ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Pineal Parenchymal Tumors: A Clinicohistopathological Study from a Tertiary Care Institute in India.

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ABSTRACT

Pineal parenchymal tumors are rare neoplasms of pineocytes lying along a broad spectrum of differentiation, from well differentiated lesions cured by simple excision to rapidly growing, disseminating tumors resistant to chemoradiotherapy. WHO partitioned this continuum into grades: I-Pineocytoma, II/III-Pineal parenchymal tumor of intermediate differentiation and papillary tumor of the pineal region and IV-Pineoblastoma. To study the incidence and histopathological features of pineal parenchymal tumors in relation to age, sex, clinical features and radiological findings. It's a 22 year study from January 1989 to December 2010 comprising retrospective and prospective cases. Pineal parenchymal tumors accounted for 0.17% of the total number of central nervous system lesions (i.e. 19/10,980 cases). Pineoblastomas predominated with 57.89% (11 cases) followed by pineocytomas 26.31% (5 cases) and pineal parenchymal tumor of intermediate differentiation 15.78% (3 cases). Males (57.89%) predominated over females (42.10%), the male to female ratio being 1.3:1. Pineocytomas were seen in the elderly while pineoblastomas occurred in the paediatric age group. The commonest symptom was visual impairment. The clinical and radiological findings were not rewarding for differentiating pineal tumors. Hence the histopathological examination remains the gold standard for diagnosis.

Keywords: Pineal, Tumors.

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ISSN: 0975-8585

INTRODUCTION

Pineal gland is located adjacent to cerebral aqueduct in posterior part of the third ventricle. Mass lesions of the pineal gland are classified into four major histological groups including germ cell tumors, pineal parenchymal tumors (PPT), glial tumors and nonneoplastic masses [1-8]. Much is known about the other tumors but pineal parenchymal tumors are rare and only limited information is available about their behaviour. PPTs arise from the pinealocytes, neurosecretery cells of the pineal gland. The 1993 WHO classification divides PPT into pineocytomas, pineoblastoma and mixed pineocytoma – pineoblastoma [9]. Accordingly PPTs show spectrum of histological features from poorly differentiated neoplasms (pineoblastomas) to better differentiated tumors (pineocytomas). Neoplasms with transitional or intermediate features were tentatively classified as mixed pineocytoma – pineoblastoma. The 2007 WHO classification of CNS tumors called this entity as pineal parenchymal tumors of intermediate differentiation (PPTID) and it also added another type as papillary tumor of the pineal region (PTPR) [10].

Obtaining a biopsy for histopathological assessment was a dangerous procedure previously with mortality rate as high as 50% [3]. Nowadays the advent of imaging systems [The computed tomography (CT) and magnetic resonance imaging (MRI)] and stereotactic biopsy technique have simplified the detection and pathological assessment of these tumors so increasing the number of neurosurgical biopsies of pineal region tumors.

Hence the current study was prompted by the need for additional information regarding the diagnosis, treatment and survival of the patients with these tumors.

Aims and Objectives

- To study the incidence of pineal parenchymal tumors in relation to age, sex and clinical features and their correlation with histopathological features
- To compare the results of our study with published data.

MATERIAL AND METHODS

The present study is a 22 year study from 1989 to 2010 (16 yrs retrospective and 6 yrs prospective) conducted in the department of neuropathology of a tertiary care institute. A total of 19 cases of PPTs were studied. The relevant clinical information such as age, sex, clinical features, laboratory & radiological findings (CT scan & MRI whenever available) were noted & studied in relation to different types of PPTs.

Complete tumor resection specimens were studied for gross morphology with respect to size, color and consistency. After fixation in 10% formalin, the tumor tissue was processed routinely for paraffin sections and stained with haematoxylin and eosin (H&E). Immunohistochemistry was performed on paraffin sections in cases. Whenever the resection was preceded by stereotactic biopsy, a squash preparation was also studied after staining with rapid H&E method. On histopathological examination tumors were classified according to WHO 2007 classification. As radiotherapy (RT) is unavailable at our institute, follow up could be obtained in 31 % of the patients who were referred to the specialized centre for RT.

RESULTS

Incidence

Out of 10,980 CNS specimens received in 22 yrs 19 cases were PPTs constituting 0.17%, highlights the rarity of these tumors.

Classification of tumors according to WHO showed that the pineoblastomas were the commonest with 12 cases (63.15%), pineocytomas four cases (21.05%) and PPTID three cases (15.78%).Table 1

In our study the youngest patient was six months old while the oldest was of 46 yrs. The age range for pineoblastoma was from six months to 35 yrs (median of 12.75 yrs). Patients having diagnosed as pineocytoma had the age range of 20 to 42 yrs (median 31 yrs) and that for PPTID was 32 to 46 yrs (median 39 yrs). Overall

pineoblastomas were common in pediatric age group between 11 to 20 yrs while pineocytomas and PPTIDs were found to be common in adults of 31 to 40 yrs of age. Table 2

There was a slight male preponderance as there were 11 males (57.89%) and eight females (42.1%) with a male: female ratio of 1.3:1.

Signs and symptoms

All the patients were evaluated at initial diagnosis & following signs & symptoms were noted. Symptoms reported by more than 10% of the patients were as follows: visual disturbances (included diminished vision, diplopia, papilloedema) in 17 cases (89.47%), headache in 14 cases (73.68%) & vomiting in 6 cases (31.57%). Impaired ambulation, giddiness & weakness were other complaints reported by 5% of the patients. Table 3

Histopathological findings

Histologically all the pineocytomas exhibited moderate cellularity arranged in diffuse sheets and irregular lobulated pattern. The cells were mature, uniform & small with round to oval bland nuclei, fine chromatin, inconspicuous nucleoli & moderate eosinophilic cytoplasm. Mitoses were infrequent & necrosis & hemorrhage were not seen. Two of four pineocytomas showed large pineocytomatous rosettes, calcification & lymphocytic infiltrate. Table 4 (Fig.1)

All pineoblastomas were highly cellular tumors except two which showed moderate cellularity. All had diffuse sheet like pattern composed of small round poorly differentiated cells with high N:C ratio, scant cytoplasm & hyperchromatic pleomorphic nuclei. Nuclear atypia (9/12 cases), brisk mitosis (5/12 cases), necrosis (4/12 cases) were consistent features of pineoblastomas. (Fig.2) Four of 12 cases showed Flexner-Wintersteiner type of rosettes. The poorly differentiated nature of pineoblastoma were appreciated on squash preparation as well so that the diagnosis of grade IV PPT could be made. (Fig.3)

PPTIDs were characterized by mixture of high & moderate cellularity. One of three showed lobulated pattern, (Fig.4) while rest two were in diffuse sheets. These tumors were biphasic with cells showing high N:C ratio admixed with cells having bland uniform cytological features. (Fig.5) One out of three cases showed necrosis & high mitotic activity in poorly differentiated component. The tumor showed positivity for synaptophysin. Table 4. (Fig. 6). Radiological findings whenever available detected only the presence of pineal region space occupying lesion, however they were not directly contributory to the final diagnoses. (Fig.7&8)

The follow up was available in 31% of the cases. All patients were referred for radiotherapy. two out of 19 cases succumbed to death, one was pineoblastoma and other was PPTID. Patients of pineocytoma showed improvement in their visual disturbances after the surgery.

Table 1: Incidence Of Pineal Parenchymal Tumors (Who Classification)

TUMOR	NO OF CASES	%
PINEOCYTOMA	04	21.05
PPTID	03	15.78
PINEOBLASTOMA	12	63.15
TOTAL	19	100

Table 2: Age wise Incidence of Pineal Parenchymal Tumors

AGE (yrs)	PINEOCYTOMA	PPTID	PINEOBLASTOMA	TOTAL
0 -10	-	-	04	04
11 – 20	01	-	05	06
21 – 30	01	-	01	02
31 – 40	02	02	02	06
41 – 50	-	01	-	01
TOTAL	04	03	12	19

ISSN: 0975-8585

Table 3: Clinical Symptoms

CLINICAL SYMPTOMS	TOTAL CASES	PERCENTAGE
Visual disturbances	17	89.47
Headache	14	73.68
Vomiting	06	31.57
Inability to walk	03	15.78
Convulsions	01	5.26
Fever	01	5.26
Giddiness	01	5.26
Weakness	01	5.26
Bladder/ Bowel Complaints	01	5.26

Table 4

Tumors	Total	Cellularity		N. Atypia	Brisk MA	Necro	HWR	PR
		M	H					
Pineocytoma	5	5	-	-	-	-	-	2
Pineoblastoma	11	2	9	9	5	4	4	-
PPTID	3	3#	3#	3*	1	1	-	-

#- All 3 cases of PPTID showed mixture of moderate& high cellularity
* All 3 cases of PPTID showed moderate nuclear atypia in poorly differentiated areas.
N-nuclear, MA-mitotic activity, Necro-necrosis, HWR-Homer Wright rosettes, PR-Pineocytomatous rosettes.

Table 5: Comparative Data - Incidence

PINEAL PARENCHYMAL TUMOR	SCHILD et al (1993)	HERNANDO et al (1994)	FRANCOIS et al (1998)	PRESENT STUDY (2011)
STUDY PERIOD	1939 -1991 (52 yrs)	1970 – 1990 (20 yrs)	1972 – 1997 (25 yrs)	1989 – 2010 (22 yrs)
NO OF CASES	30	35	76	19

Table 6: Comparative Data – Grade Of Tumors

TUMOR	SCHILD et al (1993)	HERNANDO et al (1994)	REGIS et al (1996)	FRANCOIS et al (1998)	PRESENT STUDY (2011)
PINEOCYTOMA	09	21	44	19	04
PPTID	06	03	00	28	03
PINEOBLASTOMA	15	11	45	29	12
TOTAL	30	35	89	76	19

Table 7: Comparative Data – Age

STUDIES	PINEOCYTOMA	PPTID	PINEOBLASTOMA
SCHILD et al (1993)	17 – 72 (36)	8 - 77 (32)	11 months – 66 yrs (18)
HERNANDO et al (1994)	14 – 65 (36.2)	7 months – 66 yrs (41)	1 – 39 (12.6)
FRANCOIS et al (1998)	1 – 65 (31.3)	5 – 64 (40.3)	1 - 36 (12.5)
PRESENT STUDY (2011)	20 – 42 (31)	32 – 46 (39)	6 months – 35 yrs (12.75 yrs)

ISSN: 0975-8585

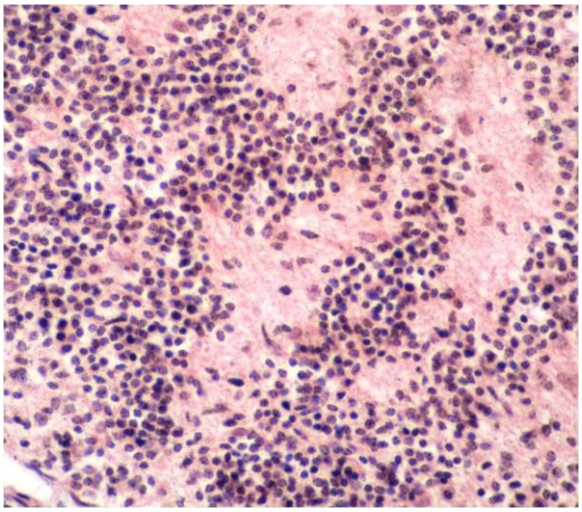

Figure 1: PINEOCYTOMA H&E 10 X
Tumor showing diffuse sheets of uniform tumor cells with round to oval bland nuclei, fine chromatin, inconspicuous nucleoli & moderate eosinophilic cytoplasm, forming large pineocytomatous rosettes

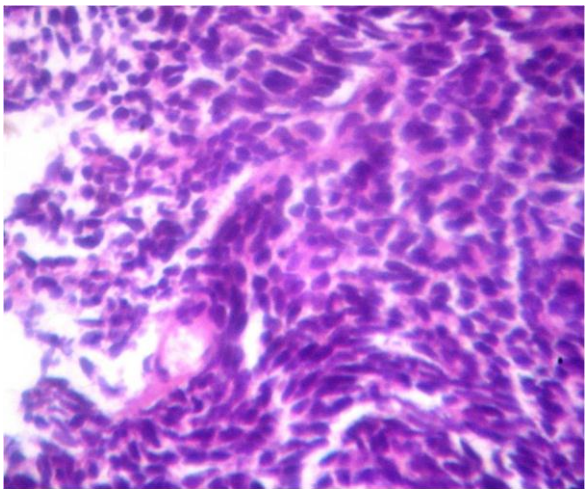

Figure 2: PINEOBLASTOMA H&E 40X
Highly cellular tumor in diffuse sheet like pattern composed of small round poorly differentiated cells with high N:C ratio, scant cytoplasm & hyperchromatic pleomorphic nuclei.

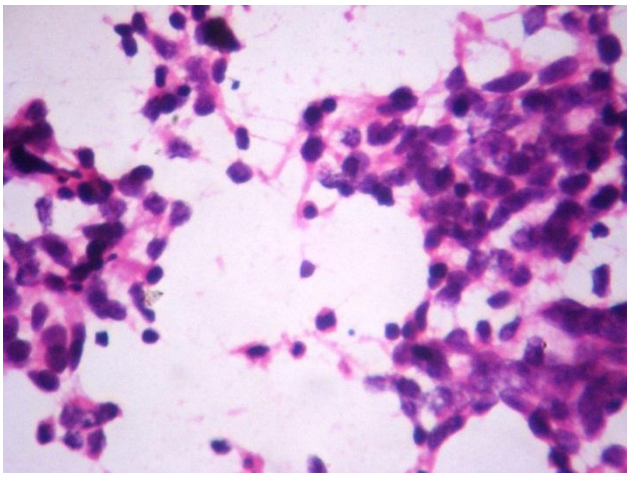

Figure 3: PINEOBLASTOMA (SQUASH SMEAR) H&E40X
The poorly differentiated nature of pineoblastoma was appreciated on squash preparation

ISSN: 0975-8585

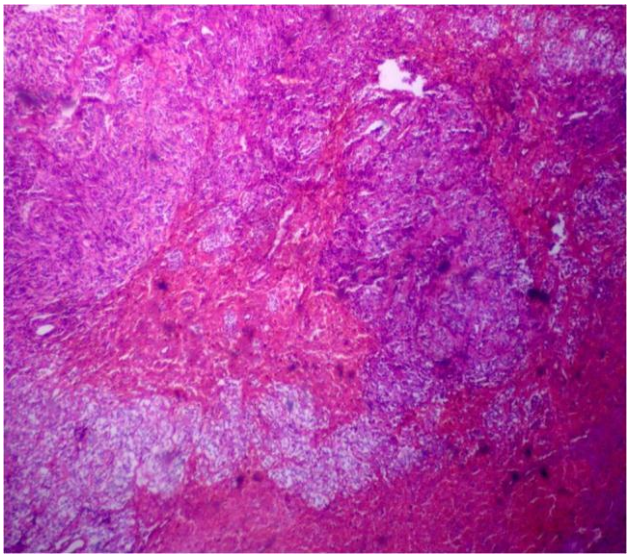

Figure 4: PPTID H&E 10 X
Tumor showing well demarcated lobulated pattern with moderately high cellularity.

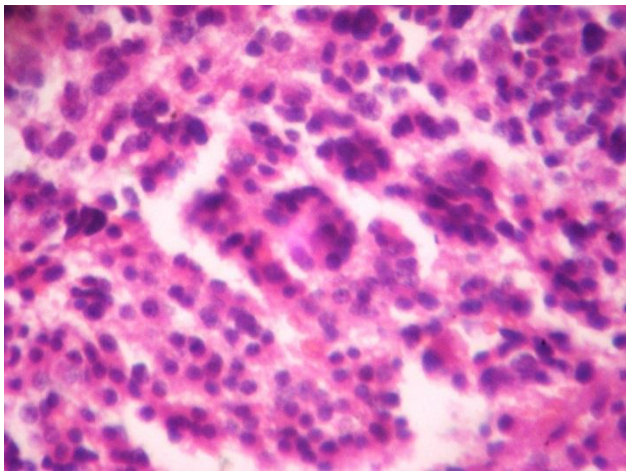

Figure 5: PPTID H&E 40 X
Tumor showing greater variation in nuclear size and shape, more coarse chromatin than pineocytoma.

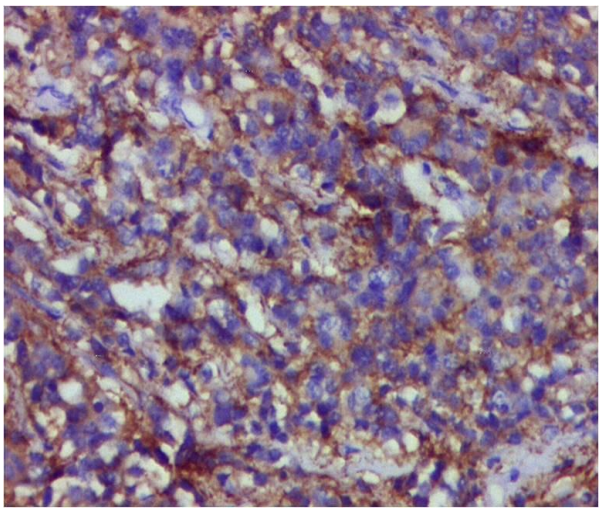

Figure 6: PPTID Synaptophysin IHC 20X
IHC showed positivity for synaptophysin in PPTID.

ISSN: 0975-8585

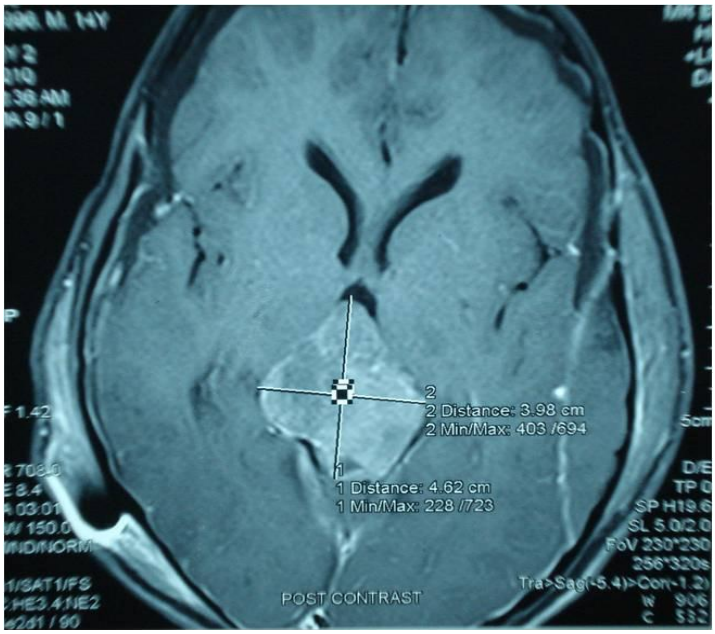

Figure 7: Post contrast MRI
MRI showing contrast enhancing mass measuring 4X3 cm in the pineal region.

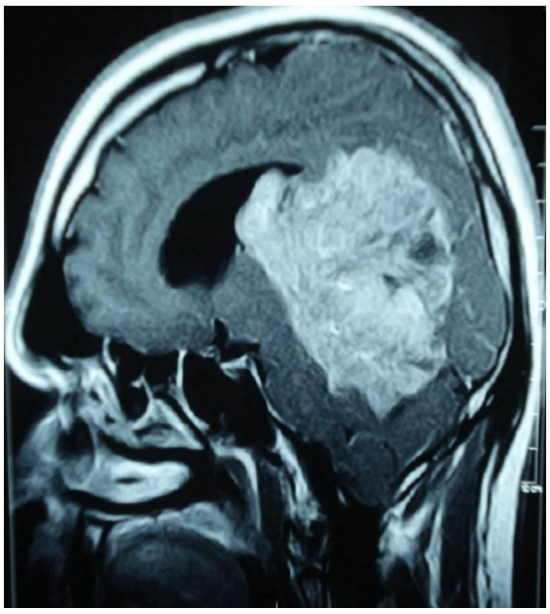

Figure 8: Post contrast MRI
MRI showing contrast enhancing heterogeneous lobulated mass in pineal region.

DISCUSSION

PPTs are the tumors that arise from pinealocytes and represent 0.4 – 1% of primary brain tumors [10]. Such rarity of the PPTs has always complicated the efforts to establish their clinicohistopathological characteristics and appropriate classification systems. According to recent WHO classification the PPTs are classified into four categories: Pineocytoma (Grade I), PPTID (Grade II/III), pineoblastoma (Grade IV) and PTPR (yet to be graded.)

Our present series is a 22 year study (16 yrs retrospective and 6 yrs prospective) from 1989 to 2010. Our data is comparable to other reported series by Schild et al and Hernando et al who reported 30 and 35 cases in 52 and 20 yrs respectively [11,12]. Table 5. The most recent data was published by Francois et al

which is the largest study of 76 cases in 25 yrs. The sample size in our study is small but considering the 22 yrs duration of the study at a tertiary care neuropathology department it only highlighted the rarity of PPTs, the observation reported by almost all other studies [11-13].

The classification of PPTs has been subject of controversy. Most divide PPTs into pineoblastoma, pineocytoma and mixed pineocytoma-pineoblastoma [14-16]. We followed the recent classification proposed by WHO and found pineoblastomas as the commonest PPTs (63%) followed by pineocytomas (21%). Studies of Schild, Regis & Francois reported similar results with pineoblastomas being the commonest PPTs [11,13,17].. Table 6.

Our results are consistent with previously reported studies by Hernando and Francois suggesting that pineoblastomas are common in pediatric age group and pineocytomas are commonly seen in adults, Table 7 and there is slight male preponderance over female for PPTs [12,13]

Our study showed concordance with Schild that visual disturbance is the commonest symptom suggesting that the signs and symptoms are related to injury to tectum, pretectal region & cerebral aqueduct.

We agree with Borit that pineoblastomas are morphologically similar to medulloblastomas [18], a high grade poorly differentiated primitive appearing tumor while pineocytomas are benign looking with pineocytomatous rosettes as their inherent feature. We also agree with Borit's consideration that homer-Wright's rosettes are a feature of pineoblastoma. Unlike Borit's series we report 3 cases of PPTID. Schild, Henrick & Rubeinsten also independently reported such tumors showing features intermediate between pineoblastoma and pineocytoma[19]. Hence we agree with Rubeinsten's conclusion that pineocytoma and pineoblastoma could not always be sharply demarcated and there are PPTs that show features transitional between these two [19]. Table 4 summarizes morphological features of all PPTs in our study.

Thus the present study highlights the clinicopathological profile and its histopathological correlate for PPTs which will help the neuropathologist to come to an accurate histological diagnosis as it will lead to the specific treatment. However because of the overall rarity and remarkable diversity of these PPTs the reports in the literature are small and more such multiinstitutional studies are needed to establish the specific treatment protocols.

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