Corticosteroid-induced Mania after Single Regional Application at the Celiac Plexus

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WE report the occurrence of symptoms of mania related to corticosteroid injection at the celiac plexus for chronic pancreatitis. Corticosteroids are associated with mental status changes, including mania, confusion, depression, hallucinations, and paranoia. The mechanism for these central nervous system (CNS) perturbations is unknown. The literature suggests that mania is second to psychosis as the most common corticosteroid-related mental state change. Although a relation to dose and daily exposure exists, we found no reports of mania related to a single regional steroid injection.2,3

Case 1

A 57-year-old woman with familial pancreatitis resulting in palliative distal pancreaticostomy presented for chronic pain. She gave a history of mania resulting from second separate previous corticosteroid trials; a brief orally administered tapered course of dexamethasone and a single intravenous injection of unknown corticosteroid for bursitis of the right shoulder. In each case, manic symptoms were reported to have been profound but brief, marked by insomnia, agitation, racing thoughts, and grandiosity. She reported no intervening episodes of mania, other than these two corticosteroid-related episodes, no other formal psychiatric history, and was taking no other medications at the time. We discussed with the patient the potential therapeutic options for providing comfort other than treatment at the celiac plexus and the possibility of mania after corticosteroid administration. Once all other appropriate options had been exhausted, we offered, and the patient accepted, corticosteroid injection with local anesthetic at the celiac plexus.4,5 The patient was not willing to consider using lithium as a preemptive mood stabilizer. Because valproic acid is associated with hepatoxicity, we chose to offer carbamazepine as the only other option for a preemptive mood stabilizer.6 Carbamazepine was given but was not tolerated because of sedation, and it was discontinued after a single dose. Celiac plexus nerve blockade was performed by standard procedure, as described later.7 There was no interventional intravascular, subarachnoid, or paravertebral injection and no hemodynamic change. The procedure was tolerated without complication. Approximately 10 min after the injections, the patient reported complete resolution of previously severe abdominal pain.

After the procedure, the patient reported no difficulty and exhibited normal behavior until approximately 25 h after the procedure. At this time, she was observed in the hospital store dressed in bright red bedroom clothing and having spent several hundred dollars. She was found to have a mental status change comprising expansive affect, racing, tangential and grandiose thoughts, pressured and loud speech, and poor insight and judgment. There was no difficulty with sleep until the night after onset of manic symptoms, which was marked by complete lack of sleep. Her manic symptoms resolved after 4 days of treatment with haloperidol and clonazepam. The doses of these medications were tapered and discontinued after 6 days without recurrence of manic symptoms.

Case 2

A 52-year-old woman with chronic pancreatitis and ampullary stenosis of the pancreatic duct presented with chronic epigastric pain. She had previously undergone endoscopic retrograde cholangiopancreatography, sphincterotomy, and surgical sphincterotomy, with recurrence of symptoms. Stent placement also failed to relieve pain. She was taking no medications at the time of presentation. Her medical history was significant for cytomegalovirus hepatitis and cholecystectomy for cholelithiasis, appendectomy, and hysterectomy. Her epigastric pain persisted, despite aggressive medical management, and she was offered an analgesic celiac plexus block with a combination of local anesthetic and corticosteroid.8,9 She gave a history of mania resulting from two previous corticosteroid trials; once associated with intravenous adrenocorticotropic hormone administration 20 yr earlier for chronic mucoid diarrhea, and a second, 18 months earlier, when she received two large oral doses of prednisone for cytomegalovirus hepatitis. On each occasion, treatment induced profound but brief symptoms of agitation and either euphoria or dysphoria associated with insomnia for several days, heightened energy, obsessive behaviors, racing thoughts, and verbosity. She reported no intervening episodes of mania.

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Accepted for publication March 12, 1996. Accepted for publication June 7, 1996.

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Key words: Psychosis; mania; Hormones; corticosteroids; Anesthetic techniques; regional; nerve blockade.

Anesthesiology, V 85, No 5, Nov 1996

Methodology

Celiac plexus nerve block was performed using 1.5 ml of 1% lidocaine and 2 ml of 0.75% bupivacaine. A 22-gauge, 4-cm needle was used to penetrate the parietal peritoneum. The needle was inserted 3 cm lateral to the lumbar spine in the midaxillary line, aiming cephalad, parallel to the 12th rib. The injection was performed under fluoroscopic guidance, and the needle was slowly removed. The injection continued until the loss of resistance was noted.

Discussion

The treatment of chronic pain often provides the opportunity to evaluate the mechanism of pain perception with single and regional injections.
CASE REPORTS

other than these two corticosteroid-related episodes, and she had no other psychiatric diagnosis. Despite the known possibility of recurrence of these symptoms, the patient chose to have the procedure. Her mental status was evaluated, before and after injection, by administering the Young Mania Rating Scale. Her precontrast injection Young Mania Rating Scale score was 2, consistent with normal mood at that time.

Celiac plexus nerve blockade was performed by standard procedure, as described later. There was no indication of intravascular, subarachnoid, or paravertebral injection and no hemodynamic change. The procedure was tolerated without complication. Immediately after the celiac plexus block, the patient reported decreased pain, which lasted 6–8 hours, after which her pain returned to its previous baseline intensity and did not subside.

The patient signed out of the hospital, against medical advice, approximately 41 hours after the celiac injection. She reported no difficulty with sleep until 72 hours after injection, at which time she experienced complete lack of sleep for 48 hours (postinjection nights 3 and 4). She described this period of insomnia as euphoric, with prominent sexual aggressiveness. She noted that after sleeping for 6 hours on the fifth postinjection night, she became irritable, with obsessive thoughts. She refused treatment for agitation. Her Young Mania Rating Scale score after celiac plexus injection at the celiac plexus was 3, consistent with mania. Manic symptoms resolved after 7 days.

Methods

Celiac plexus block was performed using bilateral posterior approach with C-arm fluoroscopic guidance, with the patient in prone position. A 20-gauge, 12-cm styled needle was inserted 6–8 cm lateral to the spinous process of the L1 vertebra, just lateral to the upper margin of L1 vertebral body. Under fluoroscopic guidance, the needle was advanced to a position approximately 1.0 cm anterior to the anterior border of L1 vertebrae on each side. Accurate placement was confirmed by bilateral injection of 5 ml of 1:1 mixture of water-soluble radiographic contrast and preservative-free saline, which revealed the usual sausage-shaped pattern of dye spread anterior to the anterior surface of the L1 and upper part of the L2 vertebrae. After negative aspiration, a 3-ml test dose of 1.5% lidocaine was injected on each side, without central or regional effects. A mixture that contained 15 ml local anesthetic solution (1:1 mixture of 1.0% lidocaine and 0.5% bupivacaine) and 2 ml (50 mg) triamcinolone was deposited on each side. Total dosage of triamcinolone was 100 mg.

Discussion

The addition of corticosteroid to a celiac plexus block provides pain relief in some, but not all, cases, and its mechanism is unknown. In both cases presented here, single regional application of corticosteroid was associated with neuropsychiatric manifestations. Since the introduction of corticosteroids into clinical practice, there have been countless reports of associated neuropsychiatric symptoms. Despite this sizable literature, questions remain as to the patient population at risk, the time course of symptoms, and the treatment options.

The incidence of neuropsychiatric effects related to repeated corticosteroid use is reported to be substantial. The high rate is, in part, related to predisposition from underlying medical conditions that may have similar CNS manifestations in the absence of corticosteroid exposure. However, there remains a consistent cause and effect relation between corticosteroid treatment and mental disturbance that is independent of underlying disease. In most studies, a proportional relation is suggested between the incidence of mental status change and corticosteroid dose as well as duration of corticosteroid exposure. The literature includes many cases in which neuropsychiatric symptoms are reported after limited corticosteroid exposure, even from topical nasal preparations.

Both patients reported on here had a previous history of brief mental status change with limited exposure to corticosteroid. In each case, there was no psychiatric history other than when exposed to corticosteroid. Whether the manic symptoms seen here could have been "functional," induced by suggestion, or a placebo response can never be ruled out completely. However, the literature has never reported such cases. The early literature does not support the commonly held suspicion that premedicating psychiatric illness predisposes to steroid-induced mental disturbance. There is no convincing evidence to suggest that a kindling effect from corticosteroid exposure. There is only a single report of persistent psychiatric illness after an exposure to steroids, although, in this case, the authors acknowledge that it is difficult to determine whether psychiatric illness would have developed in this patient anyway. If there is a "kindling effect," whereby a single episode of psychosis decreases the threshold for future episodes, these side effects become less acceptable. Although neuropsychiatric manifestations from corticosteroids may be potentially dangerous in the short term, they are usually treatable, and there is little evidence to suggest that these acute side effects lead to long-term effects. Therefore, administration of corticosteroid was elected in each case, and side effects were either treated or extinguished without treatment. It is not clear whether pretreatment with...
mood-stabilizing drugs before steroid administration is of value, but, theoretically, this may be an advantageous approach in the steroid-sensitive patient.5,10–18

Specific mechanisms to explain the CNS side effects of corticosteroids remain unclear. Recent work in a variety of animal species, including humans, suggests that corticosteroids increase mesolimbic catecholamine concentrations, particularly dopamine.19,20 The role of enhanced CNS dopamine metabolism and steroid-induced mania is not yet clear, but its significance is suggested by the therapeutic efficacy of dopamine antagonists. It would be of value to determine the incidence of corticosteroid-related adverse effects, and to correlate these adverse effects with either pharmacokinetic measures, such as peak plasma concentrations and elimination half-life, or with biological activity, such as hypothalamic-pituitary adrenal axis suppression.21,22 Because corticosteroids are known to produce a long duration of biologic effects, such as persistent suppression of the hypothalamic-pituitary adrenal axis, it appears that the duration of resulting CNS symptoms may not correlate with this timecourse. Although the cause of such events may be the same, the underlying alterations in physiology may be different, and thereby explain variations in duration of effects.

The prognosis for acute corticosteroid-related neuropsychiatric complications is usually excellent, because dosage reduction or discontinuation of therapy usually results in full recovery. Therapy for CNS side effects of corticosteroids remains directed toward controlling symptoms, primarily with dopamine antagonists such as butyrophenones, benzodiazepines such as clonazepam, and mood stabilizers such as lithium or anticonvulsants.23–25 Of particular concern with pain management, tricyclic antidepressants, which may be used as adjuvant analgesics, were reported to exacerbate manic symptoms and may be contraindicated in patients with neuropsychiatric disturbance related to corticosteroids.23-25 Whereas these cases illustrate the association of mania with regional application of corticosteroid at the celiac plexus, it is possible that other regional corticosteroid injections that are known to lead to substantial corticosteroid blood concentrations, such as epidural corticosteroids, have similar potential for neuropsychiatric complications, even with a single dose.23,25

References


