ORIGINAL ARTICLE

Utility and challenges in intraoperative consultation of spinal lesions by crush smear cytology

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ABSTRACT

Background: Various methods are used for intraoperative consultation of spinal lesions. Crush smear cytology is one such method that is accurate, rapid, and allows preservation of tissue for paraffin-embedded sections.

Aims: To study the cytomorphology of various neoplastic and nonneoplastic lesions involving and compressing the spinal cord. To evaluate accuracy and discuss diagnostic pitfalls of crush smear cytology.

Materials and Methods: Over a period of 5 years (January 2008 to October 2012), a total of 57 spinal lesions were referred for intraoperative cytology. In four cases, material was inadequate for evaluation, so we analyzed 53 cases.

Results: Majority of lesions were neoplastic accounting for 86.79% whereas nonneoplastic lesions constituted 13.20%. Most of the tumors were low grade (82.92%). Overall accuracy rate was 90.56% with accuracy of 91.30% and 85.71% for neoplastic and inflammatory lesions, respectively.

Conclusion: Crush smear technique is a simple, reliable, easy, and rapid method for diagnosing neoplastic and inflammatory lesions involving and compressing the spinal cord. It gives an immediate idea of prognosis so that surgeon can modify the operative procedure, if necessary.

Key words: Crush smear, intraoperative cytology, pitfalls, spinal lesions

Introduction

Spinal lesions can be localized and diagnosed precisely with the help of computed tomography and magnetic resonance imaging (MRI). However, intraoperative consultation for spinal lesions by crush smear cytology can provide a preliminary diagnosis so that surgeon can decide further management on the operating table.[1]

The ideal intraoperative method used should be accurate, rapid, and should allow preservation of tissue for paraffin-embedded sections. The application of smear technique as a mean of obtaining rapid diagnosis for neurosurgical biopsies is now well-established,[2-5] and is being used increasingly in many neurosurgical centers, though some of the centers still use frozen section.

In the literature, there are many studies on squash cytology of central nervous system (CNS) lesions including both brain and spinal cord.[3,4,6-10] However, very few studies are done on spinal lesions alone.[2] The aims of this study were to: (1) Study the cytomorphology of various neoplastic and nonneoplastic lesions involving and compressing the spinal cord, (2) correlate cytological diagnosis with histopathological diagnosis to evaluate accuracy of crush smear cytology, and (3) to discuss diagnostic pitfalls in the cytodiagnosis of spinal lesions.

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Materials and Methods

The study was carried out from January 2008 to October 2012 in a Tertiary Care Hospital having a well-equipped neurosurgery department, operation theater, and patients' referral. During this period, we received a total of 492 cases of CNS lesions, out of which 420 were intracranial and 72 were spinal. Out of 72 spinal lesions, only 57 spinal lesions were referred for intraoperative cytology. All the patients attending neurosurgery OPD having clinical signs and symptoms as well as imaging features suggestive of spinal lesions and who underwent operative procedure were included whereas primary bone tumors and metastatic tumors not involving the spinal cord were excluded from the study. In each patient, detailed clinical history was obtained. Informed consent was taken from each patient. All biopsies were obtained by open laminectomy procedure, and the crush smear technique described by Adams *et al*.[11] was employed for the preparation of smears. Wet smears were immediately fixed in 95% ethyl alcohol. Fixed smears were subsequently stained with rapid hematoxylin and eosin, Toluidine blue stain (in some cases), and any other stain such as May–Grunwald–Giemsa stain (wherever applicable). The entire process took 5–7 min. Smears were assigned the categories of neoplastic, inflammatory, and unsatisfactory/inadequate for interpretation. When biopsy material was adequate but was difficult to spread and the smears showing mainly blood or scanty tissue, were considered unsatisfactory for evaluation. Gliomas were graded as low and high grade. Remaining part of the tissue and more tissue whenever received later on was fixed in 10% formalin and submitted for histopathology processing by routine method. The recent WHO classification (2007)[12] was used for classification and grading of tumors.

Results

The youngest patient in the study was 9-year-old whereas the oldest patient was 75-year-old. The study shows slight male predominance with M: F ratio of 1.85. The most frequently involved spinal level was thoracic 19 cases (33.33%), followed by lumbar 13 cases (22.80%). Compartmental distribution of cases showed that most of the lesions were extramedullary of 43 cases (75.43%) among which intradural lesions were more common of 23 cases (40.35%) than extradural. Intramedullary lesions were 14 cases (24.56%). Most common complaint was nerve root pain (57.89%) followed by back pain (54%) followed by paraparesis (47%) and paresthesia (43.85%). 15 patients (26.31%) presented with sensory loss. Out of total 57 cases, 53 cases were adequate for cytological interpretation with adequacy rate of 92.98% and total four cases were inadequate for interpretation accounting for an inadequacy rate of 7.01%.

Neoplastic lesions were common and constituted 46 cases (86.79%) whereas nonneoplastic lesions constituted seven cases (13.20%) [Table 1]. Group A comprised of neoplastic lesions having a total of 46 cases. Benign nerve sheath tumor (BNST) was the most common tumor accounting for 15 cases (32.6%) followed by meningioma 10 cases (21.73%). Group B of inflammatory lesions was having a total of seven cases. Tuberculosis was the most common inflammation. Neoplastic lesions were graded according to the WHO classification of CNS tumors, 2007 [Table 2].[12]

Complete correlation was seen in 48 cases (90.56%) [Table 3]. Diagnostic discrepancy was noted in five cases (9.44%). In discrepant cases, two cases were of frank error [Table 4]. In these cases, cell lineage was wrongly diagnosed. One case of fibrous meningioma was misdiagnosed as schwannoma. One case of hemangioblastoma was misdiagnosed as pilocytic astrocytoma. Two cases had partial correlation. In these cases, cell lineage was correctly diagnosed, but grading was incorrect. One case each of high-grade ependymoma and astrocytoma was misdiagnosed as low grade ependymoma and astrocytoma, respectively. One case of tuberculosis was misdiagnosed as chronic nonspecific inflammation on cytology. Diagnostic accuracy for neoplastic lesions was 91.30% and for nonneoplastic/inflammatory lesions was 85.71%. Overall diagnostic accuracy was 90.56% [Table 5]. In the present study, sensitivity, specificity, and diagnostic accuracy of squash smear cytology for diagnosis of high-grade lesions were 77.77%,

Table 1: Cytomorphologic diagnosis of lesions on adequate smears

Cytological diagnosis	Number of cases (%)
Neoplastic	
BNST*	15 (32.6)
Meningioma	10 (21.73)
Ependymoma	5 (10.80)
Low grade	3
High grade	1
Myxopapillary ependymoma	1
Astrocytoma	4 (8.69)
Pilocytic astrocytoma	2
Low-grade astrocytoma	2
Metastasis	3 (6.52)
Multiple myeloma	1 (2.17)
Lymphoma	1 (2.17)
MRCT†	1 (2.17)
Chordoma	1 (2.17)
Paraganglioma	1 (2.17)
Lipoma	2 (4.34)
Epidermal cyst	2 (4.34)
Total (%)	46 (100)
Inflammatory/nonneoplastic	
Tuberculosis	4 (57.14)
Pyogenic abscess	2 (28.57)
Nonspecific inflammation	1 (14.28)
Total (%)	7 (100)

*BNST – Benign nerve sheath tumor; †MRCT – Malignant round cell tumor

Table 2: Grade wise distribution of lesions on cytology

Grade	Tumor	Number of cases (%)
Low grade		
I	Pilocytic astrocytoma	2
	Meningioma	10
	Nerve sheath tumor	15
	Myxopapillary ependymoma	1
	Paraganglioma	1
II	Low-grade astrocytoma	2
	Ependymoma	3
	Total	34(85)
High grade		
III	Anaplastic ependymoma	1
	Anaplastic astrocytoma	-
IV	Glioblastoma	-
	MRCT	1
	Metastasis	3
	Lymphoma	1
	Total	6 (15)

MRCT – Malignant round cell tumor

Table 3: Cyto-histopathological correlation in the study

Cytological diagnosis	Total number of cases	Consistent	In-consistent	Concur-dance (%)
Meningioma	10	10	-	100
BNST	15	14	1	93.33
Ependymoma LG‡	3	2	1	80
Ependymoma HG§	1	1	-	
Myxopapillary ependymoma	1	1	-	
Pilocytic astrocytoma	2	1	1	50
Astrocytoma LG	2	1	1	
Metastasis	3	3	-	100
Multiple myeloma	1	1	-	100
Lymphoma	1	1	-	100
MRCT	1	1	-	100
Chordoma	1	1	-	100
Paraganglioma	1	1	-	100
Lipoma	2	2	-	100
Epidermal cyst	2	2	-	100
Tuberculosis	4	4	-	100
Pyogenic abscess	2	2	-	100
Chronic nonspecific inflammation	1	-	1	0
Total (%)	53	48	5 (9.43)	90.56

‡LG – Low grade; §HG – High grade; MRCT – Malignant round cell tumor; BNST – Benign nerve sheath tumor

100%, and 95.12%, respectively, while positive predictive value and negative predictive values were 100% and 94.11%, respectively.

Discussion

Intraoperative consultation of spinal lesions by crush smear cytology is considered to be an important preliminary diagnostic tool to distinguish neoplastic lesions from nonneoplastic conditions at surgery. The goal of a pathologist in intraoperative consultation is to diagnose and grade every case definitively to optimize the surgery. In the present study, adequacy rate was 92.98%, which is comparable to those of whole CNS lesions.[13,14] In inadequate for interpretation cases, two were inflammatory lesions, one case each of hemangioma and meningioma. In these cases, smears could not be spread out properly, showed only blood or material could not be retained on the slides or showed crush artifacts due to firm texture of these lesions, and so smears could not be assessed [Figure 1]. In the present study, accuracy rate by cyto-histopathological correlation was 90.56%. In the study of 517 cases of spinal lesions by Goel *et al*.,[2] accuracy by cyto-histopathological correlation was 86.2% in case of tumors only while it was 82.4% in case of both inflammatory and neoplastic lesions. The results of the present study are comparable with those of Goel *et al*.[2] Diagnostic accuracy of our study of spinal lesions is also comparable with diagnostic accuracy of whole CNS lesions.[4,8] Out of 53 adequate cases, correct cytological diagnosis was given in 48 cases with discordance in 5 cases.

Table 4: Cases misdiagnosed on cytology

Final histopathology diagnosis	Cytodiagnosis
Fibrous meningioma	Schwannoma
Hemangioblastoma	Pilocytic astrocytoma
Astrocytoma high grade	Astrocytoma low grade
High-grade ependymoma	Low-grade ependymoma
Tuberculosis	Chronic nonspecific inflammation

Table 5: Diagnostic accuracy of spinal lesions

Lesions	Total cases	Positive correlation	Misdiagnosis	Inadequate	Diagnostic accuracy (%)
Neoplastic	48	42	4	2	91.30
Inflammatory	9	6	1	2	85.71
Total	57	48	5	4	90.56

In discrepant cases, one case each of high-grade ependymoma and astrocytoma was misdiagnosed as low grade ependymoma and astrocytoma, respectively. It may be due to the nonrepresentative sampling from low-grade area. Any high-grade glial tumor is not uniformly high grade, especially in initial stage. It varies in grade from region to region. Hence, sampling error can easily lead to the incorrect under-diagnosis of tumor. In cytological evaluation, there is tendency to disregard the necrotic debris and therefore cytology often diagnose a lower grade of tumor than histology. Similar findings had been noticed by Shukla *et al*.[14] and Kini *et al*.[10] Goel *et al*.[2] also found partial correlation due to grades and mixed tumors. One case of hemangioblastoma was misdiagnosed as pilocytic astrocytoma. This may be because of nonrepresentative sampling. Spinal hemangioblastoma

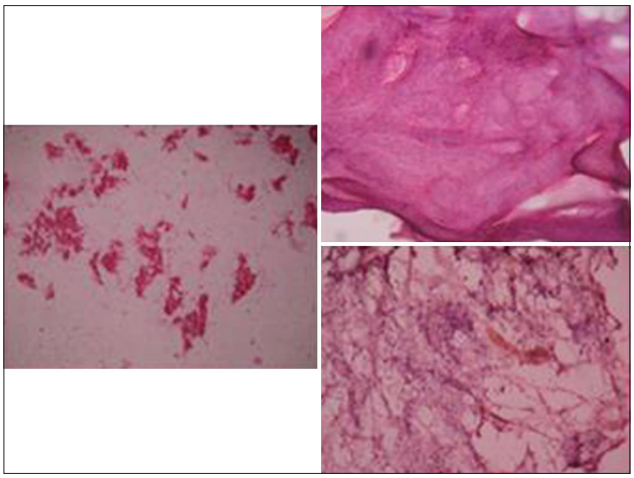

Figure 1: Photomicrograph showing drying, crushing, and spreading artifact

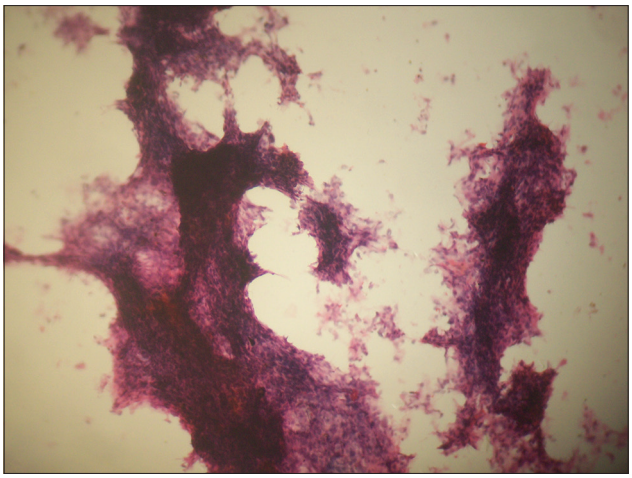

Figure 2: Photomicrograph showing tight clusters with few dissociated cells in fibrous meningioma misdiagnosed as schwannoma

also present as mural nodule such as pilocytic astrocytoma on MRI and if biopsy is taken from the cyst wall which shows only reactive piloid astrocytosis, misdiagnosis of pilocytic astrocytoma can be done. Also in hemangioblastoma, obtaining good quality smears was difficult. Similar difficulty was observed by Goel *et al*.[2] Distinction between schwannomas and meningiomas was the most common difficulty. The presence of whorls, psammoma bodies, discohesive cells at periphery of cell clusters, intranuclear inclusions, and grooving helped in diagnosing meningiomas. BNST and meningiomas were slightly firm in nature, so difficult to spread. However, it did not interfered with the cytological diagnosis in the present study as interpretation was possible by observing cells at the periphery. In such cases, selection of tissue preferably soft for smearing is also important. Iqbal *et al*.[6] also found schwannoma and neurofibroma difficult to smear, but did not face any difficulty in diagnosing them. One case of fibrous meningioma was incorrectly diagnosed as schwannoma [Figure 2]. It may be due to the presence of spindle-shaped cells arranged in fascicles and bundles, absence of psammoma bodies, whorls, and discohesive cells which make it difficult to study nuclear details. Similar finding has been reported by Mitra *et al*.[15] and Goel *et al*.[2] One case of tuberculosis was misdiagnosed as chronic nonspecific inflammatory lesion on cytology. Smears showed only fibrous tissue and few lymphocytes. Representative area was missed due to extensive fibrosis. Similar findings were observed by Iqbal *et al*.[6] Diagnostic discrepancies in our study did not have any effect on immediate management decisions by the neurosurgeon.

Over the last two decades, there are definitive advances in neuro-radio diagnostic methodologies, and also there are improvements in the cytological and histological techniques including staining methods. All these factors might have added to the higher diagnostic indices in recent studies as compared to the older ones. Discordance in our study was mainly due to sampling error, partial correlation, and difficulty in interpretation due to crush artifacts [Figure 1].

Conclusions

The smear technique is a simple, reliable, easy, and rapid method as turnaround time is around 10 min from receipt of sample to give diagnosis. It is a useful tool for the intraoperative diagnosis of spinal space occupying lesions having overall accuracy of 90.56%. As it has high positive predictive value of 100%, tumors are not over graded. Rather, cytology tends to grade tumors lower than histopathological grading. However, with these advantages, certain potential pitfalls should be given due consideration. Piloid astrocytosis in glial tissue surrounding certain tumor can lead to misdiagnosis. Correct grading of tumor is possible only to some extent, as small pieces of tumor is studied in smear preparation. Crush artifacts may interfere with interpretation. Due to time constraint, tumor can be categorized under a broad heading leading to under diagnosis.

In the end, we can conclude from this study that intraoperative cytological smears are easy to perform, inexpensive, permit high diagnostic accuracy, and is a useful alternative in centers lacking frozen section infrastructure. It can provide a preliminary diagnosis in spinal lesions enabling the surgeon to plan further management on operating table.

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Conflicts of interest

There are no conflicts of interest.

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