Leptomeningeal Inflammation and Altered CSF Chemistry in a Patient Treated with Intrathecal Morphine Infusion: Symptom Resolution with Cessation of Administration.

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Background

- Intrathecal Morphine pumps have been used to treat chronic pain for over 30 years.
- Various adverse reactions associated with Intrathecal Drug Delivery Systems have been described including neurological injury, intrathecal granuloma formation, arachnoiditis, and reactions to medications.
- Here we describe a case of bilateral lower extremity weakness and diffuse spinal cord inflammation, as well as complete symptom resolution upon cessation of drug administration, in a patient treated with intrathecal morphine infusion.

Leptomeningeal Inflammation

- A 51 year old female received an intrathecal pain pump for post laminectomy syndrome.
- After 5 years of pain control her dose of intrathecal morphine was increased (from 1.5 mg/day to 1.7 mg/day) due to an acute back strain.
- Within 2 weeks she had an episode of transient bilateral lower extremity numbness, tingling, and weakness that lasted several hours before resolving without intervention.
- 2 months later she had another, apparently spontaneous episode. Within 96 hours she had repeated lower extremity leg weakness and reported to the Emergency Department.
- Work up in the ED showed diffuse leptomeningeal enhancement (see right) and altered CSF chemistry (see below).
- The concern was for arachnoiditis vs. lymphoma.

MRI Results

- Observation of Diffuse Leptomeningeal Enhancement

Symptom Resolution

- The patient was admitted to the hospital and seen by several consult teams. Repeat lumbar puncture is shown below. Cytology showed a lymphocytosis with frequent atypical cells present.
- Other labs, including complete blood count, complete metabolic panel, CSF cultures and CSF viral panel were all unremarkable. Evaluation for malignancy did not identify an oncologic process.
- While in the hospital her intrathecal morphine dose was decreased by 10% (from 1.730 mg/day to 1.574 mg/day).
- By 3 months she had almost complete clinical resolution. CSF studies were returning to baseline (see below) and there was marked improvement in MRI enhancement.

Leptomeningeal Inflammation Re-demonstrated

- The decision was made then to wean and discontinue her intrathecal morphine, allow one month to pass and then repeat CSF studies.
- Throughout this time she demonstrated progressive incremental improvement in her strength.
- After 5 months, and at the request of the patient, her intrathecal morphine be resumed. This was done at a very low dose of 0.1 g/day which she tolerated well. Her dose was then increased to 0.2 mg/day.
- Within 3 days of the 0.2 mg/day dose she had new onset back pain, pain with ambulation, and recurrence of right anterior thigh paresthesia.
- The CSF analysis found resumption of high protein and lymphocyte values.

CSF Results - Emergency Department

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<th>Date</th>
<th>Cell</th>
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Timeline of Events

1. Intrathecal Drug Delivery System placed and infusion started.
2. Patient reports to ED for acute back strain.
3. Intrathecal morphine dose increased from 1.5 mg/day to 1.7 mg/day.
4. Patient presents with bilateral LE weakness, diffuse leptomeningeal enhancement on MRI, and altered CSF chemistry.
5. Intrathecal morphine dose decreased to 1.5 mg/day.
6. Patient reports significant clinical improvement.
7. Patient requests to restart intrathecal morphine. Dose started at 0.1 mg/day, then 0.2 mg/day.
8. Re-demonstration of LE weakness, altered CSF chemistry, diffuse enhancement on MRI.

Conclusion

- This is a case of LE weakness, pain and diffuse spinal cord inflammation, as well as complete symptom resolution upon cessation of drug administration, in a patient treated with intrathecal morphine infusion. In light of this patient’s experience, the following are considered for patients being treated with intrathecal morphine who present with acute increases in pain or a focal neurological sign. 
  - Weaning intrathecal morphine may decrease leptomeningeal inflammation and thus alleviate symptoms.
  - Consider CSF analysis +/- MRI.
  - More research is needed to evaluate serial CSF analysis as an early indicator of leptomeningeal inflammation.