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Technical Notes & Surgical Techniques

Use of intraoperative sodium fluorescein for diagnostic tissue biopsy of spinal cord lesions☆

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ABSTRACT

Background: Recent evidence suggests that fluorescein-guided microsurgery facilitates resection of intrinsic and metastatic lesions in the brain. Use of sodium fluorescein for angiography has previously been reported without non-specific diffusion into the adjacent spinal parenchyma. Diagnostic biopsy of spinal cord lesion is often challenging and the localization of such lesions intraoperatively is paramount. We present the first known report of use of sodium fluorescein for localization and diagnostic biopsy of intrinsic spinal cord lesions.

Methods: Three patients with spinal cord lesions received fluorescein sodium 10% (Alcon Laboratories INC, Fort Worth, TX, USA) at 3 mg/kg prior to surgical resection. Intraoperative visualization of fluorescence was performed using a Zeiss Pentero (Carl Zeiss AG, Oberkochen, Germany) microscope equipped with a Yellow560 filter or a Leica OH6 (Leice Microsystems, Wetzlar, Germany) equipped with a FL560 filter.

Results: Administration of sodium fluorescein resulted in lesional fluorescent contrast extravasation and facilitated surgical resection. The addition of sodium fluorescein allowed for identification and facilitated biopsy in three patients. In patients undergoing biopsy, tissue samples were positive for a diagnostic pathology.

Conclusion: Fluorescein may be a helpful microsurgical tool in guiding resection and localization for tissue biopsy of intramedullary spinal lesions. Further research is necessary to explore fluorescein sodium applications in the resection of spinal cord lesions.

1. Introduction

Sodium fluorescein (NaFl) is a biologically safe fluorescent dye that extravasates via interruptions in the blood brain-barrier (BBB) [1–3] and has been used as an adjunct to resect intracranial gliomas since the 1940s [4–7]. Advancements in fluorescent capable surgical microscopes have increased the utility of fluorescein in the resection of gliomas [8], allowing for real-time identification of tumor pathology while operating under the surgical microscope. Furthermore, usage of newer fluorescent microscopes allowed for intraoperative identification of critical neurologic structures while operating under fluorescein guidance and has facilitated safe aggressive resection of gliomas [8]. Recent studies have demonstrated relatively high sensitivity and specificity when comparing overall fluorescein staining with corresponding tumor pathology [9–17]. Additionally, the use of sodium fluorescein has also been applied to the resection of non-infiltrative and metastatic intracranial lesions [18–20].

Intramedullary spinal cord lesions present a unique surgical challenge where the identification of the lesion relies on surgical expertise and the lesion is surrounded completely by eloquent structures. Complete resection of some lesions is possible; however, for many lesions surgical biopsy is the goal of surgery. Accordingly, the advantages gained from sodium fluorescein guided microsurgery may prove beneficial for the identification and surgical management of intramedullary spinal cord lesions [21]. Physiological similarities between the spine and cranial BBB suggest similar fluorescein extravasation mechanisms and recent case reports illustrating sodium fluorescein videoangiography use for spinal arteriovenous malformations demonstrate safety and the paucity of non-specific spinal parenchymal staining [22,23]. Specifically, fluorescein sodium videoangiography offered the ability to

Abbreviations: NaFL, Sodium Fluorescein; BBB, Blood Brain Barrier; EBV, Epstein Barr Virus

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visualize fluorescent vasculature and non-fluorescein stained spinal parenchyma allowing for safe manipulation of vital spinal structures [22]. Thus far, there exists a paucity literature describing the use of sodium fluorescein use for the surgical management of intramedullary spinal lesions [21] and no such report exist describing the utility of fluorescein and spinal cord biopsies.

To our knowledge, we are the first to report the use of sodium fluorescein as an aid to biopsy spinal cord lesions. We our clinical experience with three patients who underwent fluorescein-guided biopsy of spinal lesions.

2. Clinical case presentations

2.1. Case 1

2.1.1. Presentation

55 year-old female patient without significant prior medical history presented with lower extremity weakness, saddle anesthesia and bladder incontinence. MR imaging of the patient's spine demonstrated a T1-contrast enhancing lesion at the level of T11/12 and initial CSF studies demonstrated inflammatory changes. The patient was taken to the operating room for biopsy and exploration without fluorescein-guidance and final pathology was non-diagnostic. The patient received addition CSF studies that were inconclusive, an extensive workup, started on broad-spectrum antibiotics and steroids without clinical improvement. Repeat MR imaging demonstrated increased size of the lesion (Fig. 1A and B). The patient was taken for re-exploration with NaFL guidance.

2.1.2. Operation

The patient underwent T11/12 area-exploration for biopsy of a spinal cord lesion. NaFl was administered at the time of skin incision at a dose of 3 mg/kg. After dural opening, a fluorescein microscope was utilized to visualize the lesion. Under microscopic fluorescein guidance, the lesion easily identified and biopsies were acquired (Fig. 2A and B). Final pathology was consistent with Epstein Barr Virus (EBV)-related B-Cell lymphoproliferative disease (Fig. 2C and D).

2.1.3. Post-operative follow-up

Post-operatively, the patient was at her pre-operative baseline and was started on a Rituximab, Methotrexate, Procarbazine and Vincristine chemotherapy regimen.

2.2. Case 2

2.2.1. Presentation

51 year-old male with a past medical history of HIV with right lower extremity weakness. MR imaging on initial work-up demonstrated an enlarging thoracic lesion and additional smaller lesions in his spinal cord. Work-up including systemic cultures, lumbar puncture and empiric antibiotics failed and repeat imaging demonstrated an enlarging lesion centered at the T3/4 thoracic level (Fig. 3).

2.2.2. Operation

The patient underwent T3/4 hemi-laminectomy for biopsy of a spinal cord lesion. NaFl was administered and surgery was similar to case 1 described above. Final pathology was consistent with *Mycobacterium haemophilum*.

2.2.3. Post-operative follow-up

Post-operatively, the patient was at his pre-operative baseline and was started on antibiotics.

2.3. Case 3

2.3.1. Presentation

68 year-old male without significant past medical history presented with progressive weakness of his lower extremities and a lesion centered at the level T1. After an unremarkable work-up the patient was consented for a laminectomy for tumor biopsy (Fig. 4A and B).

2.3.2. Operation

The patient underwent T1 laminectomy for biopsy of a spinal cord lesion. NaFl was administered and surgery was similar to case 1 described above. Final pathology was consistent with a primary glial neoplasm (Fig. 4C and D).

2.3.3. Post-operative follow-up

Post-operatively, the patient was at his pre-operative baseline.

3. Discussion

NaFl is a safe and readily available agent that has seen increased use in the surgical resection of cranial lesions. The benefits of NaFl use include specific and sensitive tumor staining and adjuvant

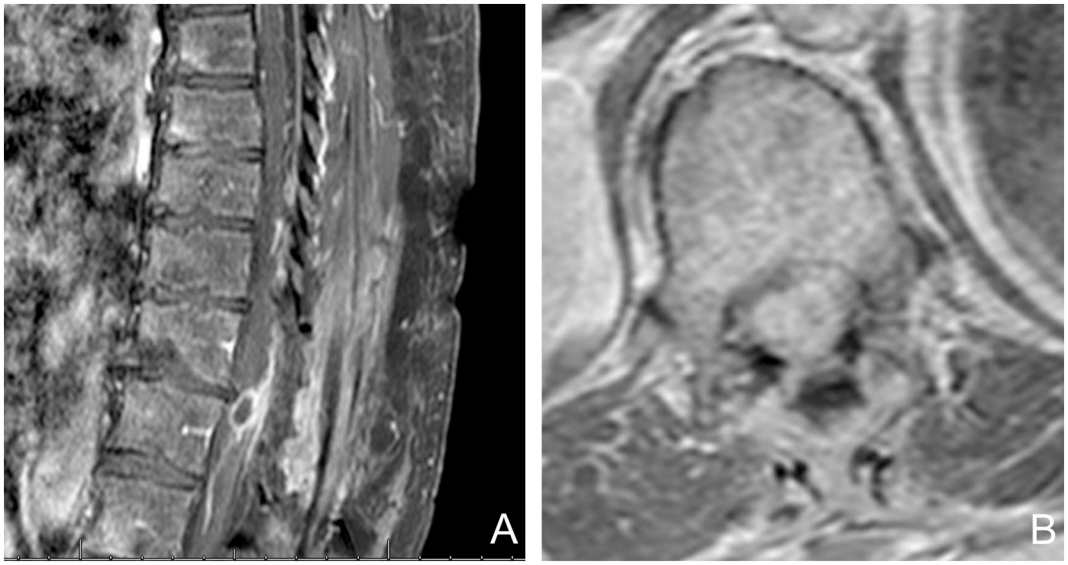

Fig. 1. 55 year-old female patient with progressive back pain and multilevel radicular symptoms with a 20 × 10 × 15 mm intradural lesion with significant mass effect in the lumbar spine, T1 weighted post-contrast images shown (A and B).

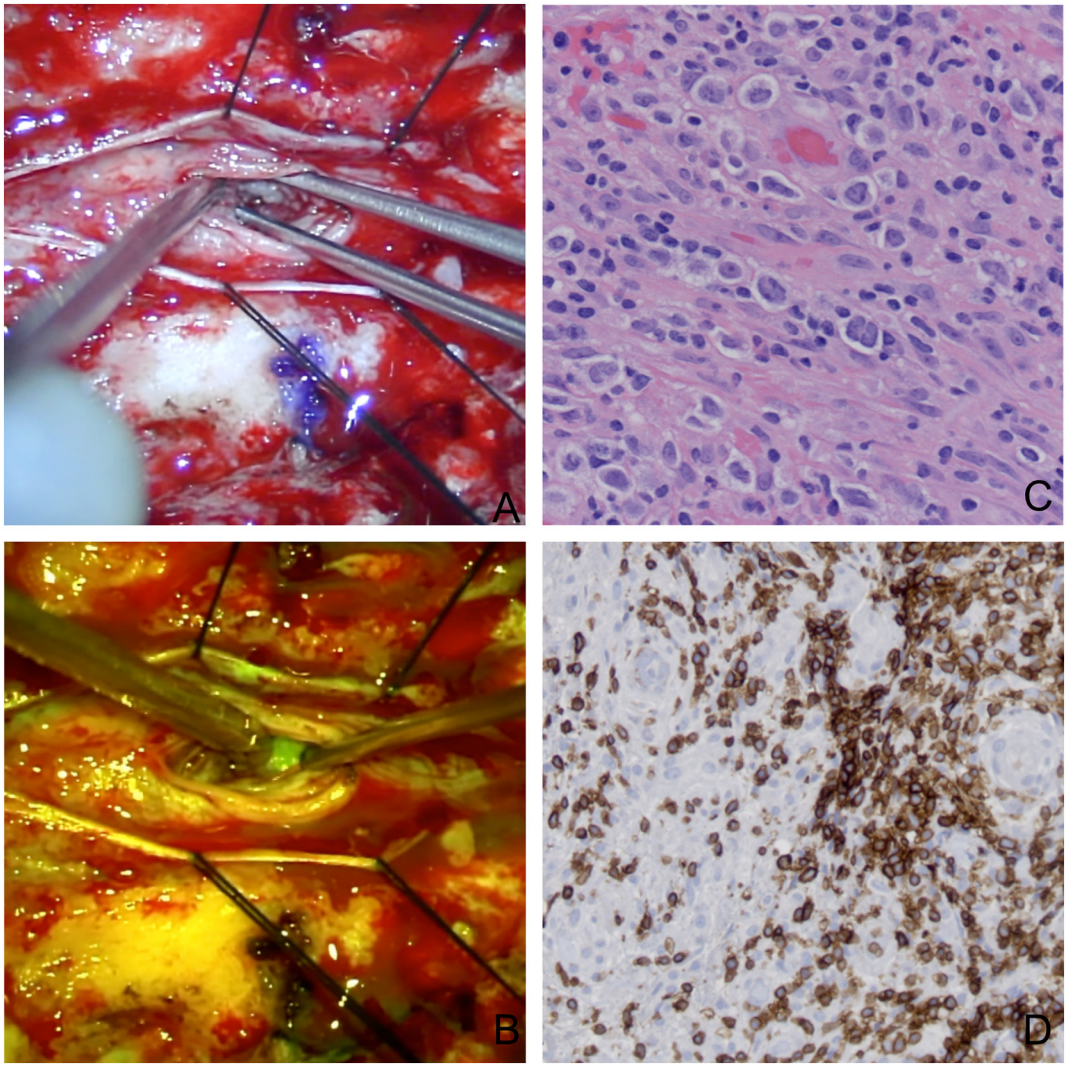

Fig. 2. Intraoperative NaFl microscopic images demonstrating lesional fluorescein during microscopic dissection and biopsy (A and B). Post-operative histological diagnosis was consistent with EBV driven lymphoma demonstrating diffuse CD-68 positive histiocytes (C and D).

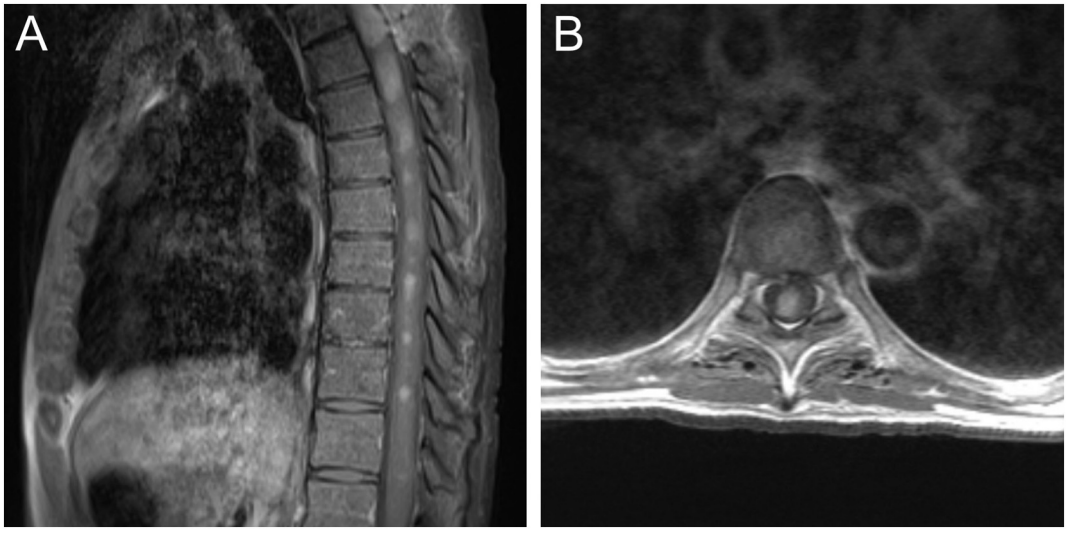

Fig. 3. 51 year-old male with a past medical history of HIV with MR imaging demonstrated an enlarging thoracic lesion and additional smaller lesions in his spinal cord (a and b).

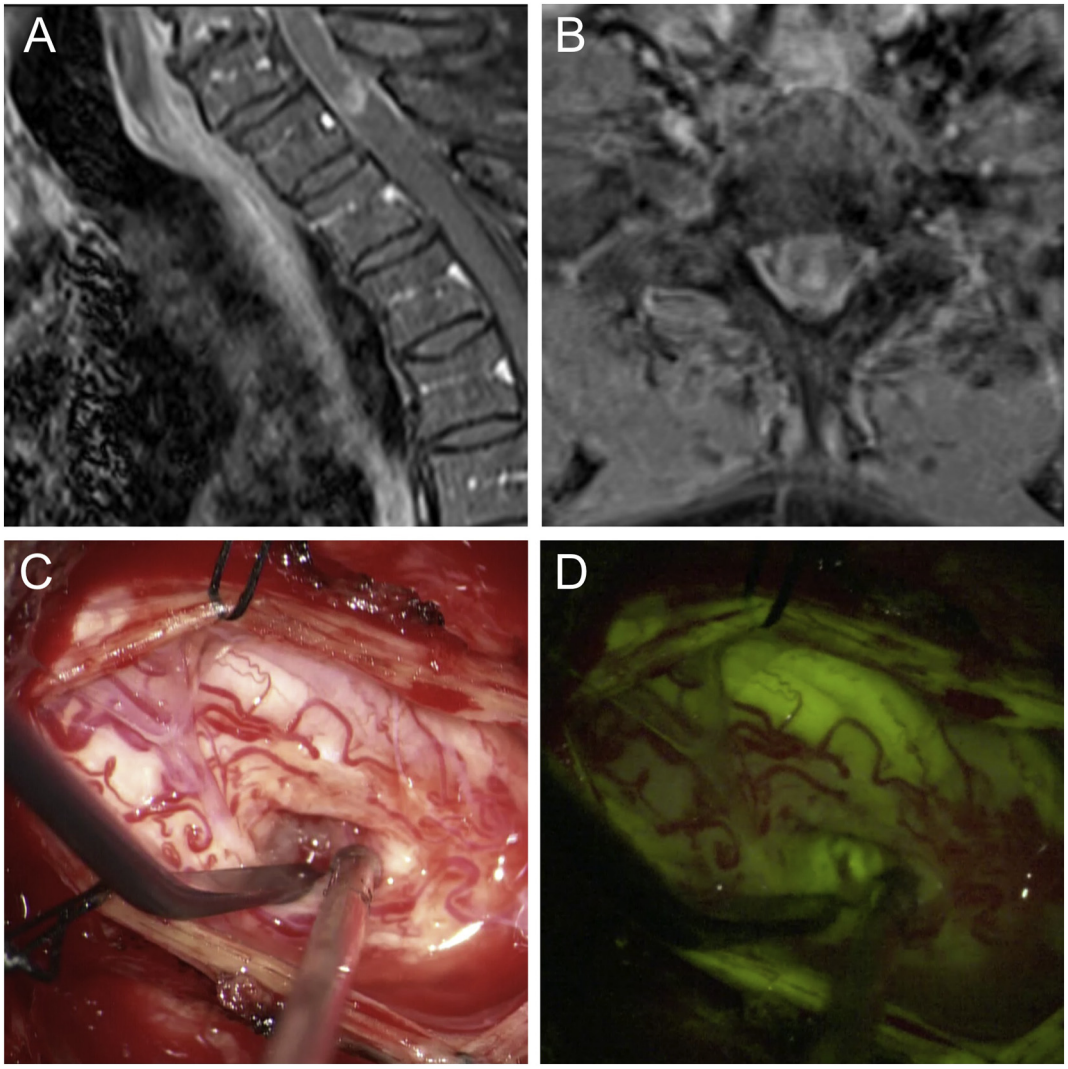

Fig. 4. 68 year-old male with progressive weakness of his lower extremities and a lesion centered at the level T1 (a and b). Intraoperative NaFl microscopic images demonstrating lesional fluorescein during microscopic dissection and tumor biopsy (c and d).

neurosurgical navigation which increased the potential for maximal safe resection of cranial lesions such as glioblastoma [7,9,11,13,16]. Thus far, there has been limited NaFl use in the spine for fluorescein-guided resection of intradural and intramedullary lesions [21,24]. Existing literature documenting NaFl use for vascular spinal pathology demonstrates minimal amount of non-specific staining within the parenchyma of the spinal cord. Our case reports (Table 1) demonstrate lesional fluorescein extravasation and the afforded ability to have microscopic fluorescein guidance for the operative management of spinal lesions.

Importantly, our illustrated cases demonstrate a proof of concept that NaFl may be useful for resection and biopsy of spinal lesions such as high-grade gliomas, pilocystic astrocytoma and ependymoma and supports the observations made by other groups [21,24]. Other studies, such as the study by Dr. Acerbi [21] demonstrate the utility of NaFL for resection of lesions. Further benefit from NaFl use may come from application to intrinsic intramedullary lesions where identification and accurate lesional biopsy is crucial and gross total resection is the goal of surgery.

Such lesions include intrinsic spinal high-grade glioma in both adult and pediatric populations. Currently, limited modalities exist for surgical navigation for the spine and the use of NaFl in such cases may increase the ability to locate and obtain diagnostic tissue for diagnosis and treatment planning. In our three patients, extensive pre-operative work-up failed to aid in the diagnosis of the patients and lesional biopsy was necessary to direct treatment. In these patients, the use of sodium fluorescein was found to be useful in the localization of pathological tissue. Final pathology demonstrated gram-positive bacteria/intramedullary abscess, EBV driven B-cell lymphoproliferative disease, and a primary glial neoplasm. In our biopsy case represented above, it was very difficult to discern abnormal tissue from spinal cord parenchyma and NaFl was extremely beneficial in the identification of abnormal tissue.

In summary, our study is the first that we know of to describe NaFl use for the biopsy of intramedullary spinal cord lesions [21]. Although systemic reactions have been reported to NaFl [25–27], existing literature, and our case presentations, demonstrate the overall safety for use of NaFl in the spine. Additional studies are warranted to fully elucidate the potential benefits and limitations of NaFl use for the resection and biopsy of intramedullary and intrinsic spinal cord lesions.

4. Conclusion

Fluorescein may be a helpful microsurgical tool in guiding identification, resection and sampling of intramedullary and intrinsic spinal lesions when complete resection is unlikely. Our clinical case reports demonstrate the initial efforts of evaluating NaFl in the spine as a biopsy tool. Further research is necessary to fully establish NaFl as a

Table 1
Patient demographics.

Patient	Age (years)	Sex	Clinical presentation	Location	Size	Histology
1	55	F	Lower extremity weakness, bladder incontinence, saddle anesthesia	T11/T12	20 × 10 × 15 mm	EBV driven B-cell lymphoproliferative disorder
2	51	M	Right lower extremity weakness	Multiple lesions	Multiple lesions	Gram + abscess
3	68	M	Bilateral lower extremity weakness	T1	6.2 mm × 4 mm	Glial cells proliferation with lymphocytic cuffing

safe and beneficial option for surgical approaches to spinal cord lesions.

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None.

Declaration of competing interest

None.

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