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Parkinsonian Symptoms during Emergence from General Anesthesia

Stanley Muravchick, M.D., Ph.D.,* David S. Smith, M.D., Ph.D.†

THE fundamental neurochemical lesion that causes idiopathic or primary Parkinson's disease (Paralysis agitans) is well established, but the anesthetic implications of dopaminergic deficiency within the basal ganglia remain unknown. The literature relevant to anesthetic practice simply cautions against the perioperative use of adjuvant drugs that are thought to have dopaminergic blocking or cholinomimetic properties.^{1,2} It remains unclear whether general anesthesia is associated with significant changes in dopaminergic

activity. We present a report of severe and prolonged dystonic muscle rigidity during emergence from otherwise routine general anesthesia in a patient who was subsequently found to have classic Parkinson's disease.

Case Report

An apparently healthy white man, 54 yr old, 178 cm, 80 kg, was scheduled for open cholecystectomy after 4 days of hospitalization for intravenous antibiotic therapy (mezlocillin, gentamycin) instituted for severe right upper-quadrant abdominal pain, nausea and vomiting, and recurrent shaking chills. All laboratory data were within normal limits except for a slightly increased gamma-glutamyltransferase, suggesting a diagnosis of chronic cholecystitis or hydrops of the gallbladder. The patient's prior annual physical examinations had revealed no objective abnormalities in any screening studies but made passing mention of complaints of persistent anxiety, a lack of a general sense of well being, and recurrent constipation. The patient also had experienced skeletal muscle spasms after taking prochlorperazine (Compazine) to treat attacks of nausea. The attending anesthesiologist who visited the patient the afternoon before surgery described a preanesthetic evaluation of ASA physical status 1. Nursing notes revealed that the patient again experienced muscle spasms of his torso and jaw within 1-2 h after he asked for and received 10 mg oral prochlorperazine for nausea. These symptoms resolved after subsequent treatment with 100 mg oral diphenhydramine (Benadryl).

* Professor of Anesthesia.

† Associate Professor of Anesthesia.

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Address reprint requests to Dr. Muravchick: Department of Anesthesia, Courtyard 402, Hospital of the University of Pennsylvania, 3400 Spruce Street, Philadelphia, Pennsylvania 19104-4283.

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Upon arrival in the operating room, the patient was sedated with 2 mg intravenous midazolam and 50 µg fentanyl. Bilateral intercostal blocks placed at a total of 12 segments required 30 ml of preservative-free 0.5% bupivacaine with 1:200,000 epinephrine. Induction of anesthesia with 375 mg thiopental and neuromuscular blockade with 75 mg atracurium for intubation and subsequent surgical relaxation was similarly routine and unremarkable. Inspired isoflurane concentrations between 0.8% and 1.25% in oxygen/nitrous oxide 30/70% produced a hemodynamically stable intraoperative course. The surgical specimen, a gall bladder with obvious hydrops, was removed 40 min after incision, and the wound was closed and infiltrated directly with an additional 15 ml of 0.5% bupivacaine. Forty milligrams edrophonium with 0.4 mg glycopyrrolate brought neuromuscular transmission, which had partially recovered spontaneously, to a fully sustained response to 50-Hz tetanic stimulation within 3 min. Intravenous atropine (0.5 mg) was given shortly thereafter to treat transient bradycardia. Arterial oxygen saturation as estimated by pulse oximetry never decreased to less than 98%, and body temperature decreased only 0.2°C.

Despite prompt resumption of spontaneous ventilation, tracheal extubation was delayed 1 h by a markedly prolonged period of emergence from anesthesia. Within minutes after discontinuation of nitrous oxide, the patient exhibited sustained rigid extension of his extremities. He failed to demonstrate any facial grimaces, nor did he respond to direct commands. There were no visible clonic contractions, muscle tremors, fasciculations, or other evidence of seizure activity or shivering. Eventually, he appeared to make purposeful efforts, turning his head and slowly reaching for the endotracheal tube, but he did not verbalize until 30 min after tracheal extubation, when he complained of inability to urinate. Over the next 45 min, he showed progressive improvement in responsiveness to questions and orientation and more normal skeletal muscle tone. The postanesthetic progress note made at this time by the attending anesthesiologist described "a dystonic, Parkinsonian-type phenomenon. . . almost certainly not a specific reaction or adverse response to the anesthetic agents used."

At no time within 24 h of surgery did this patient receive phenothiazines, butyrophenones, or any other drugs known to produce dystonic reactions or extrapyramidal side effects. Two hours after tracheal extubation, the patient's internist recommended continued avoidance of these drugs and observed "no neurologic deficit." The balance of the hospital course was remarkable only for persistent urinary retention and intermittent diarrhea. He was discharged home from the hospital on the 3rd postoperative day. Eighteen months later, overt symptoms and a definitive diagnosis of Parkinson's disease required him to markedly reduce his professional activities. Treatment with levodopa/carbidopa eventually produced dramatic improvement and he was able to resume his former responsibilities.

Discussion

This apparently healthy patient had a severe dystonic reaction on emergence from an otherwise uneventful general anesthetic. Transient hyperreflexia and posturing is common after general anesthesia before recovery of full consciousness,³ but prolonged muscle rigidity, expressionless facies, and unresponsiveness to verbal

command is unusual. Sustained tonic motor activity is associated more often with malignant hyperpyrexia and myotonia,⁴ neuroleptic malignant syndrome,⁵ or the Freeman-Sheldon syndrome.⁶ This patient did not present with a diagnosis of Parkinson's disease either established or suspected, nor did he exhibit "classic" Parkinsonian symptoms preoperatively. In retrospect, however, his susceptibility to skeletal muscle spasm and what had appeared to be nonspecific and noncontributory chronic complaints of constipation and mild depression can be recognized as prodromal symptoms of Parkinson's disease, which are especially common in individuals diagnosed in their middle adult years.^{7,8}

There are prior reports of postoperative muscle rigidity in patients who have an established diagnosis of Parkinson's disease,⁹ especially after use of fentanyl and droperidol.¹⁰ Even in normal patients, however, generalized perioperative rigidity can occur after moderate to high dosages of fentanyl,¹¹ sufentanil,¹² or Innovar.¹³ Opioid-induced muscle rigidity responds to neuromuscular blockade, but it occurs because of central nervous system effects, probably the inhibition of dopamine release. This hypothesis is consistent with observations that patients with Parkinsonism are predisposed to this narcotic side effect and with the threefold increase in the incidence of fentanyl rigidity seen in geriatric individuals,¹⁴ a patient subpopulation known to experience progressive compromise of dopaminergic activity even in the absence of overt symptoms.¹⁵ Attempts to prevent fentanyl-induced rigidity with amantadine, a stimulant for dopamine release, have not, however, been successful.¹⁶ In any case, the very small amount of fentanyl used here and the lack of any side effects within 20 min after intravenous administration suggest that opioids played little role in this dystonic event.

In contrast, potent inhalational anesthetics may increase, rather than decrease, brain extracellular dopamine concentrations during general anesthesia.^{17,18} Because the transport of dopamine by synaptosomes is impaired during and after exposure to halothane or isoflurane,¹⁹ there may be decreased dopaminergic transmission as well as accumulation of extracellular dopamine during inhalational anesthesia because of simultaneous dopaminergic receptor blockade and depressed neuronal release and reuptake of dopamine.²⁰ Haloperidol, an established dopaminergic blocking drug, produces both Parkinsonian symptoms and measurable increases in extracellular dopamine.^{21,22} Transient dystonia during emergence from general anes-

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thetia therefore could reflect any of a number of possible dopamine-mediated mechanisms. Not surprisingly, therefore, a review of the contemporary anesthetic literature does not reveal a consensus regarding specific guidelines for anesthetic selection in the perioperative management of the patient with Parkinsonism.

In summary, this report describes an apparently healthy patient who had a dramatic, prolonged period of generalized Parkinsonian-like dystonia and masklike facies during emergence from anesthesia and was later diagnosed as having Parkinson's disease. Inhalational anesthesia, perhaps in combination with adjunctive drugs commonly used in anesthetic practice, produced overt symptoms of primary Parkinsonism in a patient who had only the most subtle clinical evidence of a preexisting dopaminergic deficiency. We believe that this phenomenon has not been reported previously despite the large numbers of patients with established Parkinson's disease, because once diagnosed, dopaminergic activity has been enhanced adequately by ongoing therapy or perhaps because the perioperative symptoms were transient and sufficiently similar to routine anesthetic emergence to be overlooked.

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