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Pathology

Study of Pituitary Adenomas with Clinical, Radiological, Cytological and Histological Correlation

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Abstract: Pituitary tumours are a common type of intracranial neoplasm and, depending on the cell type of origin, have diverse endocrine and reproductive effects. Most of them are asymptomatic, however a minor portion of 10% of the tumors are symptomatic. Classification of tumors is based on the staining properties of the cell cytoplasm in to three morphologic entities: Chromophobic adenomas, acidophilic adenomas and Basophilic adenomas. The pituitary adenomas are either clinically functioning adenomas or non-functioning adenomas. The former includes GH secreting (cell) adenomas (abbreviated as GHomas), prolactin (PRL) secreting (cell) adenomas (PRLomas), TSH secreting (cell) adenomas (TSHomas), ACTH secreting (cell) adenomas (ACTHomas), and FSH secreting (cell) adenomas (FSHomas) [2]. Radiological studies have shown a prevalence of about 22.5%. Majority of the tumors are benign, a few of them have invasive behavior with rarer few metastasizing.Pituitary carcinoma is very rare. Metastatic carcinoma to the pituitary is sometimes seen, its autopsy findings are not extremely rare and common primary sites include carcinoma of the lung[2]. The present study reviews various pituitary adenomas encountered and aims to study their cytological, histomorphological and clinical characteristics.
Keywords: Pituitary adenomas, intracranial tumors, chromophoboic adenomas, basophilic adenomas, acidophilic adenomas, microadenomas, macroadenomas.

INTRODUCTION

Pituitary adenomas (PA) constitute about 10% of intracranial neoplasm. Most of them have its origin in adenohypophysis [3]. They are common in the age group of 30 to 60 years, with female preponderance in the early adult life. In males it is seen during 35 to 60 years and in females more common between 20 to 45 years [4]. Pituitary adenomas have been classified as: microadenomas (10 mm diameter), according to its size assessed by tomography and magnetic resonance; staining affinity (acidophilic, chromophobic or basophilic); hormonal activity or secretion of growth hormone (GH), prolactin (PRL), thyroid stimulating hormone(TSH), adrenocorticotrophin hormone (ACTH), follicle stimulating hormone (FSH), and luteinizing hormone (LH); and ultrastructural characteristics [5]. Magnetic resonanace imaging and CT scan studies classified the pituiutary tumors into four grades based on their sizeandlocalinvasion degree, as suggested by Hardy in 1973.

Grade I: Microadenomas, measuring less than 10mm in diameter, they minimally alter the radiographic appearance of the sella.

Grade II: Macroadenomas are bigger than 10mm in diameter; they enlarge the sella or exhibit suprasellar expansion, but not cause destruction.

Grade III: Invasive adenomas locally eroded the sella, and show suprasellar outgrowth.

Grade IV: Strongly invasive adenomas, that destroys adjacent bony structures and with suprasellar outgrowth, including bone, hypothalamus, and the cavernous sinus [6].

Intraoperative squash cytology of Pituitary adenoma had a soft texture and was easily smeared. Characteristically, there were monolayers of individual cells with little cohesiveness. Some of them showed papillary formation with vascular core. The cells had

eosinophilic granular cytoplasm, at places showing rosettes/glandular pattern [7].

Histopathology of the adenomasof pituitary gland show small uniform,round cells arranged diffusely (diffused pattern),around sinusoidal vessels (sinusoidal pattern), or covering connective-vascular axes (papillary pattern) [8].

The present study was undertaken at a tertiary care centre to exclusively study the Pituitary adenomas encountered over a period of 5 years emphasizing on clinical presentation, imaging assessment, intraoperative cytology and histomorphology.

MATERIALS AND METHODS

The present study was conducted at Osmania medical college, Hyderabad, Telangana from June 2013 to June 2018. It was a retrospective analysis of all pituitary adenomas over a period of 5 years presenting in our hospital which is a tertiary care centre in south India. The clinical manifestations, degree of invasion and cytological and histological features are analysed. All the tumours were sent to the department of cytology for Intraoperative diagnosis. Relevant clinical features were noted and correlated. Squash cytosmears were made. Rapid Haematoxylin and Eosin stain and Toluidine blue stains were employed and a diagnosis was offered. The remaining tissue as well as tissue excised was sent for routine histopathological examination. Routine processing and Haematoxylin and eosin staining was done. Special stains and immunohistochemistry were applied wherever necessary. Cytological and histopathological correlation was done.

RESULTS

In the present study which was conducted over a period of 5 years we received 561 cases of intracranial neoplasms, of which pituitary adenomas were 38 in number accounting for 6.77% of all intracranial tumors. There were 20 females and 18 males. The male to female ratio was 0.9.(Table 1)

Table 1: Gender distribution of cases

Female	Male
20(53%)	18(47%)

Radiological classification of tumors by Hardy's classification (Table2) showed than more than ¾ the of cases were macroadenomas, bigger than 10mm in diameter enlarging the sella with suprasellar expansion, but not causing destruction. 29 cases were of grade II.

Table-2: Hardy's classification of Pituitary tumours (Radiological)

	Number of patients	Percentage
Grade i	5	13.15%
Grade ii	29	76.31%
Grade iii	2	5.2%
Grade iv	2	5.2%

The initial diagnoses offered radiologically are as shown in table 3. Major diagnosis offered was pituitary space occupying lesions.

About half the number of cases i.e., 19 cases were noted in the 3rd decade. Below 20 years we had 4 cases and all of them were females. The second peak of incidence was noted in the 4th decade (Table 3).

Table-3: Radiological diagnosis of sellartumours

Sl.no	Radiological diagnosis	No. of cases
1	Pituitary adenoma	8
2	Pituitary sol	28
3	Meningioma	1
4	Lymphoma/fungal granuloma	1

Table-4: Age distribution of Pituitary adenomas

Age	No of cases	Percentage
10-20 years	4	10.52%
21-30 years	5	13.15%
31-40 years	19	50%
41-50 years	7	18.42%
51-60 years	3	7.89%
61-70 years	0	0

The overall mean age of incidence was 35.72. Among males the mean age of incidence was 38.25 and among females it was 33.07.

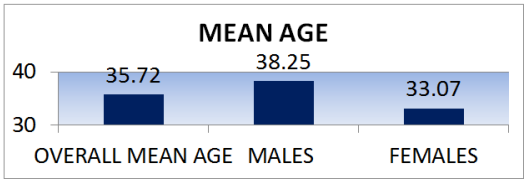

Fig-1: Mean age of incidence with gender distribution

Clinical history and symptomatology was noted in all cases .The most common complaint was visual disturbance followed by headache and amenorrhea (Table 5). The other symptoms were acromegaly, hypothyroidism, cushings syndrome, seizures.

Table-5: Incidence of various clinical symptoms

Sl.No	Symptoms	No. of cases
1	Visual alterations	31
2	Headache	29
3	Amenorrhea	15
4	Acromegaly	3
5	Cushings syndrome	2
6	Hypothyroidism	4
7	Seizures	2

Pituitary tumours can be functional and non-functional. In our study there were 24 functional tumours and 14 non-functional tumours (Fig 2). Regarding the hormonal activity among men there were 9 functional and non-functional adenomas whereas in females the functional adenomas were 15 and the non-functional adenomas were only 5(Table 6).

Table-6: Clinically functioning adenomas and nonfunctioning adenomas- in males and females

Sl.no		Funtional	Non-functional
1	Male	9	9
2	Female	15	5

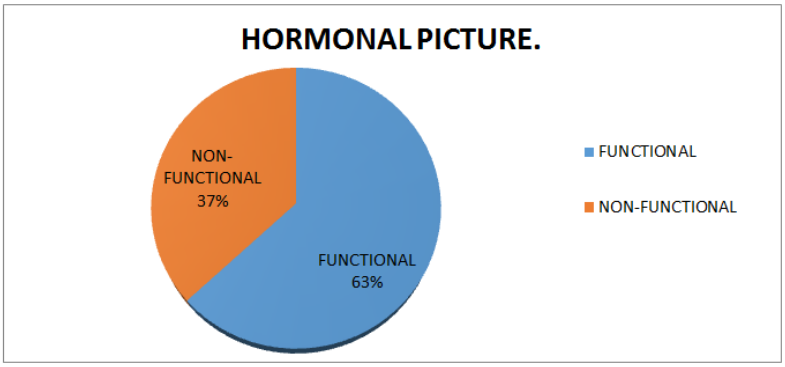

Fig-2: Distribution of functional and non-functional pituitary adenomas

Cytological squash cytology showed small groups and clusters of uniform small round cells with salt and pepper chromatin and inconspicuous nucleoli (Fig 3).

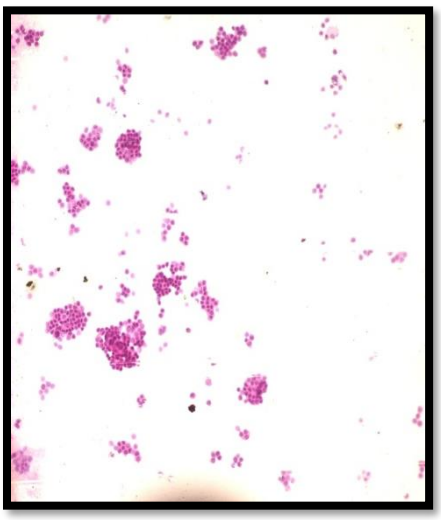

Fig 3 10x H&E Small groups of uniform bland cells with eosinophilic cytoplasm &ovoid regular nuclei with salt and pepper chromatin

Histopathological study showed cellular monomorphism with lack of acinar organization. Pleomorphic cells, uniform cytoplasmic staining, solid round uniform nuclei. Prominent nucleoli, mitotic figures may be present (fig 4 & 5).

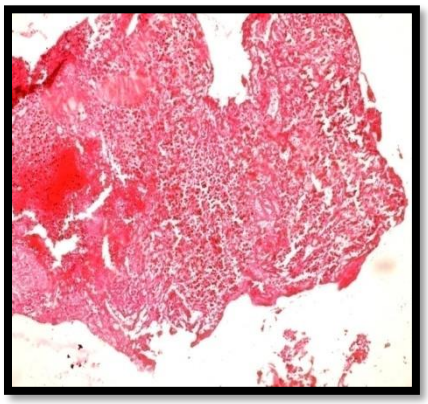

Fig-4-10X: of H & E of pituitary adenoma

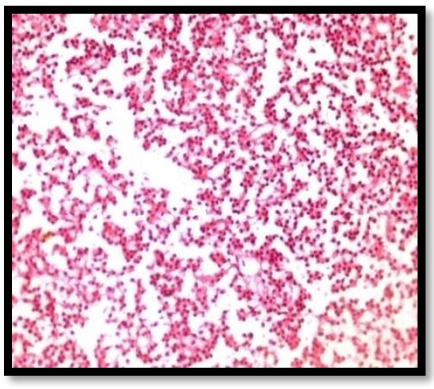

Fig-5-40X: of H & E of pituitary adenoma

The adenomas were studied histomorphologically and immunohistochemistry was applied only when in doubt. Further typing of adenomas was not done immunohisto chemically.

All the cytologically diagnosed cases were histologically proven to be pituitary adenomas. There was 100% concordance.

DISCUSSION

Pituitary gland or hypophysis lies in the base of skull, within a bony structure called sellaturcica, behind the bridge of the nose. It is a small pea sized ductless gland also called master gland of endocrine system usually attached to hypothalamus by a thin stem of blood vessels and nerve cell projections. Frontal lobe being largest accounting about 80% of total pituitary gland, main function is secretion of hormones and regulation of other endocrine glands including thyroid, adrenal and reproductive organs. Pituitary adenomas are most common in sellar region. Long natural history and low annual incidence of pituitary adenomas is impeding better clinical outcome. Increase in number of cases is ascribe to improvement in diagnostic technology which in turn increased sensitivity for detecting pituitary lesions. Great use of imaging particularly for indications like sinusitis, trauma and headache led to increase in detection of incidental pituitary tumors estimated between 0.15% to 0.3%.

Pituitary adenomas comprise nearly 15% of intracranial neoplasms and are the most common lesions in the sellar region [3]. In our study, out of 561 intracranial neoplasms, 38 cases are pituitary adenoma accounting for 6.77%.

In our study Age incidence was ranging from 20 - 60 years. According to Alma Ortiz *et al*. age incidence was correlating with our study (20 - 60 years). According to Julian Re Davis *et al*. [1] patients presented between 30 – 60 years. Higher frequency of incidence in our study between 31 - 40 years. Pituitary adenomas are rare in younger age group under 20 years. In our study there are 3 cases and all were females (16%). Women presented at earlier age (mean age 33.07yrs) at diagnosis than men (mean age 38.25yrs) because of increase symptom burden from hyperprolactinemia such as a disruption in the menstrual period and hypogonadism. Early presentation was particularly seen in prolactinomas[1].

95% of patients were symptomatic, mainly with insidious complaints, and hypopituitarism and neuro-ophthalmological symptoms were observed in 89% of the patients. The three main clinical manifestations were visual disturbances (84%), headache (76%) and amenorrhea (36%). Others being acromegaly, cushings syndrome hypothyroidism and seizures. According to S Cawich*et al*. [12] 80.7 % had visual disturbances, 72.3 %headache and 21.9% came with amenorrhea? Maria LiciaCaladoet *al*. [10] conducted a similar study in which 68.3%presented with visual disturbances 68.3% headache and 78.6 % amenorrhea. Our study is correlating with S Cawich*et al.* study with most common presentation being visual disturbance [12].

Females presented with more functional symptoms, 15 cases than nonfunctional (5 cases). Males presented with equal distribution of functional and non-functional symptoms. According to Robert Y Osamura*et al*. 68.5% are functional tumors whereas 31.5% are non-functional. According to Alma Ortiz et al 58% are functional tumors, 42% are non-functional [2].

There was 100% cytohistomorphological concurrence, similar to the studies done by Jindal *et al*. [7]. Basically the approach to pituitary adenomas is suggested by WHO by using a 5 tiered system - clinical presentation and secretory activity, size and invasiveness (Hardy's classification), histology, immunohistological profile, ultrastructural subtype.

CONCLUSION

Owing to the variety of pathologies in the sellar region & various modalities of therapeutic intervention,the pathologist has a key role in the multidisciplinary team dealing with the diagnosis and management of the patient with pituitary pathology.

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