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Central Anticholinergic Syndrome: Does It Exist?

To the Editor:—I was fascinated with Grum and Osborne's case report.[1] The number of preoperative tests were impressive, and their work-up for possible use of "drugs" was commendable.

From the signs and symptoms presented, I could not help but suspect that their patient was suffering from symptoms related to pheochromocytoma. Hypertension, tachycardia, pupillary dilation, agitation, and severe headaches all point to increased circulating catecholamines. The "dry and warm" skin is not typical of pheochromocytoma, but the patient had received glycopyrrolate, which causes dry and at times flushed skin.

It is difficult to believe that atropine, which has been in use for more than 100 yr and is still prescribed for millions of patients every day, would suddenly become so vicious and bring about the frightful syndrome called central anticholinergic syndrome! I for one, if confronted with such a clinical episode, will not diagnose "central anticholinergic syndrome" unless I have ruled out pheochromocytoma.

The author thanks Dr. Benjamin G. Covino for reviewing and correcting this correspondence.

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In Reply:—As Dr. Shamsai points out, pheochromocytoma can be considered in the differential diagnosis of a patient who suddenly presents with sudden onset of severe hypertension, tachycardia, headache, and agitation. However, there were reasons not to suspect this diagnosis in our patient, and we did not test for it. Whereas symptoms of pheochromocytoma are often provoked by activity, our patient was resting in bed while awaiting surgery. The patient had a negative family history for systemic diseases that are often associated with pheochromocytoma. During her preoperative work-up, she denied a history of cardiovascular symptoms. More compelling is her denial of previously having had a similar incident. This negative history was corroborated by a family member. The sweating that commonly occurs during an acute attack was absent, and we believe that glycopyrrolate is likely to have produced her dry skin and mucous membranes within a few minutes of administration. Although symptoms of acute catecholamine release from a pheochromocytoma may last only a few minutes, as stated in the case report the first dose of physostigmine given at the height of the patient's symptoms resulted in an immediate and dramatic decrease in her blood pressure and in the severity of her headache. A second dose given 10 min later virtually completely ablated her symptoms and physical findings. The suggestion that the episode self-terminated over a period of one half hour is not supported by the case description.

Thus, although we cannot rule out the presence of pheochromocytoma in this patient, we believe that the immediate temporal relationship between physostigmine and the cessation of the patient's symptoms argues for acute central anticholinergic syndrome following glycopyrrolate. I personally have seen two prior cardiovascular and neurologic crises immediately following administration of an antimuscarinic drug that were promptly terminated by physostigmine, and I doubt that it was mere coincidence in either case. Our report emphasizes that central anticholinergic syndrome, like pheochromocytoma, does exist and may occur more often than is commonly suspected.

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Epidural Opioid Requirements

To the Editor:—We read with interest the case report by Kreitzman and Samuels.[1] While we understand that the main point in the report is to document this patient's response to a high dose of epidural hydromorphone, we feel some issues must be clarified.

First, there was no mention as to whether this patient used opioids for pain control in the preoperative period. If he had, which drug was used, what dose, and for how long? Second, was the catheter placed in the thoracic or in the lumbar area, and was correct position of the

catheter ascertained postoperatively? Finally, what were the visual analog scale pain scores before these events occurred (between 2 PM and 4:30 PM)?

These questions are important because cancer patients who have used oral or parenteral opioids preoperatively have peridural opioid requirements significantly greater than patients not receiving opioids. Reviewing our experience in our Acute Pain Service with 1,000 patients who underwent surgery for cancer over a 2.5-yr period,* we found that patients who have been taking opioids preoperatively for pain control are a special group of patients who require two to three times the normal doses of epidural morphine when administered *via* a continuous infusion. Furthermore, psychologically they also behave differently, and we have assigned one specific anesthesiologist to deal with these special cases. In addition, young patients with metastatic sarcomas generally undergo several major surgical procedures and have experienced significant pain during the course of their disease. Thus, they learn to prevent the onset of severe pain instead of treating severe pain at its peak intensity. The patient described by Kreitzman and Samuels received 0.2-mg·h^{-1} dosage of hydromorphone, or 1.2 mg every 6 h, which is a normal dose for the average surgical patient when intermittent bolus injections are used.† It seems from his actions that his analgesic requirements were much greater than the prescribed dose.

It is also possible that this patient had a nonfunctioning or malpositioned epidural catheter and that the persistence of pain motivated his manipulation of the infusion pump in order to provide an adequate dose of opioids. If this catheter was in the epidural space, he received 3.55 mg hydromorphone in 2.5 h, which is about three times the normal dose. Yet the patient did not develop any signs or symptoms of epidural opioid overdose. As stated by the authors, hydromorphone is less lipid-soluble but more potent than morphine. We would have expected such a dose to be associated with more sedation and respiratory depression unless the patient had already been taking large doses of opioids preoperatively or the epidural catheter was outside of the epidural space.

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* Manuscript in preparation.

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In Reply:—As suggested, possible causes of increased analgesic dosage requirement include tolerance caused by preoperative opioid use and nonfunctional or misplaced catheters. Tolerance to opioid would seem unlikely here because, as stated in the case report, the patient was not receiving any medications preoperatively.[1] We also believed that our lumbar epidural catheter was functioning because the patient was subjectively and objectively (visual analog scores < 3) comfortable prior the first overdosing incident (and the next morning). Thus, since the patient had been pain-free, we doubt that his actions were related to higher analgesic requirements or persistent pain.

We believe that this was a case of curious but uneducated fingers playing with potentially dangerously unsecured pump controls. The question, which, however, is still unresolved at this time, is why this patient had no serious side effects given the pharmacologic characteristics of hydromorphone and the large dose he received.

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A Method to Prevent Tampering with an Infusion Pump

To the Editor:—In a recent case reported by Kreitzman and Samuels,[1] concern was raised about patient tampering with an epidural infusion pump. They mentioned that a simple, effective and inexpensive device, such as a locking cover for the infusion pump, would be desirable. At our hospital, we have been using an IMED infusion pump fitted with such a device (fig. 1). The cover is clear plastic and hinged at the top