Original Article

Indian Journal of Pathology: Research and Practice
Volume 13 Number 1, January - March 2024
DOI: http://dx.doi.org/10.21088/ijprp.2278.148X.13124.2

Demographic Profile of CNS Tumors and Histopathological Evaluation of Pituitary Lesions: An Institutional Study

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How to cite this article:
Jayasree Geothe, Lekshmy K S. Demographic Profile of CNS Tumors and Histopathological Evaluation of Pituitary Lesions: An Institutional Study. Ind Jr of Path: Res and Practice 2024;13(1) 13-17.

Abstract

Primary Central Nervous System tumors (CNS trs) are a diverse group of neoplasm showing significant geographic variations in incidence, morbidity, mortality, and survival. Pituitary adenomas (PA) recently termed as Pituitary Neuroendocrine Tumours (PitNET) are the commonest mass in the sellar region, can produce local, and distant effects.[1] However, some developmental, inflammatory, and neoplastic lesions may primarily or secondarily involve the sella, mimicking pituitary tumors; recognition of which is crucial for the appropriate management.

Aims: To evaluate the histopathological profile of primary CNS trs and to correlate with age, sex and site at presentation. Pituitary lesions are further analyzed to find out prevalence of non adenomatous lesions in pituitary

Materials and methods: Histologically diagnosed 79 primary CNS trs and 18 pituitary lesions are analyzed.

Results: Meningioma is the commonest brain and CNS trs. The PA being the second commonest CNS trs, constitute 17% of CNS trs, 22% of brain tumors and 78% of pituitary lesions. Other sellar lesions were single cases of Rathkeys cleft cyst (RCC), Arachnoid cyst, craniopharyngioma and pituitary apoplexy.

Conclusion: This retrospective study established a baseline profile of brain tumors and sellar lesions based primarily on the histopathological experience at a tertiary care hospital in the Southern Kerala.

Keywords: Pituitary Adenomas; Pituitary Neuroendocrine Tumours (Pitnets) Macroadenomas; Rathkey Cleft Cyst; Pituitary Apoplexy; CNS Tumors.

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Received on: 26.03.2024 **Accepted on:** 30.04.2024

INTRODUCTION

CNS trs are well known to cause significant mortality and morbidity. Even tiny benign neoplasm in the brain could have devastating effects due to their location, space occupying effects, and predisposition to undergo malignant transformation. Recent steady increase in CNS trs observed could be from availability of newer diagnostic modalities and probably from the

exposures to harmful environmental agents. More than 90% of sellar pathology are due to PA/Pit NET.[1] Locally they compress neural structures like the pituitary gland, the optic chiasmus, and the brain, more commonly may disturb several hormonal systems in the body. Other less common sellar pathologies which need consideration during management are craniopharyngioma pituicytoma, pituitary blastoma, metastatic tumors, arachnoid cysts and rare pathologies like lymphoma, paragangliomas, germinoma and Langerhan cell histiocytosis which have characteristic clinical and radiological features.[2]

The classification of PA based on tinctorial properties of cells is obsolete due to lack of clinicopathological correlation. The classification according to size (microadenomas, <1cm; macroadenomas, ≥1cm) is still relevant due to more prevalent pressure effect in the later one.

Hormone immunohistochemistry alone can sometimes be misleading due to nonspecific or diffusion type staining. The current WHO classification of PA/PitNETs is based on staining for transcription factors, antibodies against adenohypophysial hormones as well as other biomarkers including low molecular weight keratins.

The current WHO classification (5 th edition) use the terminology "PitNET/adenoma" to indicate pituitary adenoma. The term PA still can be used, but PitNET is preferred. There are no morphologic/ clinical features that distinguish locally aggressive and metastatic lesions from indolent ones. So WHO 5th Edition also encourages the use of the term "metastatic PitNET" with subtype information instead of pituitary carcinomas.

MATERIALS AND METHOD

The databases from histopathology department of SUT hospital Pattom Trivandrum, southern Kerala, for a period of 2.5 yrs between 2019 to 2021 were utilized to select patients with CNS lesions. The basic demographic data were collected, and the tumors were studied under the latest WHO guidelines. Pituitary lesions were analyzed to find out prevalence of nonadenomatous lesions. The PA are assessed in particular for determination of atypia, mitoses, pleomorphism, giant cells, inclusions, inflammatory changes, stromal hemorrhage and vascular features

RESULTS

Total number of biopsies during this period was 4056 out of which 65 were primary brain tumors (1.6%) and 14 were spinal tumors (Table 1) Commonest CNS tr was meningioma (30%) of which 16 cases were grade 1 with a female predominance. Seven cases of grade 2 and a case of grade 3 meningioma also detected. Fourteen cases of PA detected constitute 17% of CNS tumors, 22% brain tumors and 78% of sellar lesions. It was more common in females with a M:F ratio of 1:3.7 and mean age was 44 .6 yrs. Associated Rathkeys cyst (RCC) detected in two of the cases. Atypical features like increased mitosis, cellular atypia or bone invasion detected in two of the cases, but not qualifying as malignancy and did not recur in 1 year follow up period. Four cases of non-adenomatous lesions of pituitary detected including single cases of RCC, Arachnoid cyst, craniopharyngioma and pituitary apoplexy constituting 22% sellar lesions

The details of CNS Trs are shown in the Table 1.

Tumor	Number	%	Male	Female	<20 yrs	21-50 yrs	51-70 yrs	>70 yrs
Meningioma	24	30	7	17	0	10	13	1
Pituitary adenoma	14	17	3	11	0	10	3	1
Glioblastoma	7	9	5	2	0	0	4	3
Grade 2 & 3 glioma	7	9	2	5	0	5	0	2
Grade 1 glioma	3	4	0	3	2	1	0	0
CP angle tumor	7	9	3	4	0	2	3	2
Others	3	4	2	1	1	1	1	0
Total brain tumors	65	82	22	43	3	29	24	9
Spinal tumors	14	18	9	4	2	6	4	2
Total CNS tumors	79	100	31	47	5	35	28	11

DISCUSSION

In this study primary CNS Trs constituted 1.9% of total biopsies, out of which 82% were brain tumors. The predominant age group affected by brain tumors was between 21-50 years (44.6%). Overall incidence CNS tumors were more in females except in cases of glioblastoma and spinal tumors. Commonest CNS tumor was meningioma seen more in females and in age group of 51-70yrs as reported in most series PA is the second common CNS Tr, constitute 17% of CNS tumors, 21.5% brain tumors and 78% of sellar lesions which are higher than reported in literature. PA is a neuroendocrine tumor of the anterior pituitary gland typically present as small, slow growing, hormonally inactive lesions are typically identified as incidental findings on radiologic or postmortem examination, whereas small, slow growing lesions with excess hormonal activity can manifest as a clinical syndrome. Tumors that grow more rapidly, even if they are hormonally inactive, are capable of producing symptoms of an intracranial mass, such as visual field disturbances. Previous studies from pooled autopsy and radiological series showed average prevalence rates of 14.4% (range 1–35%) and 22.5% (range 1–40%), respectively indicate that pituitary tumors are fairly common in the general population.

The commonest type of microadenoma in most series are prolactinoma with mean age at diagnosis was 37.5 yrs, with a very high female preponderance (81%)[3] Prolactinomas show excellent responses to medical therapy including giant prolactinoma (tumor diameter > 4 cm). Generally, larger tumors recur more frequently than smaller adenomas after surgery. The highest recurrence rate (19%) was found in patients with inactive macro-adenomas with a follow-up of more than 2 years.[4-6]

Other microadenoma include somatotroph, thyrotroph, corticotroph, gonadotroph, null cell and plurihormonal types. Generally, there are two approaches for characterizing aggressiveness of pituitary tumor pathological and a clinical one. Histological subtyping of a PA based on cell lineage, cell type, and related characteristics provides critical clinical information for risk stratification and because of the differential response to therapies of the subtypes of PA.[3] Staining for three pituitary transcription factors, TPIT, PIT1 and SF1 is absolutely required along with hormone immunohistochemistry on routine basis to ensure accurate tumour characterization including synchronous PAs of distinct lineages. The term PitNET, NOS can be used when pathologists do not have access to ancillary tools to enable subtyping, Widely accepted grading systems also not defined for PitNETs. The predictive value of mitoses (conventional or phosphohistone-H3-assisted count), Ki-67 labeling index and p53 staining in this scenario remains unproven. In selected cases, molecular immunohistochemistry tools may be used to demonstrate global loss of menin (*MEN1*), p27 (*CDKN1B*), and SDHB protein encoded by *SDHB*) to guide further germline screening for *MEN1, MEN4* and SDH-deficient tumour syndromes[3]

Local factors like cavernous sinus and/or sphenoid sinus invasion and tumor microenvironment, are considered relevant in predicting persistent disease after surgery. Knops and hardy classification are two systems that defines extra sellar extension. Two cases of PA in our study showed these atypical features, but did not recur within one year follow up period. Prolactin-secreting tumors are most frequently responsible for cavernous sinus extension, and typically prolactin levels increase significantly when the tumor gains access to the sinus. Once in the sinus, these tumors are difficult to resect completely. They may compress cranial nerves resulting in deficits.[8]

Diagnosing the RCC is not always straight forward as it may be mistaken for a pituitary adenoma with apoplexy or a craniopharyngioma When a non-enhancing cyst like structure is demonstrated in a patient with pituitary adenoma, the possibility of a coexisting Rathke's cleft cyst (RCC) should be considered. The frequency of the combination was 14% of PA and 66% of RCC in our series which were much higher than 3.5% and 11% respectively as reported earlier.[9] Symptoms were always due to the adenoma, On MRI, they appear as a solid cystic or cystic sellar tumors. RCC can rupture causing granulomatous reaction with cholesterol crystal formation, which can be mistaken for craniopharyngiomas during surgery. Therefore, collision sellar lesion must be included in the differential diagnosis of cystic sellar lesions. The definitive diagnosis is made by histological study.[10] The coexistence of PA and RCC could be from a common embryological origin, the RCC is considered to be derived from remnants of Rathke punch, while PA is formed by proliferation of the anterior wall of Rathke pouch.[11] The pituitary stalk is usually not displaced to one side as one would expect in a pituitary adenoma. There is some variation in the types of cells lining the cyst. Ciliated

cuboidal to columnar cells, which may contain goblet cells may be seen. The contents are usually mucinous in nature Occasionally, the contents may be solid because of inspissated material. There are the occasional case reports of calcification seen within the cyst.[2]

Pituitary apoplexy was defined as the acute onset of clinical symptoms associated with haemorrhage or infarction within a normal pituitary gland or previously known PA. It is a rare endocrine emergency and should be considered in any patient with abrupt neuro-ophthalmological deterioration associated with headache. Because of the rich and the complex vascular system pituitary adenomas have a 5.4 greater chance to bleed than any other brain tumor. However, pituitary apoplexy may also occur in non-adenomatous or even the normal pituitary gland especially during pregnancy as in our case which had a fatal course. "Subclinical pituitary apoplexy" is widely used to describe pathological evidence of asymptomatic pituitary ischemia or hemorrhage.[12,13]

CONCLUSION

This retrospective study established a baseline profile of CNS tumors and sellar lesions in the Southern Kerala This study has few limitations as a relatively small sample size restricted to one tertiary care private hospital. Given the high frequency of PA/Pituitary Neuroendocrine Tumours, their potential for causing clinical pathologies, the findings of the current study suggest that early diagnosis and treatment of PA should have far reaching benefits as they mainly affect the economically active population and are associated with increased morbidity and mortality. Although the most common sellar pathology is the pituitary adenoma, attention must be drawn to the other possibilities whenever odd history, atypical hormonal disturbance or atypical imaging features are present. Only high index of suspicion of these non-adenoma lesions and recognition at least early during the surgery results in appropriate management.

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