3T proton MR Spectroscopy evaluation of spinal cord lesions

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Abstract

Objective: The objective of this study was to evaluate intramedullary spinal cord lesions using magnetic resonance spectroscopy and correlate the results with histo-pathological examination (HPE). **Materials and Methods:** Approval for this study was obtained from our institute ethical committee. *Overall, 50 patients were recruited (29 male and 21 female),* with a maximum age of 53 years and minimum age of 7 years. The mean age group of the study was 33 years. Standard magnetic resonance imaging (MRI) spine was done on a Siemens Skyra 3Tesla MRI scanner. MR Spectroscopy (MRS) was performed for all patients with intramedullary spinal lesions after getting written consent. It was performed using single-voxel method. The change in the metabolite peak was observed in each case and the results were compared with HPE. These collected data were analyzed using SPSS 16.0 version. Descriptive statistics, frequency analysis, and percentage analysis were used for categorical variables; and for continuous variables, mean and standard deviation were analyzed. McNemar's test was used to find the significance between conventional MRI MRS. In the above statistical tool, the probability value 0.05 is considered as significant level. **Results:** From our study, we observed that by applying routine MRI sequences alone, we could only detect around 58% of the cases correctly. However, when MRS was done along with the conventional MR imaging, the number of cases detected significantly increased to 84%. By applying McNemar's test and comparing the conventional MRI and MRS with HPE, it was found that statistically significant difference exists with *P* value of 0.007. **Conclusion:** MRS of the spinal cord is a promising tool for research and diagnosis because it can provide additional information complementary to other non-invasive imaging methods. It is an emerging tool and adds new biomarker information for characterization of spinal cord tumors, to differentiate benign from malignant lesions and to prevent unnecessary biopsies and surgeries.

Key words: Spinal cord tumors; spinal MR spectroscopy; 3 Tesla

Introduction

A spectrum of abnormalities may affect the spinal cord including developmental anomalies, inflammatory and infectious processes, vascular disease, degenerative conditions, as well as benign and malignant neoplasms. Patients with intramedullary spinal cord lesions commonly present with tingling pain, numbness, and weakness.

Magnetic resonance imaging (MRI) is the current imaging modality of choice in the evaluation of patients presenting with myelopathic symptoms in the search for spinal cord lesions. It is important to recognize and differentiate non-neoplastic from the neoplastic process of the spinal cord as differentiation of the two entities is extremely crucial to the neurosurgeon.

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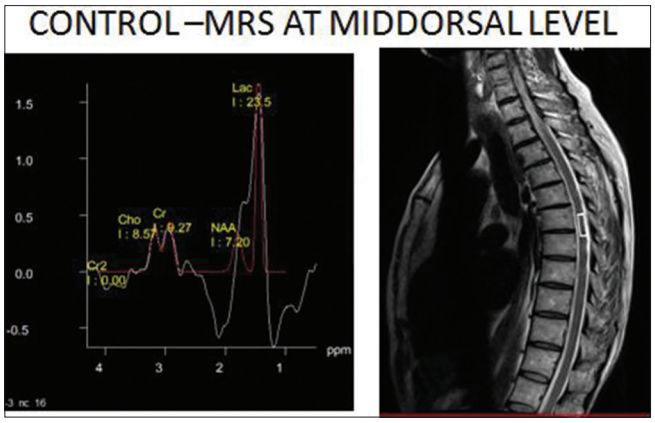

Figure 1: Single voxel MR spectroscopy at the mid dorsal cord level shows normal concentration of lactate, NAA, creatine with reduced choline

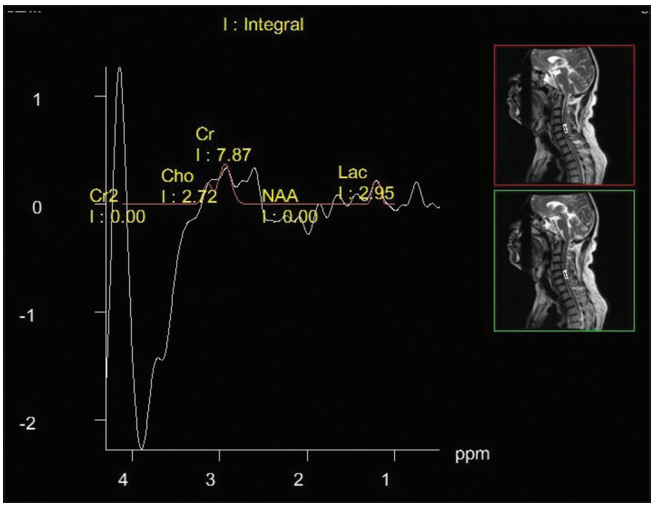

Figure 2: Control MRS at cervical level. Single voxel mr spectroscopy at the cervical cord level in another patient shows no significant increase in any specific metabolite

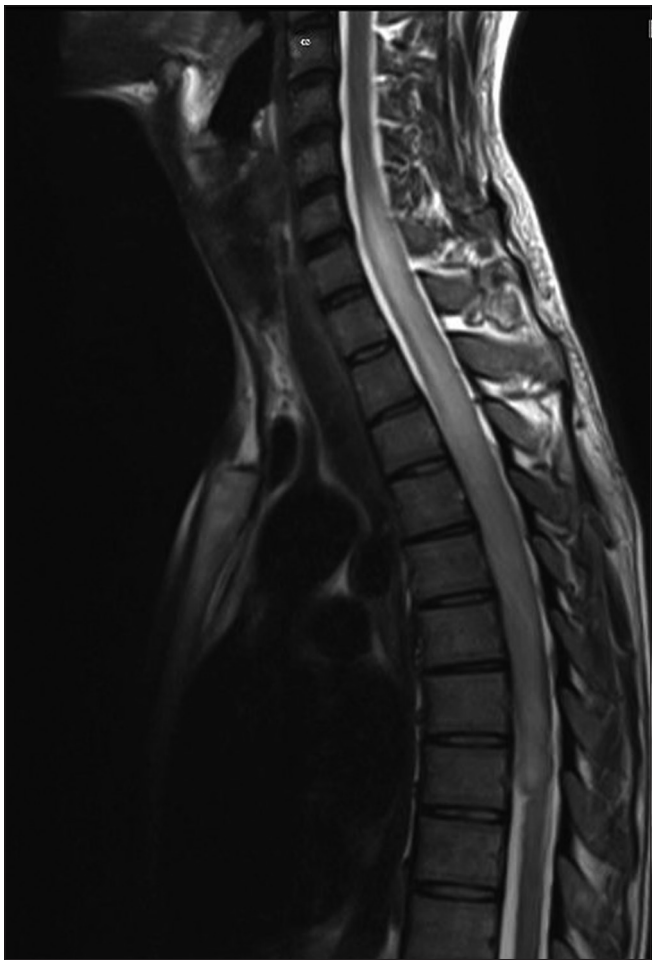

Figure 3: 30 years old male patient came with the complaints of of numbness involving all four limbs. T2 WI shows – long segment intramedullary hyperintensity from C6-D8 level with mild cord expansion

MR spectroscopy (MRS) is a non-invasive tool which helps characterize the chemical composition of human tissue. Thereby it can help better characterize pathologic processes affecting the spinal cord and helps provide important biomarkers for differential diagnosis.[1]

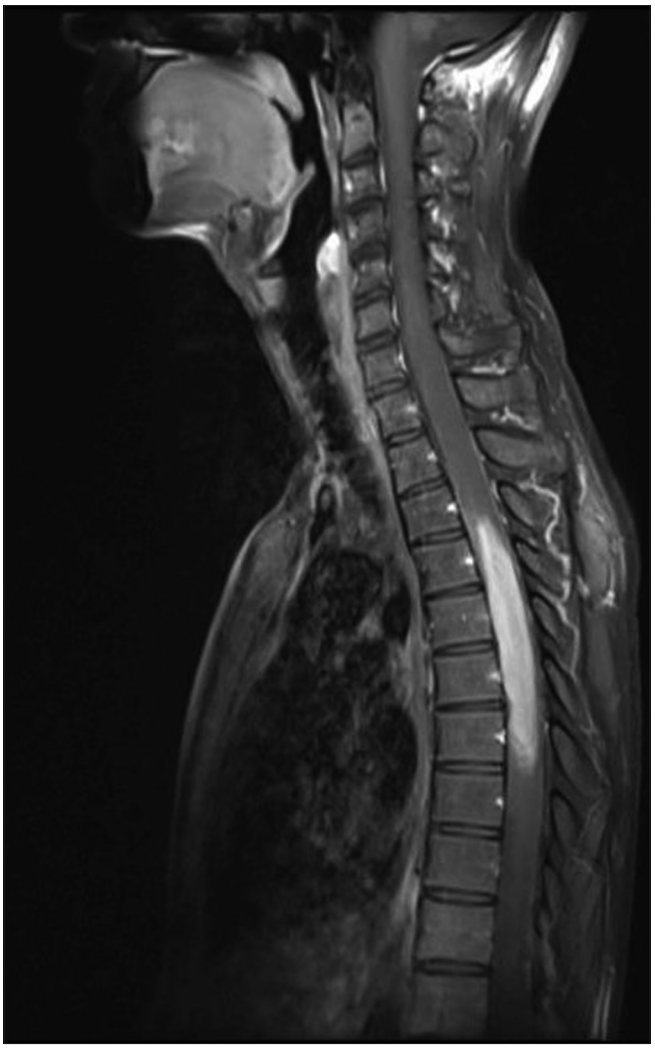

Figure 4: T1 fat sat post contrast image shows intense homogenous enhancement from D4 to D8 level

Rationale for the study

For several years, MRS has been applied in the investigation of pathologic processes involving the brain and has gained an increased acceptance by its potential in differentiating high- versus low-grade tumors, distinguishing tumor from non-tumoral tissue, differentiating solid lesions from cysts or abscesses,[2,3] monitoring the results of treatment, and occasionally predicting outcome.[4,5]

The information obtained by MRS helps differentiate benign versus malignant lesions[6] and may often prevent unnecessary invasive interventions such as surgery or biopsy. Thus, it can avoid further negative impact on patient outcome.

Materials and Methods

The study was approved by the institutional ethical clearance committee and informed written consent was obtained from all the patients and controls included in this study.

All subjects were screened with inclusion and exclusion criteria based on various neurological symptoms such as paraparesis, upper limb weakness, and back pain. Among these, only patients with intramedullary spinal cord lesions were included in this study. Patients with recurrent spinal lesions, previously operated spinal lesions, patients with contraindications for MRI (MRI-incompatible pacemaker, cochlear implant), non-consenting, and uncooperative patients were excluded from this study.

Clinical history and physical examination were obtained by evaluating neurosurgeon which included back pain, upper or lower limb weakness, and paraparesis. All the subjects were prospectively enrolled in the database for future collection of surveys and follow-ups. The goals of this investigation were focused on showing the value of MRS in the intramedullary spinal cord lesions and to compare the results with histopathological examination (HPE). This study was performed over a period of 1 year from 2015 to 2016.

MRI acquisition details

Standard 3T MRI of the spine was taken in T1 and T2 sagittal, T2 axial, and fat-suppressed T1 contrast sagittal images in a Siemens Skyra MRI Scanner. The location of lesion was identified and the characters of lesion such as solid/cystic, post contrast enhancement characters, any associated syrinx, and cord expansion were noted.

Single-voxel MRS was applied either in T2 sagittal or post contrast T1 sagittal fat-suppressed image. If the patient motion was identified, voxel position was updated and the measurement is repeated. The size of the voxel was adjusted according to the size of the lesion[7-11] and pulse gating was applied to reduce pulsation artifact. Echo Time (TE) was set at 135 and Repetion Time (TR) at 2000 ms.

The spectra were obtained with adequate homogeneity and fat suppression. The homogeneity was adequate. Manual shimming[12-14] was done in all cases and full width half maximum (FHWM) of 20 was obtained. Adequate fat

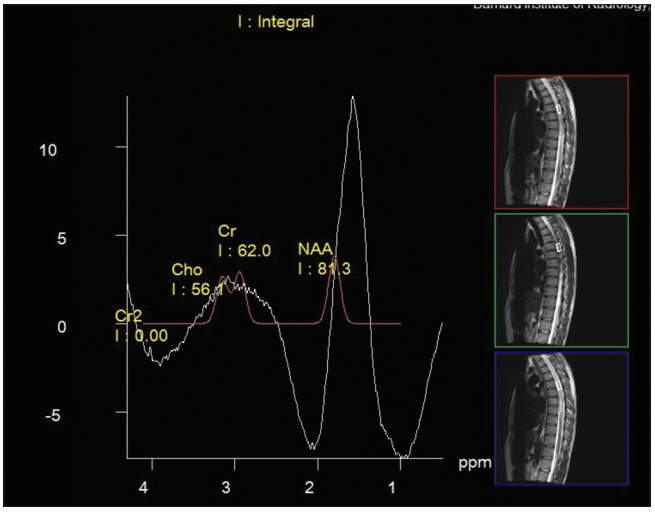

Figure 5: MR spectroscopy shows reduced NAA and creatine with lipid lactate peak at 1.3 ppm. Diagnosis: Intramedullary tuberculoma

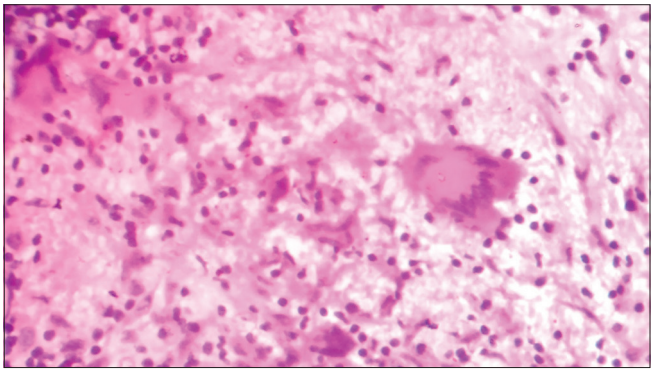

Figure 6: HPE-magnified image shows extensive areas of caseation necrosis with surrounding plasma cells and lymphocytes

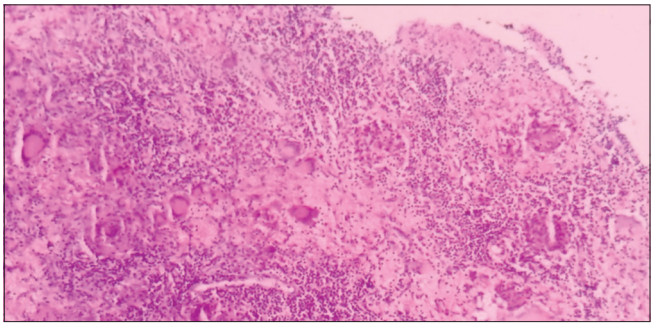

Figure 7: HPE Showed - Extensive areas of caseation necrosis with scattered epitheloid histocytes, lymphocytes, plasma cells and few neutrophils suggestive of Tuberculous etiology

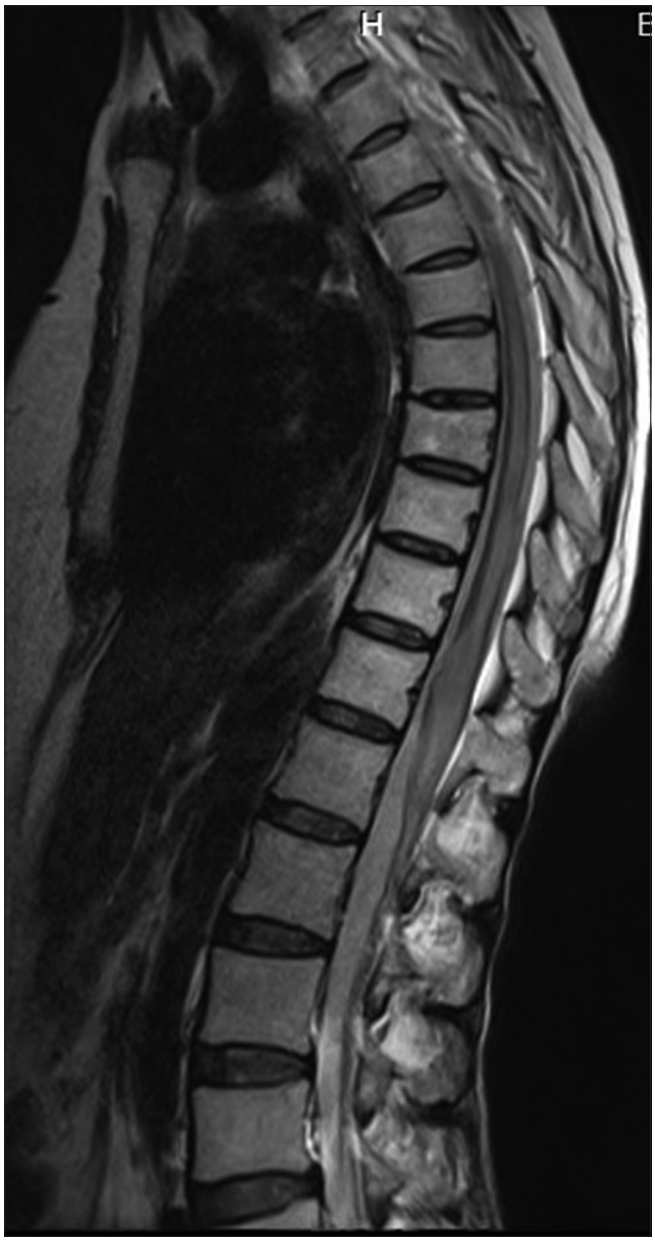

Figure 8: 56 years old female with chronic low back ache. Well defined homogenously enhancing intramedullary lesion at D12-L1 Intramedullary T2 hyperintensity noted in the lower spinal cord and conus

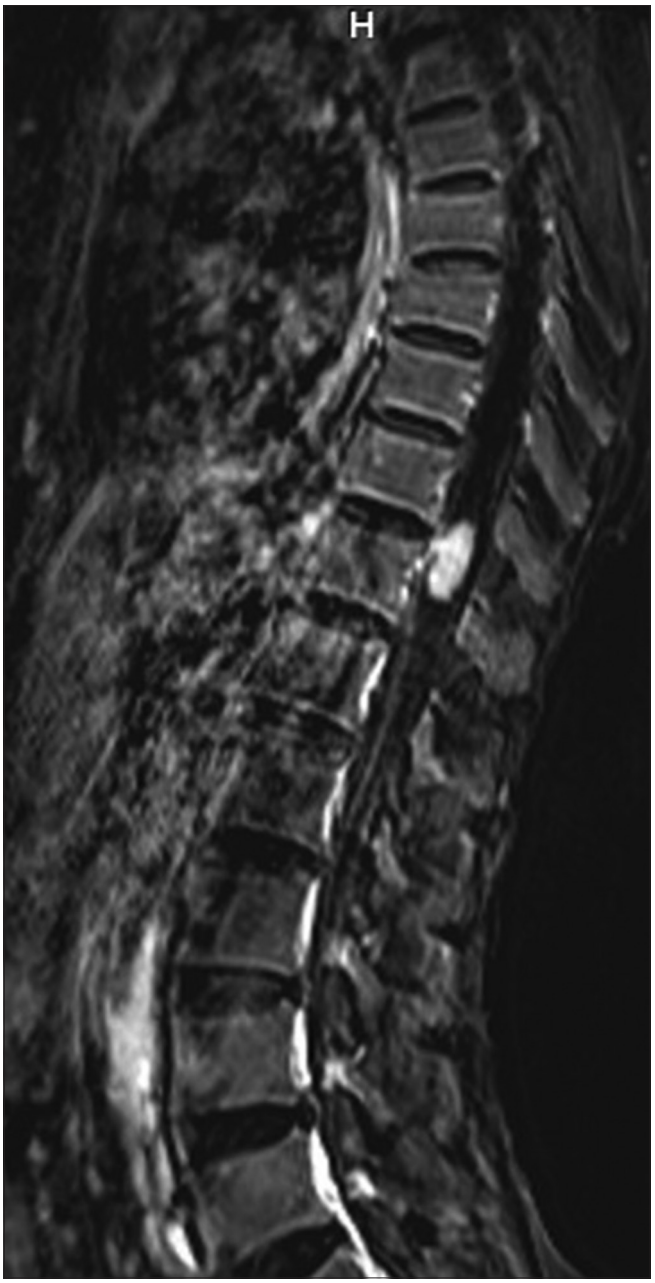

Figure 9: Well defined homogenously enhancing intramedullary lesion at D12-L1 level

suppression was obtained using chemical shift selective (CHESS) technique.

Further saturation bands were used around voxel, to avoid voxel bleeding and artifacts. Inner volume suppression bands[15,16] were applied to minimize the chemical shift displacement artifact and to reduce the influence of cerebrospinal fluid pulsations. B0 shimming, inner outer volume suppression, fat water suppression[17] were done as part of the protocol. Slice thickness was 3 mm. This sequence lasts about 5 min. The saturation pulses above and below the spectroscopy voxel facilitated flow compensation.

The time taken for acquiring T1sagittal, T2 sagittal, T2 axial, post contrast imaging, and MRS image for patients with spinal lesion was approximately 30 min and spectral processing was carried out separately which took 5 min, including data transfer to a workstation.

In MRS, single-voxel shapes were applied using rectangle shape. MRS data were acquired and post processing was done to obtain good spectrum of metabolites. Integral values of metabolites in each intramedullary spinal cord lesions were obtained. These patients were followed up for their post-operative tissue biopsy and HPE results to compare

the MRS findings. MRS was also done in normal subjects at cervical and dorsal levels for comparison and to detect the metabolite peaks.

Spinal magnetic resonance spectroscopy protocol

Overall, 50 patients were recruited (29 male and 21 female) [Table 1]. These subjects underwent standard MRI spine and MRS. Of these 50 patients, 22 patients were found to have malignant lesions. Twelve patients had histopathologically proven high-grade glioma and 10 patients had ependymoma. The remaining 28 patients were found to have benign lesions including intramedullary tuberculoma (9 patients), schwannoma (4 patients), dermoid cysts (2 patients), inflammatory lesions (7 patients) such as acute transverse myelitis, neuromyelitis optica, multiple sclerosis (3 patients), and spondylotic myelopathy (3 patients). Fifteen healthy subjects (8 male and 7 female) without any symptoms were taken as controls to find out spectrum of metabolites in a normal looking spinal cord at cervical and dorsal levels.

Statistical nalysis

The collected data were analyzed with SPSS 16.0 version (Statistical Package for Social Sciences, SPSS Inc., Chicago, IL, USA) software.

To find the significance between conventional MRI MRS, McNemar's test was used. Probability value of 0.05 was considered as significant level.

By applying conventional imaging alone, 58% of cases were detected correctly. When MRS was done along with conventional MRI, detection rate increased significantly to 84% as shown in Table 2.

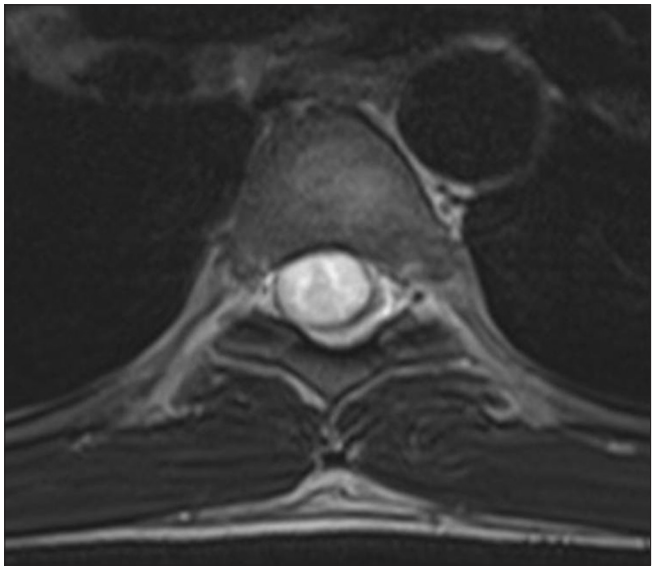

Figure 10: T2W-Intramedullary T2 hyperintense lesion with mild cord expansion

Frequency and Percentage Analysis

Comparison using McNemar's test

On comparing the conventional MRI sequences and MRS with HPE using McNemar's test, it was found that there was statistically significant difference between the above, with a *P* value of 0.007 as given in Table 3.

Table 1: 3T Spinal MRS protocol

MRI spine	TR	2000ms
T1 sagittal	TE	135
T2 sagittal	Flip angle	90degrees
T2 axial	SNR	1
T1 post contrast	Vector size	1024
	Band width	1200Hz

Table 2: Frequency and percentage analysis

	Frequency	Percent	Valid percent	Cumulative percent
Conventional				
Valid				
Yes	29	58.0	58.0	58.0
No	21	42.0	42.0	
Total	50	100.0	100.0	100.0
MRS				
Valid				
Yes	42	84.0	84.0	84.0
No	8	16.0	16.0	
Total	50	100.0	100.0	100.0

Table 3: Comparison using mcnemer test

Results	Conventional MRI	MRS
YES	29	42
NO	21	8
P	0.007	

Highly statistical significance with $P<0.01$ level

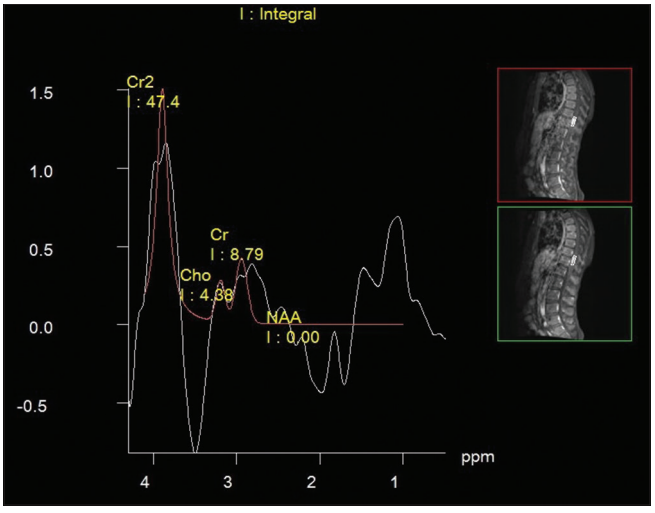

Figure 11: Lipid lactate peak with reduced choline and NAA, creatine increased due to contamination

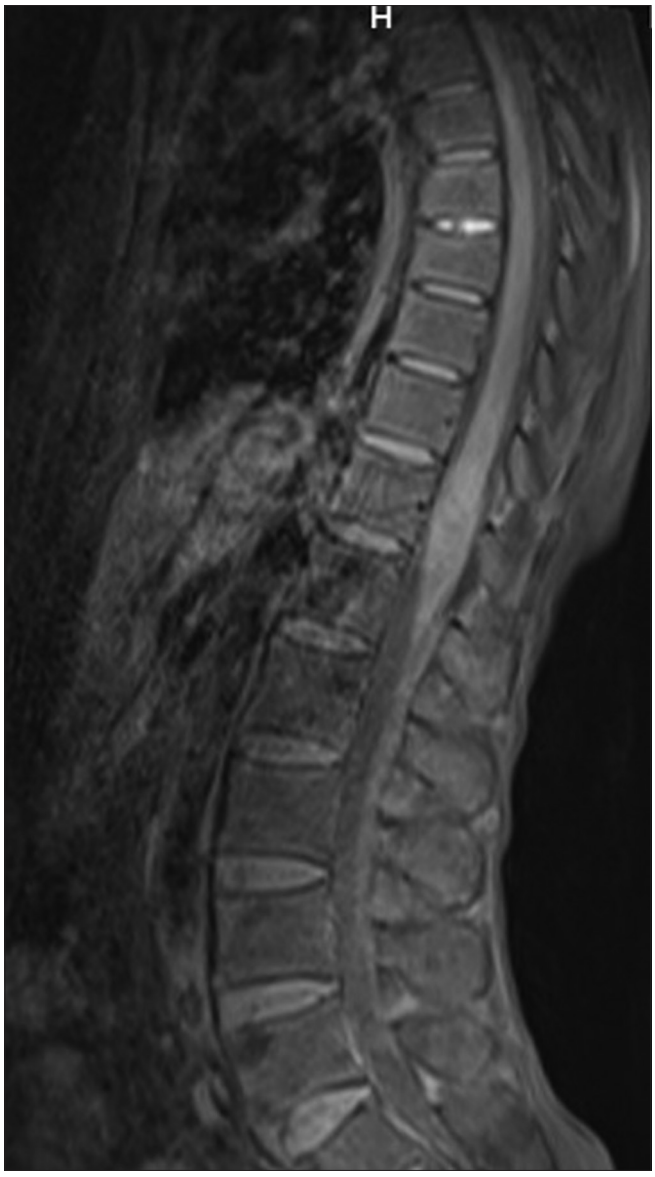

Figure 12: Pre contrast fat suppressed T1WI showing isointense nodular lesion at D12-L1 level

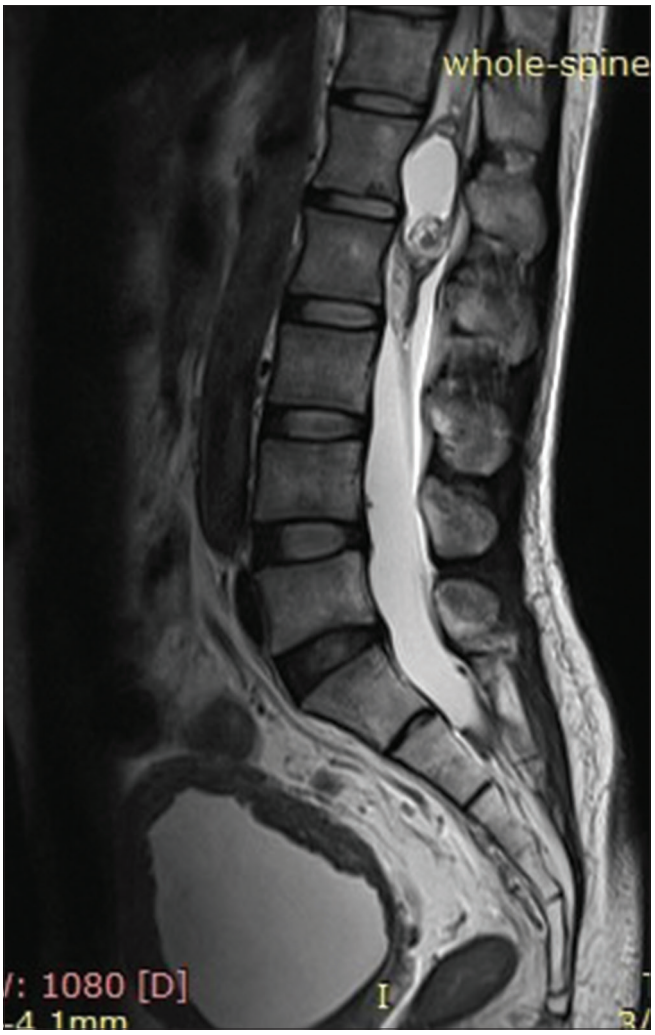

Figure 13: 37 years old male with paraparesis. Sagittal T2WI of lumbar spine revealing heterogeneous mixed intense lesion involving the conus

Results

Our study shows that among the 15 normal subjects taken as controls, a mild increase in lactate peak was observed at 1.3 ppm in few subjects [Figures 1 and 2], whereas in other subjects, metabolites were within normal limits. In contrast to controls, spectra in different pathologies in spinal cord showed a distinct change in metabolite fingerprint.

- In tuberculoma [Figures 3-12], there was a significant increase in lipid and lactate with decreased NAA. Choline was not significantly increased
- In dermoid cyst [Figures 13-19], we found lipids mixed with lactate lactate was also clearly elevated at 1.3 ppm
- In Ependymoma choline was significantly increased, NAA decreased, and lactate not very much decreased. In three patients, we observed significant increase in the creatine peak at 3.9 ppm
- In low-grade glioma [Figures 20-24], NAA decreased, lactate mildly increased, and creatine and choline significantly increased
- In glioblastoma multiforme [Figures 25-29], choline was increased, NAA decreased, and creatinewas almost zero
- In multiple sclerosis and other inflammatory lesions, a significant reduction in NAA was observed.

Discussion

Spinal MRS at higher field strengths (3 Tesla and above) provides increased signal-to-noise ratio (SNR) and can address increased B0 and B1 inhomogeneity problems,[18] encountered in lower field strengths.

The major objectives of this study were to examine the cellular changes that occur in patients with spinal cord lesions and to

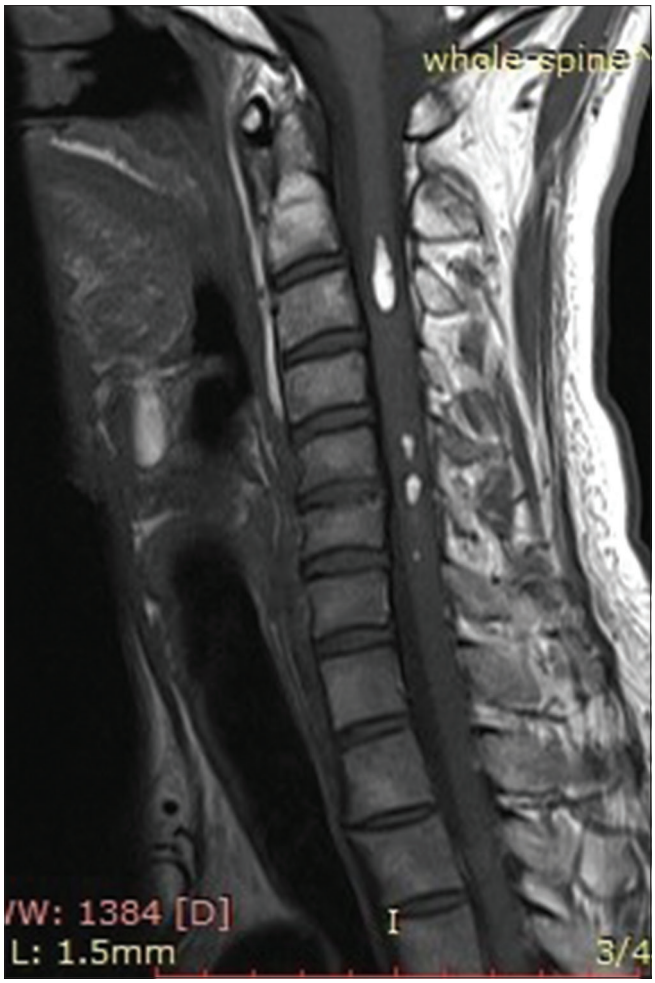

Figure 14: Sagittal T1WI of cervical spine showing multiple intramedullary fat containing lesions in the cervical spinal cord

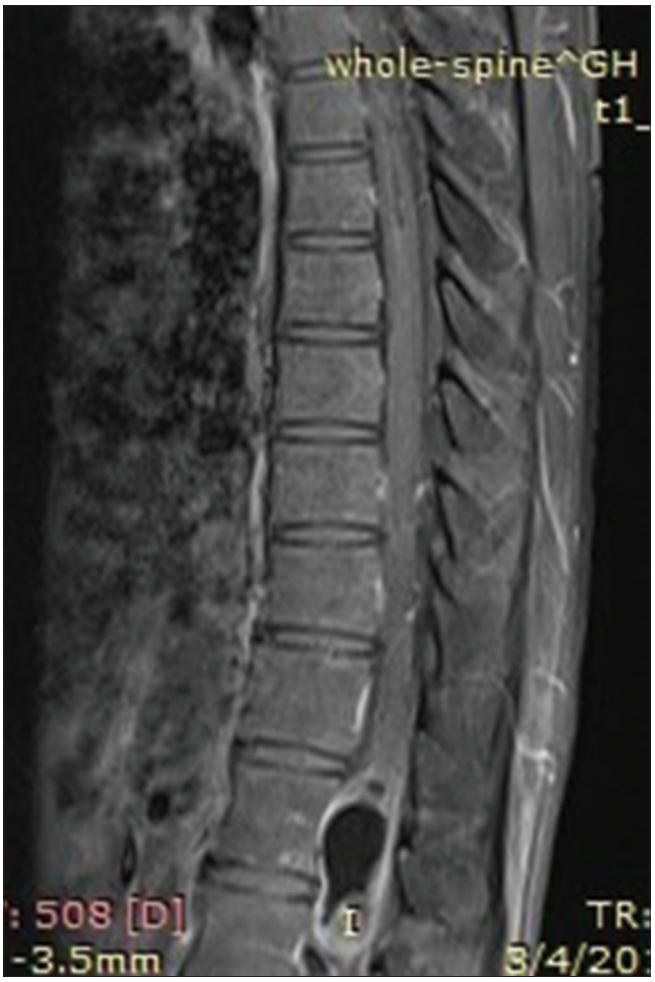

Figure 15: Post contrast FS T1WI with predominant peripheral contrast enhancement

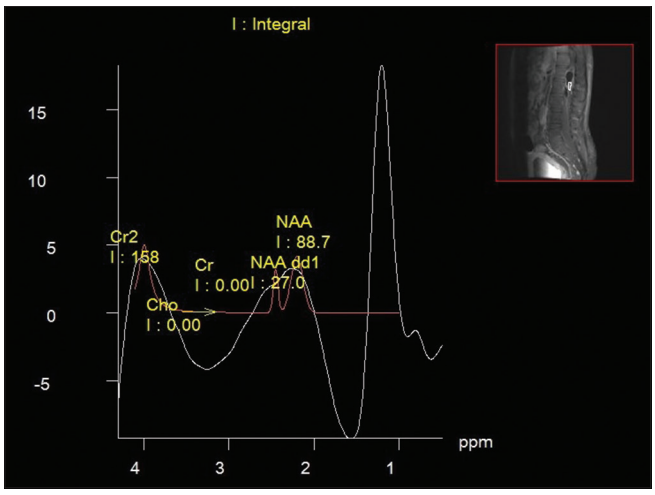

Figure 16: MRS:Lipid peak mixed with lactate. Diagnosis:ruptured intramedullary dermoid cyst

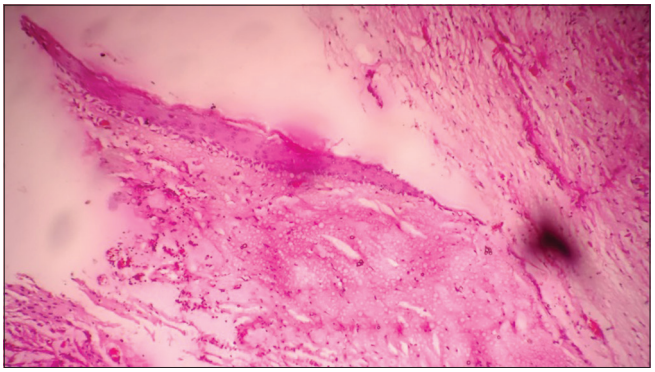

Figure 17: HPE shows stratified squamous epithelial cells supported by an outer layer of collagenous tissue

assess the feasibility of MRS to provide cellular biomarkers that could be used to differentiate spinal cord lesions.

The study protocol including T1 sagittal, T2 axial and sagittal, postcontrast, and MRS took around 30 minutes.

Spinal cord lesions are an important cause of morbidity and mortality. The need to differentiate tumors from tumor mimics is important for clinical management. MRS can

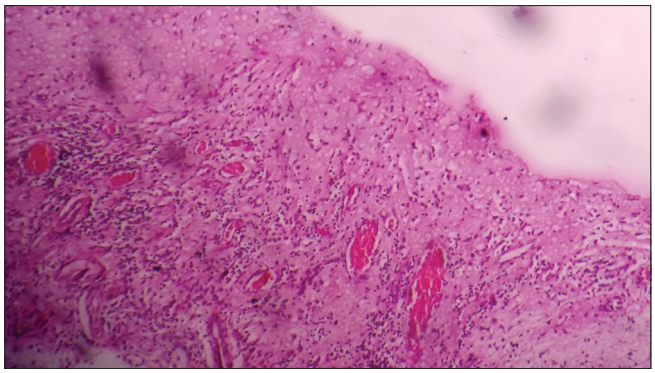

Figure 18: HPE shows stratified squamous epithelial cells associated with desquamation and breakdown of keratin

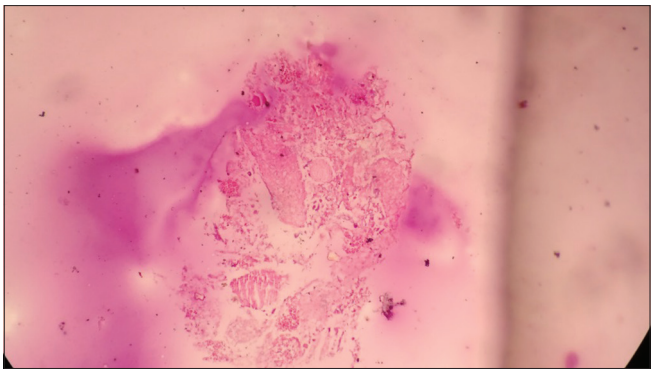

Figure 19: HPE shows desquamation and extensive breakdown of keratin

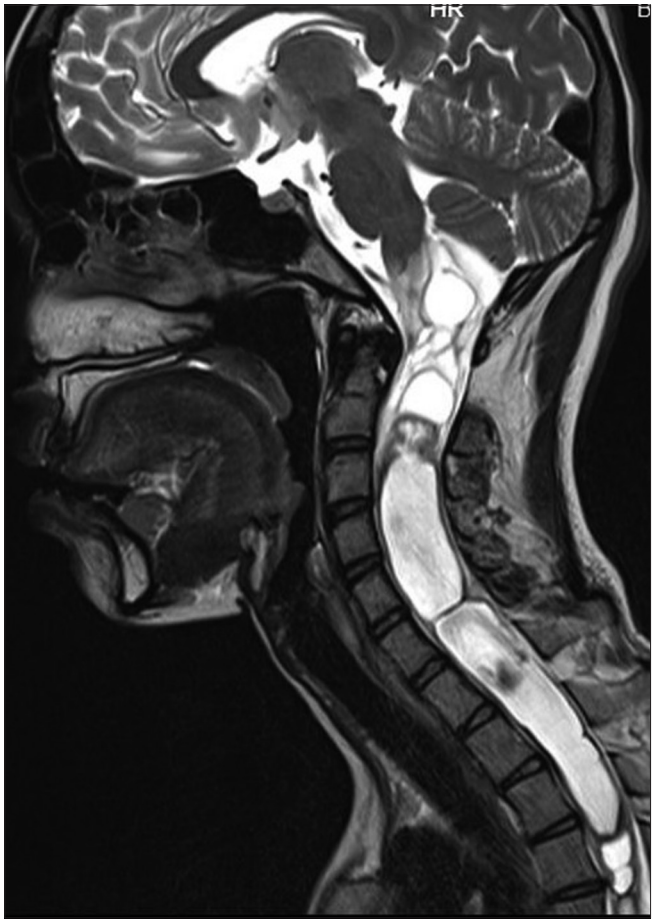

Figure 20: 20 yrs Old female patient presented with the complaints of gradual onset of quadriparesis. No history of fever. T2W sagittal image shows heterointense lesion with cystic areas causing cord expansion occupying the medulla, and cervico dorsal region

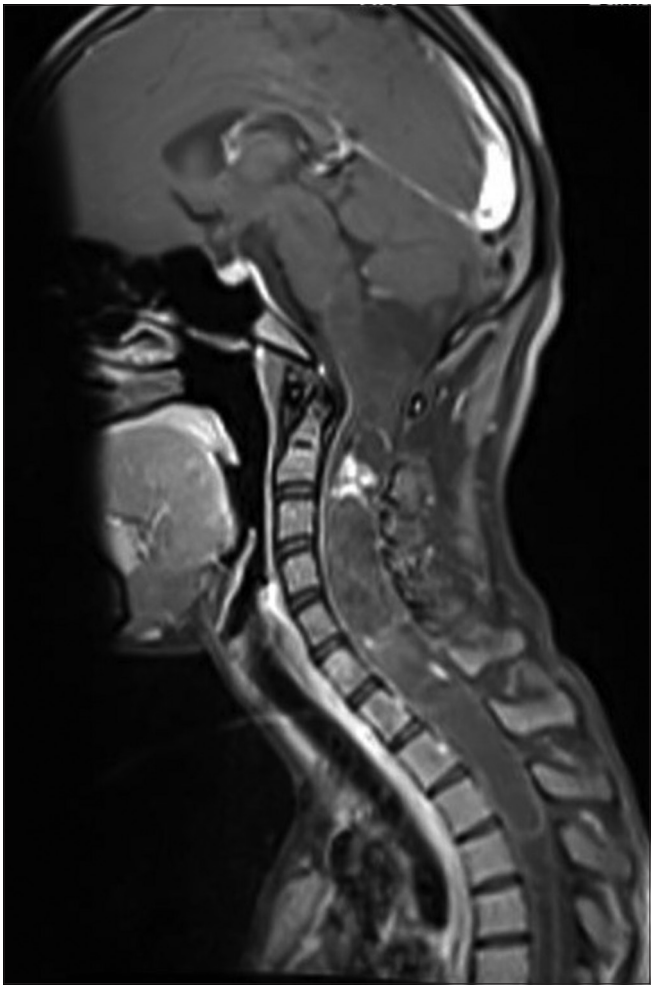

Figure 21: T1-postcontrast-heterogenouslyenhancing intramedullary lesion at cervicomedullary junction

provide information regarding cellular biochemical function in spinal cord. In our study, we evaluated the metabolite integral values in various spinal cord lesions and correlated these findings with histopathology.

Elevated choline was nearly always been observed in many malignant lesions such as astrocytoma. In case of benign lesions such as tuberculomas, lipid lactate peak [Figure 5] was mainly observed. In inflammatory conditions such as multiple sclerosis, reduction in *N*-acetyl aspartate with absence of choline was observed.

Comparison using McNemar's test

From our study, we observed that by applying conventional MRI alone, we could only correctly detect around 58% cases, whereas when MRS was done along with

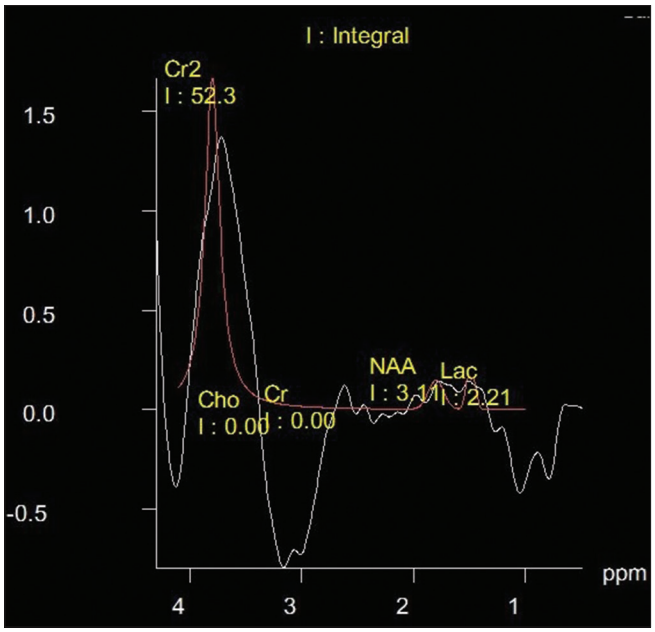

Figure 22: MR Spectroscopy- NAA reduced, lactate not very much increased and creatine increased.

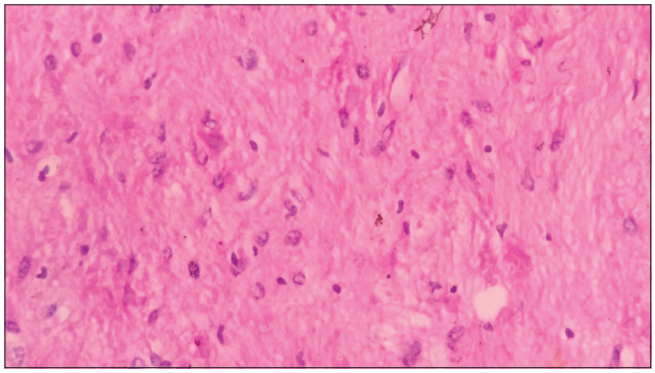

Figure 24: HPE shows neoplasm composed of cystic areas with protoplasmic astrocytes and densely cellular areas

conventional MRI, the number of cases detected is significantly increased to 84%. It is worth emphasizing that even in statistical analysis by applying McNemar's test and by comparing conventional MRI and MRS with HPE, it was found that statistically significant difference exists with *P* value of 0.007.

Our MRS findings in tuberculosis, dermoid cyst, and ependymoma also matched with those reported by Kim[19] They reported spinal MRS changes similar to changes seen in brain MRS; however, they did not show quantification with metabolite ratios.

We found the presence of lipid signals within spinal cord even in normal controls [Figures 1,2 and 30]. It is difficult to determine whether this is due to contamination from surrounding tissues or because of intrinsic properties.

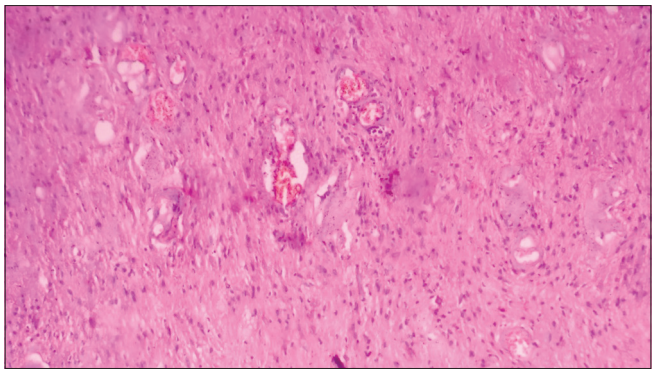

Figure 23: Biphasic neoplasm composed of looser (and cystic) areas with protoplasmic astrocytes and densely cellular areas composed of hair-like (piloid) cells, eosinophilic granular bodies, rosenthal fibers and oligodendroglial-like cells -low grade glioma

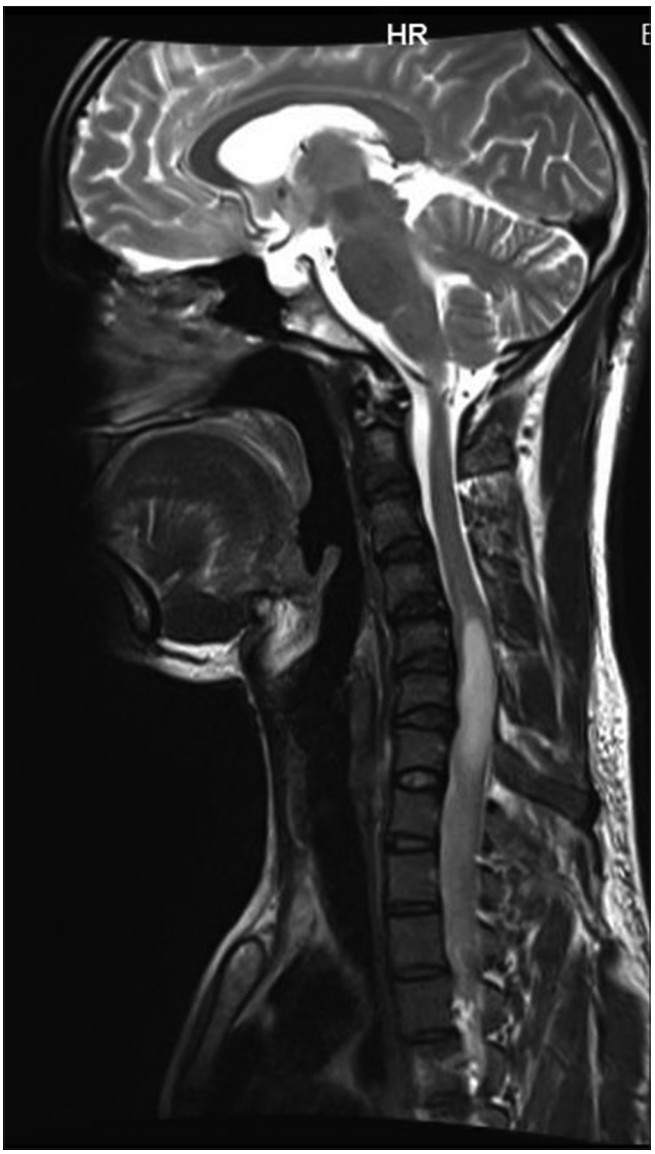

Figure 25: 30 yrs old male patient presented with progressive weakness involving both upper limb. T2WI shows intramedullary T2 hyperintensity with cord expansion extending from C5-C7

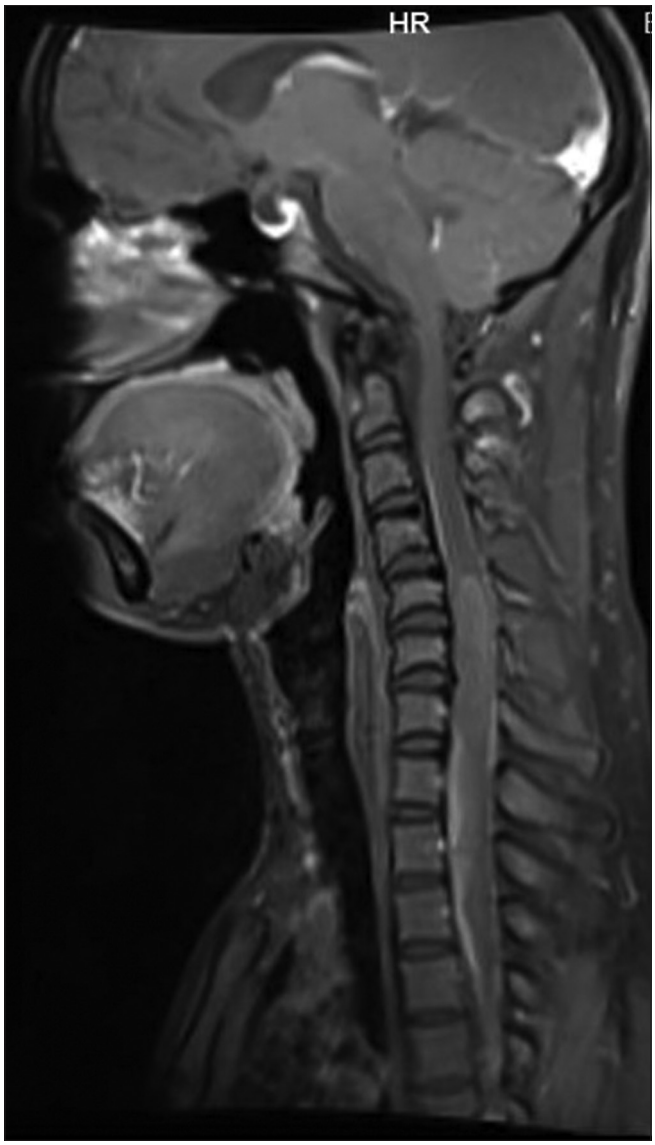

Figure 26: T1 post contrast and subtracted images show subtle enhancement within the lesion

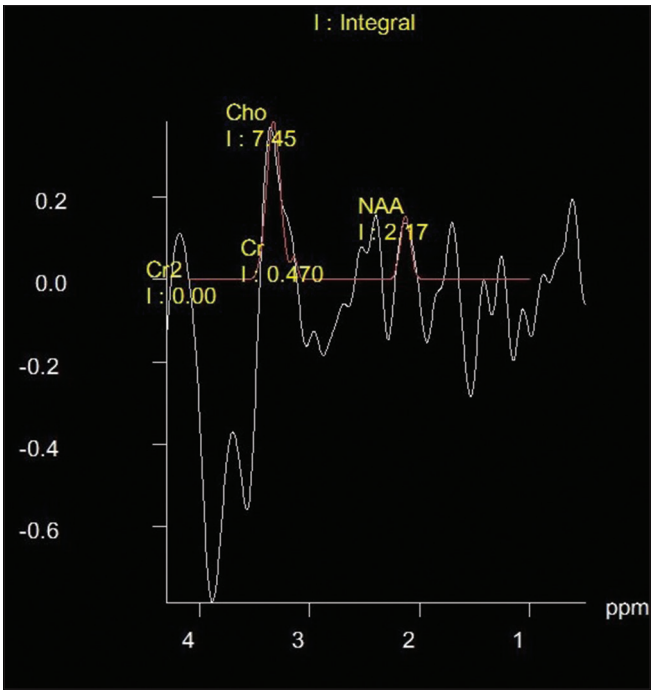

Figure 27: MR spectroscopy- choline increased, creatine almost zero, NAA is reduced. Diagnosis: Astrocytoma

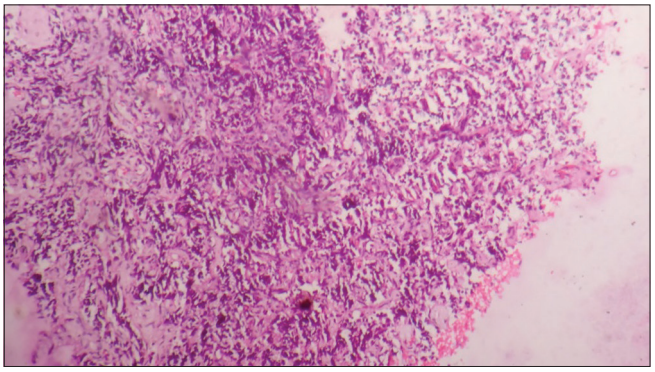

Figure 29: HPE shows increased cellularity with microvascular proliferation - Glioblastoma multiforme WHO grade 4

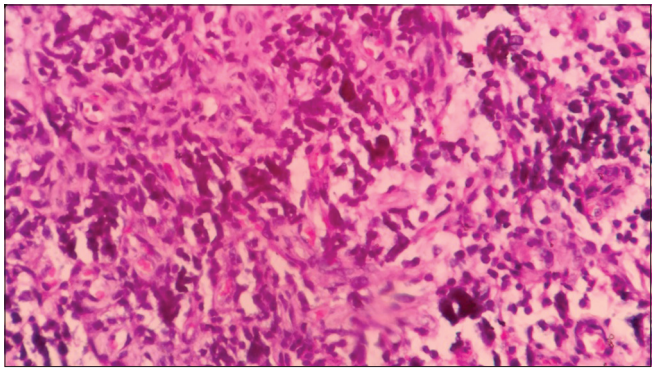

Figure 28: HPE shows mitotic figures with microvascular proliferation and pseudopalisading necrosis

However, elevated lipid peaks in a homogeneously enhancing intramedullary lesion was found be a strong predictor of tuberculoma [Figure 4], whereas elevated choline integral values in an intramedullary lesion were detected in tumors.

However, more studies with high spectral quality in larger patient cohorts are needed to increase diagnostic confidence in differentiation of intramedullary tumors and to enhance specific differential diagnoses or to provide a tool for monitoring the course of a disease.

Limitations

Spinal MRS is not as straightforward as brain spectroscopy, and the results are affected by several factors such as susceptibility changes due to anatomic in-homogeneity and small size of spinal cord for single-voxel placement. The spectral quality is also affected by cerebrospinal fluid (CSF)

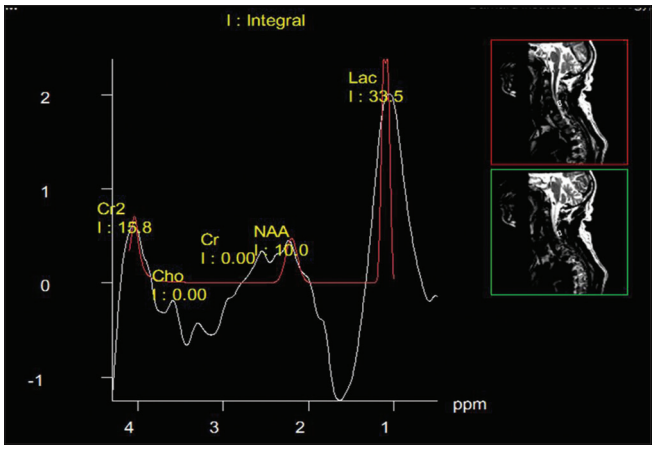

Figure 30: Control MRS at cervical level. Single voxel MR Spectroscopy at the cervical cord level shows mild increase in the lactate concentration probably due to contamination with no detectable choline

flow and cardiac and respiratory motion. These could be reduced to a certain extent by use of pulse gating in all cases.

In MRS, single-voxel shapes were applied using rectangle shape. It was difficult to include a region of interest in a normal appearing spinal cord fully on any imaging plane. In some cases, it produced potential partial volume effect or signal contamination from surrounding tissue.

Conclusion

MRS of the spinal cord is a valuable noninvasive tool for research and diagnosis because it can provide additional information in which it is complementary to other noninvasive imaging methods. It is also an emerging tool which adds new biomarker information to characterize the spinal cord tumors, to differentiate benign and malignant lesions and thereby help prevent unnecessary biopsies and surgeries. However, the application of MRS in the spinal cord is not straightforward, and great care is required to attain optimal spectral quality.

The presence of lipid peak in a homogeneously enhancing intramedullary lesion with T2 hyperintensities provides a potential useful radiological biomarker of tuberculoma of spinal cord and can prevent unnecessary interventions.

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Conflicts of interest
There are no conflicts of interest.

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