Blame it on the Pump

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Abstract
Intrathecal drug delivery a method of directly administering opioid and spasmyloytic medication to the site of action, the spinal cord. Efficacy and safety of this delivery system is well documented in cancer pain, spasticity as well as non-malignant pain. However, there are a number of recognised potential complications with this therapy. One of the most serious of which is the formation of a granuloma occurring at the intrathecal catheter tip, which appears to be related to the concentration and drug type being delivered. Evidence has indicated that delivery of high dose morphine can lead to the formation of these granulomas. Occurring in less than 3% of all patients with an intrathecal catheter, granulomas can present as an inflammatory mass on imaging with some resulting in compression of the spinal cord. Patients may present with a host of neurological symptoms dependent on the location of cord compression caused by the granuloma, including neurological deficits, myelopathy and radiculopathy.

Keywords: Drug delivery • Myelopathy • Transverse myelitis

Introduction
An important differential to consider in patients with intrathecal catheters presenting with neurological deficits is Transverse Myelitis (TM). TM is a neuroinflammatory condition affecting the spinal cord. It can present as a loss of corticospinal, autonomic and spinthalamic functional loss below the level of the lesion [1-6]. TM has been reported to result from intrathecal device related infections, but may also be a consequence of demyelinating disorders, such as multiple sclerosis and neuromyelitis optica, vascular causes and malignancies, such as lymphoma. Therefore, early recognition of the cause of TM is paramount in preventing irreversible paralysis and further neurological deficits [7]. Here we report a case of transverse myelitis, caused by a B cell lymphoma, in a patient with an intrathecal catheter.

Case Report
A 56-year-old male patient presented with a 14 days history of bladder dysfunction and deteriorating mobility on a background of intrathecal pump insertion two months prior for failed back surgery syndrome pain. Neurological examination revealed a sensory deficit to T6. Urodynamics showed an atomic bladder, requiring catheterization. Biochemical and hematological blood results were unremarkable. Spinal MRI revealed a high T6-T8 cord signal surrounding a left T7 intradural lesion (mildly hyperintense with postcontrast enhancement on T1-imaging; centrally hyperintense with a peripherally hypointense rim on T2-imaging) (Figure 1). The adjacent cord showed significant oedema. A catheter-associated granuloma was considered likely. Cerebrospinal (CSF) analysis showed lymphocytosis with no evidence of pathogens. After refilling the pump with saline, the patient was commenced on a methylprednisolone infusion (5.4 mg/kg/hour) to reduce cord oedema. Neurosurgery was consulted for removal of the apparent granuloma. However, MRI two days later revealed considerable oedema resolution and the T7 lesion was now felt to be a flow defect rather than a granuloma. Upon review, surgery was no longer indicated. Transverse myelitis was now considered the likely diagnosis and investigation into its cause was commenced. CT-TAP to out rule malignancy was normal. A repeat CSF sample demonstrated lymphocytosis (833/cm³) with 74% CD4 T-lymphocytes. CSF IgG was elevated (174 mg/l) with no oligoclonal banding found in serum. Biochemical and hematological bloods remained unremarkable. The patient was discharged with no symptoms following two weeks of steroids. He returned five weeks later with weight loss, odynophagia and night sweats. Neck MRI was subsequently performed and a metabolically active large volume tumour mass arising in right tonsil was identified (Figure 2). It was associated with active right and left cervical nodes. Small subcentimetre active foci in liver were suspicious for further malignant disease. There was no active nodal or extranodal malignant disease elsewhere. Fine needle biopsy demonstrated a high-grade diffuse large B-cell lymphoma. PET-CT confirmed no spread and bone marrow biopsy was unremarkable. The patient is currently receiving R-CHOP regimen chemotherapy.

Discussion
Neurological symptoms in patients with intrathecal pumps are often, and reasonably, attributed to complications related to the pump, however, this case demonstrates that a broader differential diagnosis should also be considered.

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Figure 1. T1 and T2 MRI of the Spine. There is high signal within the thoracic cord from T6 to T8, maximal at T7. There is an intradural extramedullary lesion to the left of the cord at the T7 level which demonstrates central T2 hyperintensity with peripheral hypointense rim. It is mildly T1 hyperintensity and demonstrates enhancement on post-contrast imaging. Although the catheter itself is difficult to identify this most likely represents a catheter tip granuloma. Given the degree of oedema within the adjacent thoracic cord, intercurrent infection cannot be excluded. There is mild prominence of the central canal of the upper thoracic spine. Posterior fixation from L3-S1 with disc spacers. Impression Enhancing intradural extramedullary lesion at the T7 level of the adjacent cord oedema. Findings are suspicious for catheter tip granuloma, intercurrent infection cannot be excluded given the degree of adjacent oedema.
early to prevent permanent consequences. While Central Nervous System Lymphomas (CNSL) is rare, accounting for 4-8% of all lymphomas, they are associated with a poor prognosis. Primary Central Nervous System Lymphoma (PCNSL) is associated with a slight male predominance, immunosuppression such as HIV and is confined to the brain, cranial nerves, eyes, leptomeninges and/or spinal cord [8]. Secondary central nervous system lymphoma (SCNSL) occurs in up to 5% of high grade and <3% of indolent lymphoma patients. The risk of SCNSL is increased in lymphomas involving the paranasal sinuses, testes, marrow or adrenals and is now assessed by the CNS lymphoma score (CNS-IPI) [9]. Adverse prognostic features for CNSL include age >60 years, elevated Lactate Dehydrogenase (LDH), elevated CSF protein and involvement of deep regions of the brain [10]. PCNSL is usually classified as a High grade diffuse large B cell lymphoma (DLBCL) of non-germinal centre cell origin with up to 16% having CARD11 mutations affecting the NFKB pathway [11]. As seen in this case, the symptoms can vary but the a transverse myelopathy can be induced by direct tumour infiltration, intravascular infiltration or most suspect in this case an immunogenic paraneoplastic syndrome. The histology of Non-Germinial Centre B cell (N-GCB) subtype High grade DLBCL determines a high risk individual despite an CNS-IPI score of 3. Treatment should involve CNS penetrating regimes with potential consolidation with an Autologous Stem Cell Transplant (ASCT), provided the patient tolerates and attains remission. This case also highlights the difficulty in diagnosis when biopsy is not amenable and must be made on CSF flow cytometry, MRI findings and PCR IGHV rearrangement [12]. It also showcases the dilemma of steroids use without histology which the patient responded to remarkably until the final presentation and tonsillar mass. In general, investigation of a patient suspected of having paraneoplastic syndrome might fail to reveal the tumour until it becomes symptomatic, typically 3-13 months later [13]. This patient showed myelopathy as presenting symptom of DLBC, which was initially believed to be related to the intrathecal pump, and therefore was only diagnosed after 1 month of presenting to the clinic.

Conclusion

In summary, while it is a common occurrence that spinal symptoms in patients with intrathecal pumps are automatically attributed to pump complications, it is evident that a wider differential diagnosis should be considered in such patients. Additionally, this case demonstrates that lymphoma may present in a variety of unusual ways and may therefore delay diagnosis. Timely diagnosis may result in improvement of symptoms and prevent metastasis.

References