

Space occupying lesions of central nervous system: A radiological-histopathological correlation study

Sunila¹, Kumarguru. B.N.^{2,*}, T S Vasana³, Manjunath. G.V.⁴

¹Former Professor, ²Associate Professor, ³Professor and Head, ⁴Vice-Principal, Former Professor and HOD, ^{1,2,4}Dept. of Pathology, ³Dept. of Neurosurgery, ^{1,3,4}JSS Medical College, Mysore, Karnataka, ²P.E.S. Institute of Medical Sciences and Research, Kuppam, Andhra Pradesh, India

***Corresponding Author:**

Email: kumarguru1978@yahoo.com

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Abstract

Introduction: Radiological imaging modalities are important pre-operative diagnostic tools to detect the central nervous system [CNS] lesion. Radiological findings can be used by pathologists to narrow down the differential diagnoses. Radiological diagnosis requires confirmation by histopathology

Aims: 1. To study various patterns of central nervous system [CNS] lesions in histopathology.

2. To correlate radiological diagnosis with histopathological diagnosis.

3. To evaluate the diagnostic efficacy of radiological diagnosis.

Settings and Study Design: Analytical study at tertiary care hospital.

Materials and Methods: Eighty eight cases were analyzed. Histopathological evaluation was done from biopsy samples sent in formalin. Tissue processing was done by standard operating procedure. Tissue sections were routinely stained by H&E. Special stains were performed in selected cases. Radiological diagnosis was correlated with histopathological diagnosis and concordance was calculated.

Statistical Analysis: Frequencies, Chi-Square Test and Crosstabs were used for calculation.

Results: Histopathological diagnosis of eighty eight cases included neoplastic lesions [90.9%] and non-neoplastic lesions [9.09%]. Correct diagnosis was achieved by radiology in 36 cases [45%] by complete concordance. However, diagnostic accuracy improved considerably [85%] after applying partial concordance criteria. For the detection of neoplastic lesions, radiological diagnosis had sensitivity of 96.25%, specificity of 50% and efficacy of 92.04%. The p value, determining efficacy of radiological investigations for detecting CNS neoplasms was statistically significant [p<0.005].

Conclusions: Radiological investigation is a reliable diagnostic tool for space occupying central nervous system lesions. It has high sensitivity and is highly efficacious investigative modality.

Keywords: Biopsy, Neoplasms, Tissue.

Introduction

Space occupying lesions [SOLs] of Central Nervous System [CNS] are important cause of neurological morbidity and mortality.^{1,2} SOLs may be neoplastic or non-neoplastic.¹ They may follow a serious clinical course even when they are inflammatory lesions or benign neoplasms.² Early diagnosis is necessary to plan appropriate intervention. Radiological investigative modalities like computed tomography [CT] and Magnetic resonance Imaging [MRI] are important preoperative diagnostic tools to detect the lesion.¹

Interpretation of histopathology of CNS tumors is significantly aided when viewed in perspective of clinical, per-operative and radiological findings. Radiological imaging is an important component of diagnosis and planning treatment.³ Radiological findings can be used by pathologists to narrow down the differential diagnoses.⁴ However, radiological diagnosis of SOL requires confirmation by histopathology. Radiological investigation is supportive for an accurate histopathological diagnosis. Hence,

histopathology considered as gold standard for diagnosis of CNS lesions.²

Since brain biopsy is an invasive procedure, every effort should be made to establish an accurate diagnosis pre-operatively. Treatments strategies differ from one type of brain neoplasm to another type.⁵ Majority of the patients have fairly characteristic presentation. However, many patients with intracranial lesions may have atypical presentation secondary to intra-tumoral haemorrhage, arterial occlusion, cerebral infarction or tumor involvement of silent areas. Such lesions pose a diagnostic challenge and needs pre-operative radiological evaluation.⁶ The present study was undertaken to find out the concordance between Radiological diagnosis and histopathological diagnosis and determine the diagnostic efficacy of radiological investigation.

Materials and Methods

The study was conducted in the department of pathology from January 2010 to September 2012 for a period of two years and eight months. It was an

analytical type of study. Eighty eight cases were analysed.

Inclusion Criteria: All neurosurgical cases for histopathological examination were performed and preoperative radiological [CT scan or MRI or both] diagnosis was available.

Exclusion Criteria: Those neurosurgical cases in which histopathological was inconclusive, those cases in which subsequent histopathological examination was not performed; and those cases in which radiological diagnosis was not available

Tissue samples sent in 10% formalin were allowed to fix for 24 hours. Gross examination was done and bits were given. Paraffin embedded sections were routinely stained by H&E. Special stains [PAS, reticulin] were employed in selected cases.

Radiological diagnosis [CT scan or MRI] was compared with that of histopathology. When both CT scan and MRI diagnosis was available, MRI diagnosis was considered for concordance. Available clinical details, radiological and laboratory investigation data were documented. All primary CNS tumors were histologically categorised according to 2007 WHO [World Health Organization] classification.⁷ Those lesions not included under WHO classification were categorised as unclassified lesions.

Statistical Analysis: Frequencies, Chi-Square Test and Crosstabs were used for calculation. Radiological diagnosis was compared with histopathological diagnosis and the diagnostic efficacy of radiological investigation was evaluated. All statistical calculations were done through statistical software STATA version 13.

Results

Eighty eight cases were analyzed. The CNS lesions ranged from 1yr to 75 yr. Lesions were most common in seventh decade [mean = 45.07 yr]. Females were affected in majority of cases [59.09%] with M:F ratio of 1:1.4. CNS lesions were more common in intracranial region [84.09%] than spinal cord region [15.90%]. Frontal region [24.32%] was the most common intracranial site of involvement. Thoracic region [85.71%] was the most common site of involvement in the spinal cord region.

Out of 88 cases, 80 cases [90.9%] were neoplastic lesions constituting the majority and eight cases [9.09%] were non-neoplastic lesions. The distribution of various neoplastic and non-neoplastic CNS lesions and their diagnostic accuracies are enumerated in Table 1. Among the neoplastic lesions, neuroepithelial tumors (32.95%) constituted most common tumor. Lymphoma (1.13%) and chordoma (1.13%) constituted least common tumors.

The diagnostic accuracy was 45.45% by complete concordance and increased to 82.95% on applying partial concordance criteria. Neoplastic lesions showed better concordance than non-neoplastic lesion. Among neoplastic lesions, the metastatic tumors, haematopoietic tumor, chordoma, meningial tumors, cranial and paraspinal nerve tumors showed better concordance than pituitary neoplasms and neuroepithelial tumors. But sellar tumor showed poor concordance. Among non-neoplastic lesions, cystic lesions and vascular lesion showed better concordance than inflammatory lesions. But necrotic lesion [Infarction] showed poor concordance. [Table 1]

Table 1: Diagnostic accuracy of CNS lesions

S. No	Histopathology	Cases [n=88]	DACC	DAPC
	Neoplastic lesions	80 [90.9%]	36 [45%]	68 [85%]
1	Neuroepithelial tumors	29 [32.95%]	4 [13.79%]	22 [75.86%]
	Astrocytic tumors	19 [21.59%]	2 [10.52%]	14 [73.68%]
	Embryonal tumors	4 [4.54%]	1 [25%]	2 [50%]
	Oligodendroglial tumor	1 [1.13%]	0	1 [100%]
	Ependymal tumor	3 [3.4%]	1 [33.33%]	3 [100%]
	Oligoastrocytic tumor	1 [1.13%]	0	1 [100%]
	Neuronal and mixed neuronal tumor [Ganglioglioma]	1 [1.13%]	0	1 [100%]
2	Meningial tumors	20 [22.72%]	15 [75%]	19 [95%]
	Meningotheliomatous meningioma	9 [10.22%]	7 [77.77%]	9 [100%]
	Fibroblastic meningioma	3 [3.4%]	3 [100%]	3 [100%]
	Transitional meningioma	2[2.27%]	2 [100%]	2 [100%]
	Psammomatous meningioma	2[2.27%]	2 [100%]	2 [100%]
	Hemangioblastoma	1 [1.13%]	1 [100%]	1 [100%]
	Atypical meningioma	1 [1.13%]	0	1 [100%]
	Angiomatous meningioma	1 [1.13%]	0	0
	Hemangiopericytoma	1 [1.13%]	0	1 [100%]
3	Cranial and paraspinal nerve tumors	15 [17.04%]	10 [66.66%]	14 [93.33%]
	Schwannoma	14 [15.9%]	9 [64.28%]	13 [92.85%]

	Neurofibroma	1 [1.13%]	1 [100%]	1 [100%]
4	Pituitary neoplasm	7 [7.95%]	5 [71.42%]	6 [85.71%]
5	Metastatic tumors	5 [5.68%]	2 [40%]	5 [100%]
	Adenocarcinoma	4 [4.54%]	2 [50%]	4 [100%]
	Squamous cell carcinoma	1 [1.13%]	0	1 [100%]
6	Sellar tumors	2[2.27%]	0	0
	Adamantinomatous craniopharyngioma	2[2.27%]	0	0
7	Lymphoma and haematopoietic tumors	1 [1.13%]	0	1 [100%]
	High grade lymphoma	1 [1.13%]	0	1 [100%]
8	Unclassified tumor	1 [1.13%]	0	1 [100%]
	Chordoma	1 [1.13%]	0	1 [100%]
	Non-neoplastic lesions	8 [9.09%]	4 [50%]	5 [62.50%]
1	Cystic lesions	3 [3.4%]	3 [100%]	3 [100%]
	Rathke cyst	1 [1.13%]	1 [100%]	1 [100%]
	Epidermoid cyst	2[2.27%]	2 [100%]	2 [100%]
2	Inflammatory lesions	3 [3.4%]	1 [33.33%]	1 [33.33%]
	Tuberculoma	2[2.27%]	1 [50%]	1 [50%]
	Acute inflammatory lesion	1 [1.13%]	0	0
3	Vascular lesions	1 [1.13%]	0	1[100%]
	Arterio-venous malformation	1 [1.13%]	0	1[100%]
4	Unclassified	1 [1.13%]	0	0
	Necrotic lesion	1 [1.13%]	0	0
	Total	88	40 [45.45%]	73 [82.95%]

DACC: Diagnostic Accuracy by Complete Concordance

DAPC: Diagnostic Accuracy after Considering Partial Concordance

The term "Complete concordance" was applied to the cases in which radiological diagnosis was exactly identical to the final histopathological diagnosis. "Partial concordance" was applied to cases in which radiological diagnosis showed minor deviation from final histopathological diagnosis but the lesion belong to the same category or one of the radiological differential diagnoses matches with final histopathological diagnosis. "Discordance" was considered in cases where radiological diagnosis differed significantly from the final histological diagnosis with respect WHO grades and/or CNS lesion categories.

Primary CNS neoplasms were categorized according to WHO grades and their diagnostic accuracies are enumerated in Table 2. WHO Grade I tumors constituted the most common primary neoplastic CNS lesion. WHO grade III tumors constituted the least common primary neoplastic lesion.

The diagnostic accuracy was 43.93% by complete concordance and increased to 72.72% on applying partial concordance criteria. Concordance was better in WHO grade II and WHO grade I than WHO grade III. Concordance was relatively poor in WHO grade IV. [Table 2]

Table 2: Diagnostic accuracy in WHO grades of primary neoplastic lesions of CNS

S. No	Who Grades of Primary CNS Neoplasms	Cases [n= 66]	DACC	DAPC
1	Grade I	42 [63.63%]	26 [61.90%]	33 [78.57%]
2	Grade II	9 [13.63%]	1 [11.11%]	8 [88.88%]
3	Grade III	2 [3.03%]	0	1 [50%]
4	Grade IV	13 [19.69%]	2 [15.38%]	6 [46.15%]
	Total	66	29 [43.93%]	48 [72.72%]

DACC: Diagnostic Accuracy by Complete Concordance

DAPC: Diagnostic Accuracy after Considering Partial Concordance

The Statistical values were calculated by Galen and Gambino method. For the detection of neoplastic lesions, radiological diagnosis had 77 true positive cases, four false positive cases, three false negative cases, four true negative cases, sensitivity of 96.25%, specificity of 50%, false positive error rate of 4.54%,

false negative error rate of 3.4%, positive predictive value of 95.06%, negative predictive value of 57% and diagnostic efficacy of 92.04%. The p value, determining efficacy of radiological diagnosis for detecting CNS neoplasms was statistically significant [p<0.005].

Discussion

Histopathology is considered as the gold standard investigation for the evaluation of CNS lesions. Radiological investigation is the only means for pre-operative assessment. Radiological techniques help to localize CNS lesions and plan surgery. Radiological diagnosis of SOL requires confirmation by histopathology.² Space occupying lesions of CNS have a wide spectrum of histopathological patterns. The present study emphasizes the significance of correlation between pre-operative radiological diagnosis and histopathological diagnoses.

Dogar T et al² and Goyani BR et al⁸ observed that most of the cases were seen in fourth decade in their study. Kaki RR et al⁹ documented that CNS lesions were common in fifth decade in their study. In contrast to the other studies, the present study showed clustering of cases in the seventh decade. Jindal N et al,¹ Dogar T et al,² Goyani BR et al⁸ and Tesfay M et al¹⁰ observed male predominance in their study. In contrast, Kaki RR et al⁹ and the present study showed female predominance in their study. In the studies conducted by Dogar T et al,² Goyani BR et al⁸ and Kaki RR et al,⁹

parietal region was the most common site of involvement of CNS lesions. In contrast, Jindal N et al² and the present study documented frontal region as the most common site of involvement of CNS lesions.

The distribution pattern of various CNS lesions in the present study was compared with other studies. In all the studies, neoplastic lesions were more common than non-neoplastic lesions. Among neoplastic lesions, neuroepithelial tumors were commonest followed by meningeal tumors. Dogar T et al² and Pant I et al⁴ documented similar observations in their studies. In contrast, Kaki RR et al,⁹ Tesfay M et al¹⁰ and Mahmoud MZ et al¹¹ found meningeal tumor as the commonest neoplastic lesion in their study. Haemopoietic tumors were least common neoplastic lesion in the present study. Pant I et al⁴ and Tesfay M et al¹⁰ documented similar observation in their study. Among non-neoplastic lesions, Cystic lesions were the most common lesion in most of the studies except Dogar T et al² in which inflammatory lesion was commonest non-neoplastic lesion. [Table 3]

Table 3: Comparison of distribution of various space occupying lesions of CNS

S. No	CNS lesions	Present study	Percentage	Kaki RR et al ^[9]	Percentage	Pant I et al ^[4]	percentage	Tesfay M et al ^[10]	percentage	Mahmoud MZ et al ^[11]	Percentage	Dogar T et al ^[2]	Percentage
1	Neuroepithelial tumors	29	32.95%	14	28%	100	49.01%	15	15.62%	0	0	48	47.05%
2	Meningeal tumors	20	22.72%	17	34%	44	21.56%	38	39.58%	38	38%	18	17.64%
3	Cranial and paraspinal nerve tumors	15	17.04%	3	6%	26	12.74%	1	1.04%	0	0	8	7.84%
4	Pituitary neoplasm	7	7.95%	3	6%	0	0	14	14.58%	27	27%	9	8.82%
5	Metastatic tumors	5	5.68%	3	6%	10	4.9%	3	3.12%	7	7%	1	0.98%
6	Sellar tumors	2	2.27%	0	0	19	9.31%	0	0	0	0	3	2.94%
7	Lymphoma and haematopoietic tumors	1	1.13%	0	0	5	2.45%	1	1.04%	0	0	0	0
8	Germ cell tumors	0	0	0	0	0	0	0	0	1	1%	0	0
9	Unclassified tumors	1	1.13%	0	0	0	0	2	2.08%	0	0	1	0.98%
10	Cystic lesions	3	3.4%	6	12%	0	0	14	14.58%	0	0	4	3.92%
11	Inflammatory lesions	3	3.4%	4	8%	0	0	8	8.33%	22	22%	10	9.8%
12	Vascular lesions	1	1.13%	0	0	0	0	0	0	5	5%	0	0
13	Unclassified	1	1.13%	0	0	0	0	0	0	0	0	0	0
	Total cases	88		50		204		96		100		102	

Out of 88 cases, 15 cases [17.05%] were misdiagnosed [Discordant]. Misdiagnosed cases and probable cause are summarized in Table 4. The reasons for misdiagnosis were mainly radiological similarity of the lesions and interfering factors like presence of

haemorrhage, necrosis and edema. Pant I et al⁴ had also analysed misdiagnosed cases in their study. Similar to the present study, Pant I et al⁴ had documented that low grade astrocytoma and medulloblastomas were misdiagnosed as ependymoma. Low grade astrocytoma and ependymoma may be considered as close

differentials depending on the location. Medulloblastomas was misdiagnosed as ependymoma because of areas of haemorrhage and infiltrative growth pattern in their study.⁴ One case of angiomatous meningioma was misdiagnosed as cystic glioma because of solid cystic nature and increased vascularity of the lesion. Tesfay M et al¹⁰ opined and concluded in their study that varying degree of perilesional

edema seen in meningioma is also a feature of gliomas, metastasis and infection. Iwama et al mention that signal intensities of gliomas on MRI did not correlate with the malignancy of the tumor. Tovi et al concluded in their study that though the degree of malignancy of the lesion as a whole can be assessed by MRI, it does not allow gliomas to be clearly delineated.⁴

Table 4: Discordant cases of CNS lesions

S. No	Histopathology	Discordant cases	Radiological diagnosis	Probable causes for mis-diagnosis
	Neoplastic Lesions			
	Neoplastic lesions	12 [15%]		
1	Neuroepithelial tumors	7 [24.13%]		
A	Astrocytic tumors	5 [26.31%]		
	Glioblastoma	2 [28.57%]	1. Haemorrhagic lesion	Vacularity of the lesion and haemorrhage
			2. Metastasis	Involvement of left temporal and parietal lobe and Similar features
	Pilocytic astrocytoma	2 [50%]	1. Malignant tumor	Heterogeneous nature of the lesion and mass effect
			2. Pituitary adenoma/ Craniopharyngioma	Unusual Location of the tumor
	Fibrillary astrocytoma	1 [50%]	Medulloblastoma/ Ependymoma with obstructive hydrocephalus	Presentation as ill-defined nodular lesion with mass effect and location near fourth ventricle
B	Embryonal tumor	2 [50%]		
	Anaplastic medulloblastoma	1 [50%]	Ependymoma	Similar features of the lesion and location
	Primitive neuroectodermal tumor	1 [100%]	Meningioma	Lobulated nature of the lesion with mass effect
2	Meningial tumors	1 [5%]		
	Angiomatous meningioma	1 [100%]	Cystic glioma	Solid-cystic nature and increased vascularity of the lesion
3	Cranial and paraspinal nerve tumors	1 [6.66%]		
	Schwannoma	1 [7.14%]	Meningioma	Similar radiological features
4	Pituitary neoplasm	1 [14.28%]	Rathke cleft cyst	Cystic nature, similar location
5	Sellar tumors	2 [100%]		
	Adamantinomatous craniopharyngioma	2 [100%]	1. Pituitary macroadenoma/ Haemangioma	Similar location of the lesion
			2. Third ventricle cyst	Similar location and cystic nature of the lesion
	Non-Neoplastic Lesions			
	Non-neoplastic lesions	3 [37.5%]		
1	Inflammatory lesions	2 [66.66%]		
	Tuberculoma	1 [50%]	Malignant glioma	Involvement of left frontal lobe and parietal lobe and mass effect
	Acute inflammatory lesion	1 [100%]	Pituitary macroadenoma	Similar location of the lesion
2	Unclassified	1 [100%]		
	Necrotic lesion	1 [100%]	Anaplastic astrocytoma	Vasogenic edema and location of the lesion in white matter of left temporal lobe and parietal lobe

In the present study, concordance was 71.21%. Pant I et al⁴ documented a higher concordance [96.07%] in their study. In contrast, Dogar T et al²

observed lower concordance [68%] in their study. In the present study, diagnostic accuracy by complete concordance [DACC] and diagnostic accuracy after applying partial concordance criteria [DAPC] was calculated. But other studies had not clearly specified

about criteria followed to consider concordance. This may be important because, not all the cases diagnosed by radiology can perfectly match with histopathological diagnosis, which is considered as gold standard.

For the detection of meningioma, Tesfay M et al¹⁰ observed sensitivity of 80% and specificity of 95%. For the detection of gliomas, sensitivity was 71% and specificity was 85.7% in their study. However, overall sensitivity and specificity for detection of neoplastic lesion was not mentioned in the study.¹⁰ In the present study, for detection of neoplastic lesions by radiology, sensitivity and specificity were 96.25% and 50% respectively. In contrast, Kaki RR et al⁹ documented lower sensitivity [92.5%] and higher specificity [70%]. Similarly Jindal N et al¹ had also documented lower sensitivity [90%] and higher specificity [57%]. This reflects failure to consider non-neoplastic lesion while offering radiological diagnosis in the present study.

Tesfay M et al¹⁰ documented diagnostic efficacy of 88.6% for meningiomas and 83% for gliomas in their study. For the detection of neoplastic lesions, the diagnostic efficacy in the present study was 92.04%. Kaki RR et al⁹ had observed lower diagnostic efficacy [88%] in their study. Similarly, Jindal N et al¹ had recorded a lower diagnostic efficacy [84.2%] in their study. In contrast, Goyani BR et al⁸ recorded a diagnostic a higher efficacy [98.57%] because, only MRI was used as investigative modality in their study. Jindal N et al,¹ Kaki RR et al⁹ and the present study used both CT and MRI as investigative modalities.

Each investigative modality has its own advantages and disadvantages. In view of low specificity of the radiological diagnosis in the present study, it may be suggested that, in addition to radiological impression, neurosurgeon can also consider other diagnostic modalities such as intra-operative squash smear cytology and intra-operative frozen section to plan or modify further management.

Conclusion

Radiological investigation is a reliable diagnostic tool for space occupying central nervous system lesions. It may be considered as an important supportive and complimentary tool to histopathological diagnosis. Radiological similarity of the lesions and presence of interfering factors are important contributory factors for diagnostic pitfalls. Radiological investigation has high sensitivity and is highly efficacious for the diagnosis of neoplastic CNS lesions. However, in view of low specificity, multimodality approach may be beneficial for management of the patient.

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