CASE REPORTS

Cardiovascular Depression after Brachial Plexus Block in Two Diabetic Patients with Renal Failure

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In diabetic patients, the 5-yr mortality rate may exceed 50% after the development of cardiovascular autonomic neuropathy.[1] Many of these deaths are not explained by postmortem studies. Recently, episodes of bradycardia and hypotension unresponsive to atropine and ephedrine have been reported during general anesthesia in diabetic patients with advanced autonomic neuropathy.[2–4] A more recent study has demonstrated an increased cardiovascular lability in anesthetized diabetic patients.[5]

This report describes progressive bradycardia and hypotension that developed suddenly in two diabetic patients approximately 20 min after brachial plexus block was performed for creation of an arteriovenous shunt. The cardiovascular depression responded promptly to external cardiac massage and epinephrine or isoproterenol. Both patients had evidence of advanced autonomic neuropathy and died of cardiorespiratory arrest at home within a few years of these incidents.

CASE REPORTS

Case 1. A 64-yr-old man, 170 cm and 54 kg, was admitted for creation of an arteriovenous shunt. The patient had hypertension and a 30-yr history of adult-onset type II diabetes mellitus and was in renal failure secondary to diabetic nephrosclerosis. The patient complained of post-prandial fullness, occasional bouts of diarrhea, a severe burning pain and lack of sweating in both lower extremities, and severe orthostatic hypotension that prevented him from standing without assistance. Current medications included ferrous sulfate, prazosin, furosemide, and NPH and regular insulin. Physical examination was remarkable for angiopathic retinal changes and decreased sensation of the lower extremities. Blood pressure was 168/98 mmHg. Heart rate was 78 beats per min. Chest roentgenogram showed a mild cardiomegaly without evidence of congestive heart failure. Electrocardiogram showed changes consistent with previous inferior wall myocardial infarction and nonspecific ST-segment and T-wave abnormalities, but the patient denied remembering symptoms suggestive of angina pectoris. The hemoglobin was 7.8 g/dl. The total protein was 7.0 g/dl, with albumin 2.8 g/dl. The serum creatinine and blood urea nitrogen concentrations were 5.0 mg/dl and 72 mg/dl, respectively. The serum potassium and

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glucose concentrations were 4.2 mEq/l and 128 mg/dl, respectively. Arterial blood gas values were pH, 7.38; Pa_{O_2}, 85 mmHg; and Pa_{CO_2}, 29 mmHg.

The patient received morphine sulfate 8 mg im approximately 2 h before the operation. Insulin was withheld. In the operating room, diazepam 7.5 mg was given intravenously in increments of 2.5 mg. Left interscalene block was performed using 45 ml 0.25% bupivacaine and 0.75% lidocaine, eliciting paresthesias in the distribution of the ulnar nerve. Blood was not aspirated during the injection. Oxygen 6 l/min was given by nasal cannula. A satisfactory motor and sensory block in the distribution of the left brachial and cervical plexuses was obtained in 15 min. Horner's syndrome was not present. Vital signs were stable.

A few minutes later, the blood pressure and pulse rate decreased rapidly from 160/100 to 78/52 mmHg and 72 to 30 beats per min, respectively. The patient remained lucid and was breathing normally throughout. Ephedrine 15 mg iv elicited no response. The bradycardia progressed to asystole. The trachea was intubated; the lungs were ventilated with 100% oxygen; and external cardiac massage was performed. Atropine 1.2 mg was administered without response. However, the heart rate responded quickly to isoproterenol 0.2 mg iv. Venous blood drawn during the resuscitation, *i.e.*, approximately 20 min after injection of the local anesthetic solution, was analyzed for drug concentrations and revealed serum concentrations of diazepam of 0.1 μg/ml, lidocaine 3.2 μg/ml, and bupivacaine 1.8 μg/ml. Serum concentrations of glucose and potassium were reported as 180 mg/dl and 4.4 mEq/l, respectively. Ventilation was manually controlled for approximately 20 min when spontaneous ventilation returned. Fluoroscopy showed bilateral diaphragmatic movement. The pupils remained equal and reactive.

In the recovery room, arterial blood gas values were within normal limits, and the electrocardiogram showed no evidence of myocardial ischemia. The endotracheal tube was removed. Sensory examination revealed total sensory and motor blockade of the left neck and upper extremity, with slight sensory impairment and some weakness of the right upper extremity. Serial cardiac enzyme values and electrocardiograms ruled out myocardial ischemia or injury. Two weeks later, an arteriovenous anastomosis was created under general anesthesia with isoflurane in nitrous oxide and oxygen, and fentanyl. The patient was discharged home on the 6th postoperative day.

One year later, the patient had an amputation of the right lower extremity under spinal anesthesia for peripheral vascular disease. During admission, the patient was noted to have frequent episodes of asymptomatic hypoglycemia. One month after the amputation, in the dialysis center just prior to hemodialysis, the patient suddenly developed bradycardia that progressed to asystole. The patient responded to external cardiac massage and epinephrine. The electrocardiogram revealed a sinus rhythm with a first-degree arterioventricular (AV) block that eventually reverted to sinus rhythm. The chest roentgenogram was normal.

One month after the incident in the dialysis center, the patient's cardiovascular reflexes were studied. The details of the methods used and the definition of normal values are described elsewhere.[6] There was essentially no RR-variation during deep breathing, *i.e.*, the maximum–minimum heart rate, 1 beat per min (normal is ≥10 beats per min). The Valsalva ratio (the ratio of longest RR-interval after release to the shortest RR-interval during strain) was 1.02 (normal value is

>1.10). There was no change in diastolic blood pressure during the 4-min handgrip test. The findings were consistent with advanced cardiac parasympathetic and generalized sympathetic neuropathy. Several months later, the patient died suddenly at home. Postmortem examination was not performed.

Case 2. A 62-yr-old man, 173 cm and 66 kg, was scheduled for creation of an arteriovenous shunt for hemodialysis. The patient, a known hypertensive, had a 17-yr history of type II diabetes mellitus and was in renal failure secondary to diabetic nephrosclerosis. The patient had had a recent episode of congestive heart failure. He also had a hypotonic neurogenic bladder and decreased sweating in the lower extremities, and complained of orthostatic dizziness. Current medications included ferrous sulfate, chlorthalidone, methyldopa, a potassium supplement, and NPH insulin. Pertinent findings on physical examination included resting tachycardia 112–115 beats per min, blood pressure 170/98 mmHg, and blindness due to previous enucleation of the right eye and neovascularization with scarring of the left retina. Pain and temperature sensations were decreased, and there was loss of hair in the lower extremities. The serum blood urea nitrogen concentration was 160 mg/dl, and the serum creatinine concentration was 11.8 mg/dl. The serum potassium and glucose concentrations were 3.8 mEq/l and 249 mg/dl, respectively.

After admission, peritoneal dialysis was performed. The preoperative hemoglobin was 6.1 g/dl, hematocrit 19.0%, serum sodium 138 mEq/L, serum potassium 4.5 mEq/l, serum blood urea nitrogen 112 mg/dl, serum creatinine 9.2 mg/dl, and total protein 5.6 g/dl, with albumin 2.9 g/dl. Arterial blood gas values were pH, 7.34; Pa_{O_2}, 75 mmHg; and Pa_{CO_2}, 26 mmHg. Chest roentgenogram was normal. Electrocardiogram showed a sinus tachycardia and nonspecific ST-segment and T-wave abnormalities.

The patient received morphine 10 mg and hydroxyzine 50 mg im 90 min before the operation. In the operating room, fentanyl 50 μg iv was given. By eliciting paresthesia in the distribution of the median and ulnar nerves, a left axillary block was performed with 40 ml of 1.25% lidocaine with epinephrine 1/200,000. Blood was not aspirated at any time during the injection. A satisfactory motor and sensory block was obtained 15 min later. Oxygen 6 l/min was given by nasal cannula. The patient was conscious, and the vital signs were stable.

Approximately 25 min after the block was performed and shortly after incision, the patient suddenly began to snore loudly and the heart rate was observed to have decreased from 98 to 58 beats per min and the blood pressure to have decreased from 192/80 to 100/40 mmHg. There was no response to atropine 0.6 mg iv. The bradycardia and hypotension quickly progressed; there was no palpable pulse and the heart rate was 30 beats per min. The trachea was intubated and external cardiac massage was started. A repeat dose of atropine 0.4 mg iv and administration of ephedrine 10 mg iv were ineffective, but epinephrine 0.3 mg iv resulted in the rapid return of sinus tachycardia and blood pressure. The patient was arousable, breathing spontaneously, and followed commands. Small incremental doses of metaraminol were administered for maintenance of blood pressure, and the operation was completed without further incident.

Serial cardiac enzyme studies and electrocardiograms ruled out myocardial infarction. After hemodialysis, the patient underwent an uneventful cystoscopic examination under general anesthesia with halothane in nitrous oxide and oxygen.

The patient died at home of sudden cardiorespiratory arrest approximately 2 yr after the incident described above. No autopsy was performed.

DISCUSSION

Both patients had long-standing diabetes with evidence of widespread microangiopathic organ involvement, *i.e.*, nephropathy, retinopathy, and peripheral somatic neuropathy, and were in renal failure secondary to diabetic neuropathy. Both patients had orthostatic symptoms and sweating abnormalities in the lower extremities, in addition to some of the other symptoms of autonomic neuropathy, *e.g.*, gastroparesis, intermittent nocturnal diarrhea, or neurogenic bladder. The results of cardiovascular reflex studies performed in the patient with incapacitating orthostatic hypotension (case 1) were consistent with denervation of the heart and generalized sympathetic neuropathy. Although cardiovascular reflexes were not studied in the other patient, who suffered from frequent orthostatic dizziness, it may be assumed that this patient had had advanced cardiovascular autonomic neuropathy since abnormal results are almost always present in diabetics with peripheral neuropathy, retinopathy, or nephropathy, as are the clinical symptoms of autonomic neuropathy.[1] In addition, renal failure is associated with abnormality in the baroreceptor system.[7]

Intravascular injection of local anesthetics is unlikely to have been the cause of the cardiovascular collapses that developed in our patients. Both interscalene and axillary approaches were achieved by injecting a local anesthetic at the site where a distinct paresthesia was elicited. Blood was not aspirated at any time during the injection in either patient. Serum concentrations of local anesthetics measured at the time of resuscitation in one patient were within the ranges expected to occur with the doses employed.[8] In addition, the cardiovascular depression due to intravascular injection would be expected to develop sooner. Similarly, complications of interscalene block, *e.g.*, intrathecal injection, extensive epidural spread, or phrenic nerve paralysis, are unlikely to have occurred. Anesthesia was confined in the distribution of the brachial and cervical plexuses, and fluoroscopy excluded phrenic nerve paralysis. Bilateral sympathetic blockade may have occurred in this patient (case 1), since a large amount of local anesthetic deposited in the vicinity of the paravertebral space travels into the epidural space, as demonstrated by the contralateral spread of anesthesia in our patient.[9] However, Horner's syndrome did not occur. These complications of interscalene block are not known to occur when the brachial plexus is blocked by the axillary approach.[10]

Page and Watkins postulated that death (in cases unexplained by autopsy) in diabetics may be due to abnormalities in the chemoreceptor pathways secondary to neuropathy.[2] The 12 perioperative cardiorespiratory or respiratory arrests they reported were associated with general anesthesia, depressant drugs, or pneumonitis. But a subsequent study in diabetics showed that the chemoreceptor pathways appeared intact,[11] and other reports have described multiple cardiac arrests in long-term diabetic patients under general anesthesia in whom venti-

lation was mechanically controlled and without evidence of hypoxia.[3,4] These communications suggest that respiratory depression may not necessarily be the primary cause of some of the cardiorespiratory arrests that have been described in diabetic patients. Our patients had received morphine plus diazepam or fentanyl prior to the brachial plexus block, but the doses were not excessive. However, benzodiazepines potentiate the respiratory effect of opiates.[12] Although respiratory depression due to these drugs could not be ruled out, respiratory symptoms were not observed in either patient prior to the cardiovascular depression. Instead, one patient who received fentanyl appeared to be hyperpneic at the time of the incident. The other patient suddenly developed another cardiorespiratory arrest approximately 1 yr later in the absence of any medication and shortly before hemodialysis.

High tissue concentrations of local anesthetics depress the myocardium and the peripheral vasculature,[13-15] but the serum concentrations resulting from various forms of neural blockade do not show significant cardiovascular effects even in patients with severe coronary heart disease.[16-18] However, the cardiovascular depression developed in our patients at the point when the peak serum concentration of local anesthetics is expected to occur after brachial plexus block, approximately 20-25 min after the injection.[19] This coincidence suggests that myocardial depression may have been related to the systemic toxic effects of local anesthetics. Both patients had a relatively high dose of local anesthetics. The combined serum concentration of local anesthetics that we measured in one patient was equivalent to approximately 11 μg/ml lidocaine at the time of resuscitation. Although this concentration approaches the seizure threshold in humans, it is below that which produces cardiovascular collapse.[20] Both patients responded to the resuscitation easily, whereas resuscitation may be extremely difficult in patients receiving a cardiotoxic dose of local anesthetics, particularly bupivacaine.[20]

The cardiovascular system, in the absence of sympathetic innervation, is less able to withstand hypoxia, blood loss, or toxic substances. A recent study demonstrated impaired cardiovascular homeostatic response to general anesthesia in diabetic patients with advanced autonomic neuropathy.[5] Nevertheless, cardiovascular autonomic neuropathy alone, i.e., autonomic denervation of the heart and generalized sympathetic neuropathy, may not solely explain the cardiovascular collapse in our patients. Similar cardiovascular depression has not been reported in nondiabetic patients with coronary artery disease or in nondiabetic patients receiving beta-adrenergic antagonists or those with a transplanted heart. In one patient, however, diazepam given intravenously prior to the block may have contributed in the pathogenesis of the collapse. Diazepam depresses cardiovascular function in combination with high-dose morphine and may potentiate the cardiac toxicity of local anesthetics.[21] It has been reported that diazepam increases the incidence of bupivacaine-induced tachyarrhythmia in rats.[22]

Our patients both had abnormal ST segments as well as T waves, and either cardiomegaly on admission or a recent episode of congestive heart failure, which may have been secondary to hypertensive and/or coronary heart disease. They both were hypertensive, and one had electrocardiographic evidence of previous myocardial infarction. However, a survey of cardiac function in diabetic patients has shown a close relationship between left ventricular function and microvascular complications of diabetes.[23] Therefore, diabetic cardiomyopathy may not be excluded in either of our patients since both had widespread microangiopathic involvement as evidenced by advanced retinopathy, nephropathy, and peripheral neuropathy.

The primary cause of the cardiovascular depression that developed in our patients remains to be elucidated. However, the presence of advanced autonomic neuropathy, the clinical evidence of heart disease, and the timing of the cardiovascular collapse that corresponded to expected peak concentration of local anesthetics suggest that the episodes may have been due to the depressant effects of relatively high serum concentration of local anesthetics on myopathic hearts in patients devoid of sympathetic compensation. Premedication and intraoperative sedation may have shared in the pathogenesis. Although regional anesthesia may be considered a preferred anesthetic technique in diabetic patients,[24] our experience suggests that there is a need for caution when large quantities of local anesthetics are injected into patients with long-term diabetes and evidence of widespread microangiopathic involvement of organs, and renal failure in particular. Acidosis and decreased plasma protein concentrations are often associated with renal failure and may increase pharmacologically active unbound drug concentration in the plasma and intracellular drug concentrations.[25] Similarly, it appears prudent to exercise caution in the administration of drugs such as diazepam, fentanyl, and midazolam when used in conjunction with regional anesthesia in these patients.

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Excessive Airway Pressure Due to Ventilator Control Valve Malfunction during Anesthesia for Open Heart Surgery

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Ventilator malfunction can be classified as failure of the breathing circuit, of the bellows assembly, or of the control assembly.[1] The most commonly cited causes for

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breathing circuit malfunction include leaks,[2,3] disconnections,[4,5] or misconnections[5,6] in the breathing circuits. Morbidity or mortality can result from a no-flow (no-ventilation) state resulting in hypoxia, or from excessively increased airway pressure resulting in barotrauma.[5–9]

In this case report we describe North American Drager AV-E ventilator malfunction due to a defective valve in the ventilator control assembly that regulates gas inflow to the ventilator bellows chamber. The continuous flow of gas to the bellows induced a no-ventilation state and at the same time caused the patient's airway pressure to increase to hazardous levels.

CASE REPORT

A 44-yr-old, 73-kg man was scheduled for elective coronary artery bypass surgery. Preoperatively, systemic arterial and flow-directed