Hemiparkinsonism as a complication of an Ommaya reservoir

Case report

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The authors describe the case of a 28-year-old woman who developed the following symptoms in her right hand: a lasting resting tremor, transient focal rigidity, and paresthesia. These deficits occurred following treatment with intrathecal methotrexate via an Ommaya reservoir which was placed too deeply, resulting in trauma to the contralateral mesencephalon.

KEY WORDS □ Ommaya reservoir □ ventricular catheter □ parkinsonism □ methotrexate

The intraventricular Ommaya reservoir is a preferred method for delivery of intrathecal chemotherapy in terms of therapeutic efficacy and patient comfort. The most common complication is infection, estimated to occur in 3% to 15% of patients or once in every 153 reservoir-months. Less frequent problems include reservoir malfunction, hemorrhage, and focal seizures. Pericatheter necrosis and leukencephalopathy have been reported in patients who received intrathecal methotrexate, particularly when combined with irradiation. To our knowledge, parkinsonism has not been described as an outcome of intraventricular reservoir placement or the drugs injected by this means.

Function of the catheter was restored after it was withdrawn 3.5 cm; during this maneuver unusual resistance was encountered. Methotrexate injections were resumed 2 months later. Postoperatively, the patient noticed paresthesia and stiffness of the right hand and right perioral area; these resolved over 6 weeks but were succeeded 4 months later by a persistent 3 to 5 cycle/sec resting tremor of the right hand, chiefly of the thumb and index finger, involving at times the forearm and right foot, and disappearing with intention. Magnetic resonance imaging revealed a small signal-void focus in the former path of the catheter tip (Fig. 2) and showed no signs of leukencephalopathy.

Physical examination, which took place after anticholinergic therapy had been initiated, did not disclose other features of parkinsonism such as bradykinesia, rigidity, abnormality of gait, loss of postural reflexes, or autonomic dysfunction. No ballismus, chorea, or ataxia was present. No deficits were detected in language, attention, memory, strength, sensation, or ocular motility. There was no family history of parkinsonism, and serum ceruloplasmin was normal. The patient had undergone no irradiation. Parenteral and oral medications had included Adriamycin (doxorubicin hydrochloride), vincristine, prednisone, cyclophosphamide, actinomycin D, 6-mercaptopurine, and carbustine. The tremor failed to improve after cessation of the antiemetic drugs metoclopramide and thiethylperazine. Three years later, the patient's leukemia is in remission.
The tremor has not progressed but has reduced in intensity with trihexyphenidyl.

Discussion

Posttraumatic parkinsonism has been described following penetrating injury to nigrostriatal tracts, but such cases are rare because midbrain injury is often fatal. In our patient the trauma was exceptionally limited and, aside from transient paresthesia, was confined to the motor system. It is of interest that no symptoms were noted for more than a year following insertion of the catheter but occurred after it was withdrawn from the midbrain. This may be attributed to disruption of tissue ingrowth in catheter fenestrations or to increased methotrexate exposure to tissue within the hollow catheter track which ordinarily would not have been brought into contact with intrathecally injected agents.

The site of injury resembles the electrolytic lesions induced in monkeys by Ward, et al., in 1948, particularly those of their monkeys TM1 and BR12 which developed Parkinson-like tremors immediately following focal ablation within the mesencephalic tegmentum in locations that approximate the signal void area seen in Fig. 2A. More extensive than our patient’s lesion, theirs extended into the pontine tegmentum. Monkeys TM6 and BR14 probably failed to develop tremor because the lesions were more medially placed and insufficiently destroyed the substantia nigra or its outflow to the striatum.

The small artificial mesencephalic cavity left in the wake of the catheter tip would have allowed methotrexate to pool in direct proximity to the substantia nigra. Unlike the immediate tremor produced experimentally in monkeys by Ward, et al., our patient did not experience tremor until several months after catheter withdrawal and after intrathecal methotrexate was resumed. The reason for this is uncertain but could have been the addition of chemical to mechanical injury. Exposure of methotrexate to divided tissue might have been capable of inducing parkinsonism, interrupting dopaminergic projection to the striatum by inhibition of the biosynthesis of tetrahydrobiopterin, an essential cofactor for tyrosine hydroxylase. The susceptibility of this biopterin pathway to degeneration has been postulated to explain idiopathic parkinsonism, although administration of exogenous tetrahydrobiopterin has been therapeutically disappointing. Fortunately, leukovorin rescue was not part of our patient’s protocol, since intrathecal injections of folic acid in rats have resulted in excessive stimulation and eventual injury of nigral gamma-aminobutyric acid (GABA)ergic and dopaminergic neurons.

Asymmetric tremor, this patient’s major symptomatic feature, is not typical of juvenile onset Parkinson’s disease. Its course did not correlate with administration of metoclopramide or thiethylperazine, drugs which are known to reversibly precipitate or unmask evolving parkinsonism. We conclude that our patient’s tremor was a complication of trauma combined with metabolic insult to the substantia nigra. Paresthesia may be explained by trauma to the medial and ventral trigeminal lemnisci, which also lie in the catheter’s path.

The fascination of this unusual case lies in its anatomically discrete lesion and definable clinical correlate. It also emphasizes the importance of routine postoperative CT verification of intraventricular catheter placement prior to injection of cytotoxic agents. In cases such as this, ultrasonic guidance represents a potential method of observing catheter position intraoperatively, when immediate recognition of unforeseen difficulties would allow prompt correction to be made.

References


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