

# Blame it on the pump

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October 27, 2020

## Abstract

A patient presented with cauda equina syndrome signs on a background of intrathecal pump implantation for chronic pain. Initial investigations were consistent with a granuloma, a common complication of intrathecal pumps. CSF cytometry revealed a lymphocytosis. This patient represented 2 months later with neck signs secondary to a B-cell-lymphoma.

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**Keywords:** Intrathecal pump, Granuloma, Haematology, Lymphoma, Transverse Myelitis

**Key Learning Points:** Although it is a common occurrence that spinal symptoms in patients with intrathecal pumps is automatically attributed to pump complications, it is evident that a wider differential diagnosis should be considered in such patients

## Abstract

A patient presented with cauda equina syndrome signs on a background of intrathecal pump implantation for chronic pain. Initial investigations were consistent with a granuloma, a common complication of intrathecal pumps. CSF cytometry revealed a lymphocytosis. This patient represented 2 months later with neck signs secondary to a B-cell-lymphoma.

## Introduction

Intrathecal drug delivery a method of directly administering opioid and spasmolytic medication to the site of action, the spinal cord (1). Efficacy and safety of this delivery system is well documented in cancer pain, spasticity as well as non-malignant pain (2). 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 (1). Evidence has indicated that delivery of high dose morphine can lead to the formation of these granulomas (3, 4). 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 (5). 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.

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 spinothalamic functional loss below the level of the lesion (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 intra-theal 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 (SynchroMed<sup>TM</sup> II; Medtronic; Minneapolis, USA) insertion two months prior for failed back surgery syndrome pain. Neurological examination revealed a sensory deficit to T6. Urodynamics showed an atonic 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) cytometry flow 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 were 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 rule malignancy was normal. A repeat CSF sample demonstrated lymphocytosis (833/cm<sup>3</sup>) 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 were 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 early to prevent permanent consequences.

While central nervous system lymphomas (CNSL) are rare, accounting for 4-6% 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 SCNSL, 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-Germinal centre B cell (N-GCB) subtype High grade DLBC 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 flowcytometry, 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 is 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.

### Authorship

Kirk Levins: Pain clinician, writing, editing and formatting manuscript

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## Acknowledgments

The authors wish to thank the patient for their kind permission to proceed with this case report. We would also like to thank St Vincent's Anaesthesia Fund for funding for publication of this manuscript.

## Conflict of Interest Statement

The authors declare no conflict of interest.

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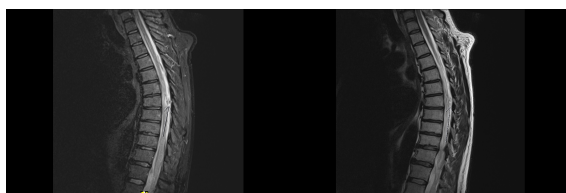
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## Figure Legend:

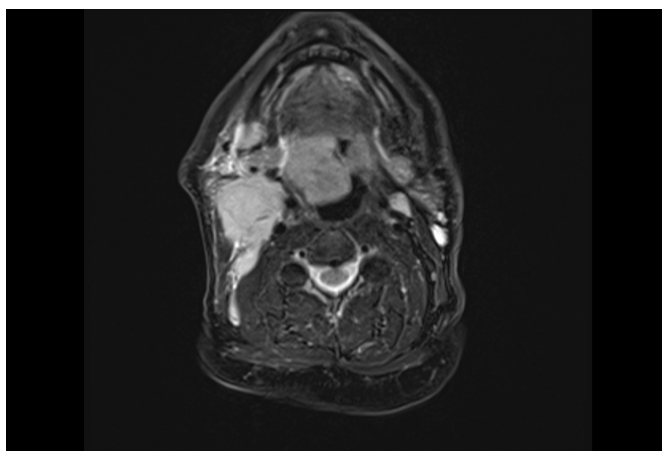
**Figure 1.** T1 and T2 MRI of the spine demonstrating an enhancing intradural extramedullary lesion at the T7 level of the adjacent cord oedema.

**Figure 2.** MRI of 5.3 cm right tonsillar malignancy centred on the right palatine tonsil. This extends inferiorly to abut and displaces the epiglottis with effacement of the right vallecula. There is lateral involvement of the constrictor muscles and extension across the midline.

**Figures:**



**Figure 1.** T1 and T2 MRI of the spine demonstrating an enhancing intradural extramedullary lesion at the T7 level of the adjacent cord oedema.



**Figure 2.** MRI of 5.3 cm right tonsillar malignancy centred on the right palatine tonsil. This extends inferiorly to abut and displaces the epiglottis with effacement of the right vallecula. There is lateral involvement of the constrictor muscles and extension across the midline.