemoglobin concentration between 5.0 and 6.7 g/dl.[10] Administration of 500 ml autologous blood not only restored the hemodynamics in our patient, but also led to what can be interpreted as an overshoot in $\dot{V}o_2$, which might have served to meet a possible oxygen debt.

Based on the above data, it may be hypothesized that chronic polycythemia can be compensated for by peripheral shunting of the blood. This adaptive response to conditions of increased blood viscosity does not seem to change during acute hemodilution, thereby decreasing the tolerance for acute isovolemic hemodilution. One might argue that advanced age or the chronic use of a β-blocking agent may have influenced the critical point of hemodilution. However, in clinical studies it has been demonstrated that these factors do not result in a functional impairment of the compensatory mechanisms at work during hemodilution.[11,12]

In conclusion, from the results of the presented case it may be hypothesized that chronic polycythemia can be compensated by peripheral shunting, of which the exact

nature is subject for further investigation. Although extrapolation beyond this case will be difficult, one should be cautious with acute hemodilution to subnormal levels in chronically polycythemic patients in the meantime, because this may be deleterious for the patient.

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The Use of Hypotensive Technique in Conjunction with Brachial Plexus Block Anesthesia for Surgery of the Upper Extremity

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SURGERY to internally fix pathologic fractures of the humerus may result in substantial blood loss for several reasons. For one, it is difficult to apply an effective tourniquet because of the proximal location of many of these lesions. Furthermore, pathologic humeral lesions may be highly vascular, leading to bleeding when excised.[1,2] We report the use of hypotensive anesthesia, in conjunction with interscalene block anesthesia, to manage surgery in a patient with such a lesion.

Case Report

The patient is a 70-yr-old man (95 kg, 170 cm) who had a pathologic fracture to his left humerus. His medical history was notable for renal stones, benign prostatic hypertrophy, and gout, all of which were well-controlled. His only medication was allopurinol. His physical exam was remarkable for decreased range of motion of the left arm, due to pain. He had normal motor and sensory function of left wrist flexors and extensors. The radiographic films of the left humerus revealed a pathologic fracture of the shaft with a 2-cm, round, lytic lesion in the proximal humeral diaphysis (fig. 1). A bone scan revealed uptake in the region of the pathologic fracture, as well as symmetric uptake at the acromioclavicular and sacroiliac joints thought to be consistent with degenerative arthritis. All preoperative blood work was normal except for lactate dehydrogenase level of 561 U/l. His preoperative blood pressure was 150/80 mmHg, with a heart rate of 70 beats/min.

An interscalene block was performed before the administration of sedation by seeking a shoulder paresthesia with a 23-gauge needle. A mixture of 30 ml mepivacaine (1.5%), 20 ml bupivacaine (0.75%), and 200 μg epinephrine was injected in divided doses. Within 2 min, the pain in the arm resolved and the patient was sedated and put in the lateral decubitus position. Inflatable Shoulder-Floats (Trimline Medical Products, Branchburg, NJ) were placed beneath the chest wall and head to decompress the dependent shoulder and keep the neck aligned. Lateral stability was maintained with a bean bag. The patient was sedated with a mixture of intravenous fentanyl (100 μg/h) and propofol (200 mg/h). A 20-gauge catheter was then inserted into the dependent radial artery. Hypotension was induced with 20 mg hydralazine. Mean arterial pressure decreased from 90 mmHg to approximately 55 mmHg. Thirty minutes later, 2 mg metoprolol was given intravenously in divided doses, which reduced the heart rate from 80 to 70 beats/min. Mean arterial pressure and heart rate remained stable thereafter. Sao_2 was 97–98% throughout surgery, with the patient receiving nasal oxygen at 3 l/min.

An approximately 17-cm-long incision was made posteriorly from the triceps insertion continuing proximally. The radial nerve was dissected out and visualized. The pathologic fracture site was identified and a frozen section revealed a plasmacytoma. The fracture was fixed with a plate and screws. Bone cement mixed with tobramycin was then placed into the bone defect for additional stability, followed by copious irrigation and closure. Intraoperative blood loss was estimated to be 400 ml and 1,500 ml lactated Ringer's intravenous fluid was administered.

The patient's course that evening in the postanesthesia care unit was uneventful, and he was soon transferred to the floor with an intravenous morphine patient-controlled analgesia. On postoperative assessment later that evening, he was found to be comfortable, with some residual decreased sensation in the hand as well as weakness of his wrist extensors. On postoperative day 1, the patient had complete return of sensory and motor function. He received a total dose of 30 mg intravenous morphine via patient-controlled analgesia, which was ini-

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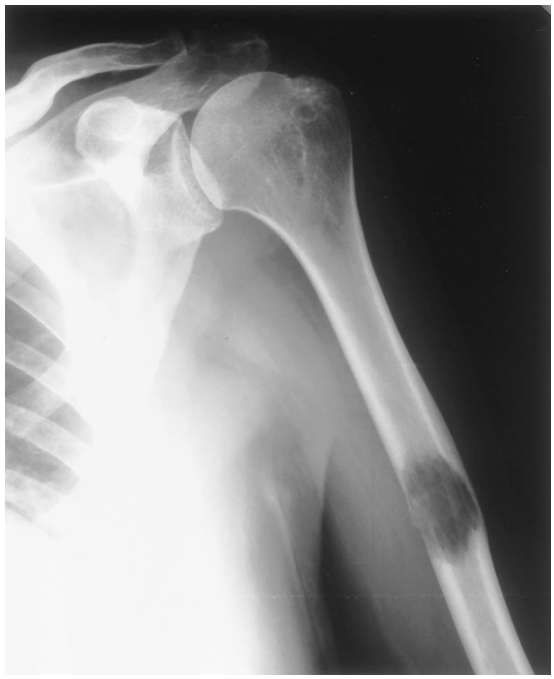

Fig. 1. Preoperative anteroposterior radiograph of the left humerus demonstrating lytic lesion in the proximal one-half diaphysis, with pathologic fracture.

tiated 4.5 hours after surgery. Approximately 30 h after starting his intravenous morphine patient-controlled analgesia, he was converted to oral analgesics. His preoperative hemoglobin was 15.8 mg/dl, and 13.1 mg/dl the next day. He did not require any transfusion of blood products. He was discharged after an uneventful hospital course on postoperative day 4.

Discussion

Conventional anesthetic approaches in this case would include brachial plexus block with normotension or general anesthesia with either normotension or induced hypotension. As a tourniquet was likely to encroach upon the surgical field, it was decided that intraoperative hypotension would be a better alternative to reduce the possibility of significant blood loss during surgery. Induced hypotension for upper extremity surgery is typically performed with general anesthesia.[3] One of the appeals of a brachial plexus block is that it is easier to control pain immediately after surgery. By inducing intraoperative hypotension with a brachial plexus block, we were able to achieve the benefits of control of bleeding during surgery with effective pain control immediately after surgery.

Hypotension was readily induced by using hydralazine with only a slight compensatory tachycardia. Heart rate was maintained throughout surgery at approximately 70 beats/min and mean arterial pressure 55 mmHg after the administration of apresoline and metropolol. Thereafter, stability was maintained with little intervention other than intravenous sedation with propofol and crystalloid administration. This may have been partly because of effective sedation and optimal patient positioning, as well as an intense brachial plexus blockade. In addition, an interscalene block may partially block the cardiac accelerator nerve to the sinus node,[4] minimizing the tendency to reflex tachycardia with hypotension.

Induced hypotension in elderly patients with vascular comorbidities during general anesthesia remains controversial.[3] By contrast, induced hypotension (mean arterial pressure 45–55 mmHg) with extensive epidural blockade in the elderly and in patients with hypertension or atherosclerotic heart disease appears to be safe when properly administered.[5–7] On the other hand, a well-conducted general anesthetic with induced hypotension in elderly high-risk patients lying flat may be equally safe, although this is yet to be documented in large series of patients.

This patient recovered well from the surgery, requiring no blood transfusion and moderate doses of narcotic postoperatively. Induced hypotension in combination with brachial plexus block may be a useful approach in selected cases such as this.

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Severe Oxyhemoglobin Desaturation during Induction of Anesthesia in a Patient with Congenital Methemoglobinemia

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CONGENITAL methemoglobinemia is a rare disease caused by the oxidation of iron from the ferrous to the ferric state in the protoporphyrin ring, which forms the prosthetic group (heme) of hemoglobin.[1] The current report presents a patient with congenital methemoglobinemia who developed severe oxyhemoglobin desaturation during induction of anesthesia.

Case Report

The patient was a 22-yr-old man who was scheduled for turbinectomy 1 month ago in another institution, but the operation was cancelled after induction of anesthesia with thiopental because the patient developed severe cyanosis and multiple ventricular extrasystoles. The patient was ventilated with 100% oxygen, which was followed by improvement of cyanosis and restoration of normal sinus rhythm.

The patient was rescheduled in our institution for the same surgery. Preoperative medical clearance did not reveal any cardiopulmonary disease and he was not on any medication. He was premedicated with meperidine (60 mg), promethazine (25 mg), and atropine (0.5 mg) intramuscularly. In the operating room, it was noticed that the patient's fingers and lips were blue.

Pulse oximetry on room air revealed an oxygen saturation measured by pulse oximetry (Spo_2) of 91%. The pulse oximeter was checked on the anesthetist's finger and showed an Spo_2 of 98%. Congenital methemoglobinemia was suspected. An arterial canula was inserted before induction of anesthesia, and an arterial blood gas analysis, measured by ABL700 series radiometer (Copenhagen, Denmark), revealed the following results: arterial oxygen concentration (Sao_2), 96.8% (functional saturation); partial pressure of alveolar oxygen (PAo_2), 90 mmHg; oxyhemoglobin, 79.2% (fractional saturation); reduced hemoglobin, 2.2%; carboxyhemoglobin, 0.2%; methemoglobin, 18.4%; hematocrit, 54.7%; hemoglobin, 17.9 g/dl. Lidocaine, 1 mg/kg, was injected intravenously before induction of anesthesia in order to minimize pain during the subsequent intravenous propofol administration, and to blunt the hemodynamic response to tracheal intubation. The patient was not preoxygenated before the injection of lidocaine. The patient immediately developed unconsciousness and apnea, associated with severe cyanosis and a decrease in Spo_2 to 79%. An arterial blood sample for gas analysis was taken, and intermittent positive pressure ventilation with 100% face mask oxygen was started; the Spo_2 increased from 79% to 91%. Arterial blood gas analysis during the apneic episode showed a Pao_2 of 60 mmHg, associated by a decrease of the oxyhemoglobin saturation to 72%, although there was no significant change of the methemoglobin concentration. Repeating arterial blood gas analysis after ventilation with 100% oxygen revealed the following: Sao_2, 99.5%; Pao_2, 481 mmHg; oxyhemoglobin, 80%; methemoglobin, 19.4%. Methylene blue, 1 mg/kg, was injected intravenously over 3 min. The patient regained consciousness 10 min later, and the Spo_2 increased from 79% to 96%. An arterial blood gas analysis showed the following: Sao_2, 99.6%; Pao_2, 324 mmHg; oxyhemoglobin, 93.9%; methemoglobin, 4.7%. The operation was cancelled.

A summary of the changes in the pulse oximetry, the arterial blood gases, as well as the methemoglobin concentrations on room air during apnea, after ventilation with 100% oxygen, and after methylene blue administration, are shown in table 1.

Discussion

The current patient had congenital methemoglobinemia, as evidenced by the high methemoglobin concentration (18.4%), and the low fractional oxyhemoglobin saturation (79.2%), in the presence of a normal Pao_2 and the absence of exposure to any oxidant stress. The intravenous administration of lidocaine was complicated by severe oxyhemoglobin desaturation that was managed by ventilation with 100% oxygen and administration of methylene blue.

The normal hemoglobin molecule contains a reduced (ferrous) iron molecule [Fe^{++}]. Hemoglobin-containing iron in the ferric state [Fe^{+++}] is termed methemoglobin. In normal individuals, a small amount of the hemoglobin in erythrocytes is oxidized to methemoglobin. Methemoglobin is reduced to deoxyhemoglobin enzymatically, hence methemoglobin concentration remains less than 2%. Cytochrome b5 reductase (nicotinamide-adenine dinucleotide reduced form [NADH] reductase) is the enzyme responsible for methemoglobin reduction. Patients homozygous for this enzymatic deficiency have congenital methemoglobinemia.[2] The acquired form of methemoglobinemia results from exposure to an appropriate oxidant stress in sufficient quantities to overwhelm the metabolic process that reconverts methemoglobin to hemoglobin.[3] In patients with acquired or congenital methemoglobinemia, cyanosis is detectable when methemoglobin concentration exceeds 1.5 g/dl. Our patient presented with cyanosis without exposure to any oxidant stress because he had a methemoglobin concentration of 3.29 g/dl (18.4%). The absorbance characteristics of methemoglobin are such that the pulse oximeter shows an Spo_2 around 85%, regardless of the Pao_2.[4]

When the iron in a hemoglobin molecule is oxidized to

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Table 1. Changes in Pulse Oximetry, Arterial Blood Gases, and Methemoglobin Concentrations on Room Air, during Apnea and Ventilation with 100% Oxygen, and after Methylene Blue Administration

		Arterial Blood Gases			
	Pulse Oximetry (%)	Sa_{O_2} (%)	Sf_{O_2} (%)	Methemoglobin (%)	Pa_{O_2} (mmHg)
Room air	91	96.8	79.2	18.4	90
Apnea	79	91	72	18	60
Ventilation with 100% oxygen	91	99.5	80	19.4	481
Methylene blue	96	99.6	93.9	4.7	324

$$Sa_{O_2} = \text{functional saturation} = \frac{O_2Hb}{O_2Hb + RHb} \times 100\%.$$

$$Sf_{O_2} = \text{fractional saturation} = \frac{O_2Hb}{O_2Hb + RHb + COHb + MetHb} \times 100\%.$$

Pa_{O_2} = arterial oxygen tension.

the ferric state, not only the heme group is incapable of combining with oxygen, but the affinity of the remaining heme groups for oxygen is increased because of allosteric effects. This is the molecular basis of the left-shifted oxyhemoglobin dissociation curve in patients with methemoglobinemia. Thus, methemoglobinemia can severely limit oxygen delivery not only because the oxygen carrying capacity of the hemoglobin molecule is reduced, but also because the oxygen carried by the remaining normal heme groups is less readily released to the tissues.[5]

Our patient developed severe cyanosis on a previous occasion and ventricular extrasystoles after an induction dose of thiopental. The severe oxyhemoglobin desaturation is not attributed to an increased methemoglobin concentration, because thiopental is not known to be an oxidant stress. In the second occasion, he developed unconsciousness, apnea, and a decrease of Sp_{O_2} to 79% after intravenous lidocaine. Local anesthetics such as prilocaine and benzocaine have been associated with methemoglobin formation.[3,6] However, it is controversial whether lidocaine can induce methemoglobinemia.[7–9] In our patient, lidocaine administration did not worsen methemoglobinemia. In fact, what presumably occurred is that even a "normal" degree of respiratory depression or decreasing Pa_{O_2} after any respiratory depressant, and not lidocaine *per se* (which would be unnoticed in normal patients), resulted in marked desaturation in a patient with congenital methemoglobinemia who had only a modest amount of normal hemoglobin available.

In our patient, the severe oxyhemoglobin desaturation after lidocaine administration was managed by ventilation with 100% oxygen. Also, the intravenous administration of methylene blue 1 mg/kg reduced the methemoglobin concentration from 18.4% to 4.7%. Methylene blue is the cofactor for nicotinamide-adenine dinucleotide phosphate reduced form [NADPH] methemoglobin reductase. This enzyme remains inactive physiologically, but will be activated by methylene blue.[1] It is recommended that patients with congenital methemoglobinemia should be adequately oxygenated before, during and after recovery from anesthesia, in order to avoid hypoxemia and prevent further detrimental decrease in the oxyhemoglobin saturation. Also, methylene blue may be administered prophylactically before induction of anesthesia.

The current report presents a patient with congenital methemoglobinemia with methemoglobin concentration of 18.4% and Sp_{O_2} of 91%. The oxygen delivery in the patient may be compromised by the decreased oxyhemoglobin concentration and by the shift of the oxyhemoglobin dissociation curve to the left. The patient developed severe oxyhemoglobin desaturation after intravenous administration of lidocaine. Worsening of methemoglobinemia did not cause the patient's cyanosis. In fact, what presumably occurred is that even a "normal" degree of respiratory depression after any respiratory depressant (which would be unnoticed in normal patients) may have resulted in marked desaturation in a patient with congenital methemoglobinemia.

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Sickle Cell–induced Peripheral Neuropathy following Spinal Anesthesia for Cesarean Delivery

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SICKLE cell disease is a group of hematologic disorders caused by a single base substitution of the β-globin subunit of hemoglobin. When deoxygenated, the affected erythrocytes can polymerize, metamorphosing from flexible nourishing cells to unyielding obstacles that occlude blood flow and result in tissue and nerve ischemia. Affecting 1 of every 600 African-Americans and a significant percentage of African, Mediterranean, and Indian individuals, sickle cell disease is the most common clinically significant hemoglobinopathy in the United States.[1] We report a case of a lower extremity peripheral neuropathy induced by a sickle cell vasoocclusive crisis after spinal anesthesia for cesarean delivery.

Case Report

A 25-yr-old African-American, primaparous woman with a 31-week breech presentation, singleton gestation, was admitted for premature rupture of membranes, chorioamnionitis, and severe oligohydramnios. Past medical history was notable for severe sickle cell disease (Hemoglobin *SS*), which in the previous 2 yr had required a permanent portacath placement and frequent hospital admissions for management; two months previous, the patient had been admitted for pneumonia and management of a vasoocclusive crisis. With the decision for a cesarean delivery and the administration of antibiotics, the patient was taken to the operating room and placed in the right lateral decubitus position. Following the placement of standard monitoring, an intravenous lactated Ringers bolus and aseptic preparation, a spinal anesthetic (12 mg hyperbaric bupivacaine, 0.75%, with 10 μg fentanyl), was placed on the first attempt with a 25-gauge Whitacre needle at the L3–L4 interspace. The patient was placed supine with a left lateral tilt and the delivery proceeded uneventfully with no hemodynamic, anesthetic or obstetric complications.

Postoperatively, the spinal blockade underwent an expected sensory and motor resolution. A single dose of 30 mg intramuscular ketorolac was given to alleviate mild abdominal and bilateral shoulder discomfort, and the patient was started on a hydromorphone patient controlled intravenous analgesia pump. On the morning of postoperative day 1, the patient reported weakness, numbness, and tingling of the lower left extremity, a location consistent with previous vasoocclusive pain crises. On examination, decreased deep tendon reflexes (1/2), and diminished strength and sensation of the affected limb consistent with a L3–L5 plexopathy was noted. The lower right extremity had a normal examination, and neither back discomfort nor bladder and bowel involvement was observed. Conservative therapy with fluids, oxygen by nasal cannula, and additional pain relief were administered, and a slight improvement in symptoms was noted by that evening.

On postoperative day 2, the patient awoke with significant dyspnea, pleuritic chest pain, and severe discomfort of the upper and lower back, shoulders, and the lower left extremity. On examination, fine inspiratory and expiratory crackles, tachypnea and tachycardia, but a stable blood pressure, were observed. Although consistent with a sickle crisis, the symptoms were also suggestive of a pulmonary embolus. A ventilation–perfusion scan indicated a greater than 50% likelihood of a pulmonary embolus; however, as anticoagulation was being discussed with hematology consultants, the patient's clinical condition progressed to include bilateral motor and sensory deficits in a T11–S2 distribution with diminished bowel and bladder control. While urgent neurology consultation was obtained, magnetic resonance imaging of the lumbosacral spine was performed that demonstrated no evidence of an epidural hematoma. Despite negative lower extremity noninvasive studies and the inability to confirm the diagnosis of a pulmonary embolus with a pulmonary arteriogram because of the patient's refusal of the procedure, empiric therapy with intravenous heparin and oral enoxaparin was started. Significant interval improvement occurred in the pulmonary and lower extremity symptoms and the patient was discharged on postoperative day 9, with complete motor, bladder and bowel recovery, and a mild sensory deficit of the lateral aspect of the left heel.

Discussion

The ability to polymerize when deoxygenated is unique to sickle hemoglobin and responsible for the cellular injury observed with the disease. A disease with variable expression, the symptoms of sickle disease are modified by several factors, the most influential being genotype, of which the homogenous *SS* disease has the most significant morbidity and mortality.[2] Although no single mechanism is responsible for vasoocclusion, the leading catalyst is believed to be the cellular efflux of potassium induced by deoxygenation, which in turn produces an increase in the density and tendency of sickle cells to interact with each other, endothelial cells, and plasma constituents.[3] These adhesive interactions often lead to endothelial cell damage and vasoconstriction, and ultimately culminate in acute, sometimes fatal, episodes of vasoocclusion.[4] While neurologic sequelae frequently occur, they are principally confined to the brain and its circulation[4]; only rarely are the spinal cord or peripheral nerves involved.

In our case, sickle cell disease complicated the diagnosis of progressive neurologic symptoms. Although the unilateral deficit was initially similar in expression and distribution as previous sickle occlusion attacks, the re-

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cent postpartum status mandated additional considerations, including alterations because of pregnancy, as well as obstetric and anesthetic complications. Pregnancy and delivery *per se* are commonly associated with neurologic injuries; 1 in 2,600–6,400 deliveries is affected in such a manner.[5] Frequently unilateral, these postpartum injuries are usually preceded by prepartum or intrapartum neurologic symptoms, prolonged labors, or instrumental deliveries.[5] Spinal anesthesia, which can also be unilateral in distribution and recovery, is rarely associated with significant or persistent neurologic injuries[5]; when they do occur, some indication is usually noted during the placement of the technique. In prospectively investigating 40,640 spinal anesthetics, Auroy *et al.*[6] noted only 24 cases of neurologic injury (19 radiculopathy, 5 cauda equina syndrome), of which two thirds experienced pain on needle insertion or local anesthetic injection. Although transient neurologic syndromes occur with modest frequency, including in patients undergoing cesarean delivery, the classic symptoms of low back pain and or dysesthesia with radiation to the buttocks, thighs, or legs were not consistent with our case. As our patient experienced an uncomplicated cesarean delivery without prolonged retractor use or a preceding labor, and an equally uncomplicated placement and hemodynamic sequlae from a spinal anesthetic, the influence of the pregnancy, as well as obstetric and anesthetic complications, as the etiology for the deficit was less compelling. While sickle cell–induced peripheral neuropathies are usually bilateral, unilateral symptoms have been reported,[7] as with our patient just 2 months previously.

Although symptomatic improvement after therapy directed towards a sickle cell occlusive crisis was initially observed, the acute onset and progression of clinical signs suggestive of a pulmonary embolus and a possible epidural or spinal hematoma prompted additional diagnostic and treatment considerations. The diagnoses of pulmonary emboli and central neuraxial hematomas have distinct and dichotomous therapeutic goals. Although thrombolytic and fibrinolytic agents are the recommended treatment for pulmonary emboli, the use of such therapies has the potential to cause or extend hematomas. With a ventilation–perfusion scan indicative of a pulmonary embolus and a magnetic resonance imaging scan negative for a hematoma, thrombolytic therapy was commenced, and an almost complete resolution of symptoms occurred. Although the treatment of sickle cell disorders does not routinely include anticoagulants, recent evidence strongly supports the inhibition of sickle erythrocyte adhesion to the endothelium by heparin[8]; moreover, in the setting of sickle cell–induced cerebral thrombosis, the use of heparin has been recommended.[9] Of interest, although epidural analgesia has been promoted as a method to effectively treat sickle cell crises unresponsive to conventional management,[10] we chose to avoid this option because of the administration of anticoagulants and the potential to obscure signs of neuropathy progression or regression.

Despite the favorable outcome in our patient, this case underscores the need to consider the independent influences of pregnancy, labor and delivery, obstetric and anesthetic interventions, as well as the established comorbid conditions when presented with a peripheral neuropathy in a patient with sickle cell disease.

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