A STUDY OF PITUITARY MACROADENOMAS-DIAGNOSIS AND MANAGEMENT IN A TERTIARY CARE HOSPITAL
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ABSTRACT: INTRODUCTION: Pituitary tumors are one of the common primary brain tumors accounting for 10% to 15% of all primary brain tumors¹. These tumors have a high incidence between the third and sixth decades of life. The morbidity associated with pituitary macroadenomas may include permanent visual loss, ophthalmoplegia, and other neurological complications. Advances in the medical and surgical management of the tumors and the availability of hormonal replacement therapies have contributed to their successful management.

AIM OF THE STUDY: To study the clinicopathological manifestations and management of pituitary macroadenomas.

MATERIALS AND METHODS: This is a prospective study, comprising of 25 patients of pituitary macroadenomas studied over a period from 2009 to 2012 in the department of Neurosurgery, Andhra Medical College, King George Hospital, Visakhapatnam. It is a Tertiary Care Hospital.

DISCUSSION AND ANALYSIS: Pituitary macroadenomas, particularly prolactinomas respond well to medical therapy. But most of the macroadenomas need surgical intervention for relief of clinical and endocrinological symptoms.

CONCLUSION: Pituitary adenomas are benign intracranial tumors which can attain a large size. Presentation usually occurs with visual disturbances, headache and endocrine disturbances. Incidence of these tumors is most common between third and fourth decades of life. Majority of this tumor are nonfunctioning with most of them having suprasellar or parasellar extension at the time of diagnosis. Transcranial intradural approach was an effective method for large tumors with suprasellar and parasellar extensions.

KEYWORDS: Pituitary tumors, Macroadenoma.

INTRODUCTION: Pituitary tumors are one of the common primary brain tumors accounting for 10% to 15% of all primary brain tumors.¹ These tumors have a high incidence between the third and sixth decades of life. They are uncommon in the paediatric age group, comprising only 2% of all primary paediatric brain tumors.² Pituitary tumors are more common among women, particularly premenopausal women. Genetic predisposition to pituitary tumors is uncommon and is seen with the multiple endocrine neoplasia type 1 (MEN-1) syndrome. Only 3% of the pituitary tumors are seen associated with this disorder, and only 25% of affected patients develop pituitary adenomas, and most of these are macroadenomas associated with excess levels of growth hormone or prolactin or both.³,⁴ As a general rule, functioning pituitary tumors tend to be more common among younger adults, whereas nonfunctioning adenomas become more prominent with increasing age.¹,⁵,⁶ The morbidity associated with pituitary macroadenomas may include permanent visual loss, ophthalmoplegia, and other neurological complications. Mortality rate associated with pituitary macroadenomas may include permanent visual loss,
ophthalmoplegia, and other neurological complications. Mortality rate associated with pituitary tumors is low. Tumor recurrence is also a possibility. Advances in the medical and surgical management of the tumors and the availability of hormonal replacement therapies have contributed to their successful management.

**AIM OF THE STUDY:** To study the clinicopathological manifestations and management of pituitary macroadenomas.

**MATERIALS AND METHODS:** This study is a prospective study, comprising of 25 patients of pituitary macroadenomas studied over a period from 2009 to 2012 in the department of Neurosurgery, Andhra Medical College, King George Hospital, Visakhapatnam. It is a Tertiary Care Hospital.

**Inclusion Criteria:** All patients with symptomatic pituitary macroadenomas with significant suprasellar and parasellar extensions.

**Exclusion Criteria:**
- Micro adenomas.
- Tumors confined to sella.

All patients were assessed by noting their consciousness level, presence of visual disturbances, headache or any features of raised intracranial pressure and presence of any features suggestive of hormonal disturbances. All investigations such as complete blood examination, random blood sugar, blood urea, serum creatinine, X-ray of skull, contrast enhanced computerized tomography and Gadolinium enhanced MRI brain were done. Endocrine screening was done by basal measurements of prolactin, growth hormone, ACTH, FSH, LH, TSH, T3 and T4, serum cortisol, IGF-1 and testosterone and estradiol. Provocative, dynamic and special hormonal assays are performed to define a specific endocrinopathy. All the patients were subjected for pterional craniotomy and excision/decompression of tumor. Post-operative radiation, pharmacotherapy was given wherever necessary. All the patients were observed from 6 months to 2 years for any residual tumor with symptoms and recurrence.

**DISCUSSION AND ANALYSIS:** Pituitary macroadenomas, particularly prolactinomas respond well to medical therapy. But most of the macroadenomas need surgical intervention for relief of clinical and endocrinological symptoms. In this study 72% of patients were in the fourth and fifth decade with mean age of 39 years. Female patients were more with a 2:1 ratio as compared to male patients. Visual disturbances was the most common presenting symptom (96%) followed by headache (68%). Endocrinological symptoms were found in 36% of patients. The ratio of non-functioning tumors was more than functioning tumors with a ratio of 2:1. Among the functioning tumors, 6 were growth hormone secreting tumors and 3 were prolactinomas, and these prolactinomas could be managed medically. In growth hormone secreting tumors, serum growth hormone levels were <40ng/ml in 4 patients and >40ng/ml in 2 patients. In prolactinomas, serum prolactin levels were <400ng/ml in two patients and >400ng/ml in one patient. In tumors
other than prolactinomas serum prolactin levels ranged from 10-150 ng/ml which may be due to stalk effect.

All patients were operated by pterional transcranial intradural approach. Near total excision of the tumor was done in 80% and decompression was done in 20% of patients. Improvement in vision was seen in 87% of patients, static in 6% and transient deterioration was seen in 6% of patients. Headache, acromegaly and galactorrhea improved in all patients. Normal serum growth hormone levels were achieved in 4 patients and <10ng/ml in 2 patients. Serum prolactin levels less than 20ng/ml were achieved in all. Postoperatively 8% of patients developed meningitis and transient diabetes insipidus. Vision was static in 8% of patients. One patient with recurrent tumor died in the immediate post-operative period due to hypothalamic disturbance. Adjuvant therapy was given in patients who underwent decompressive surgery with significant residual tumor. All patients were followed up both clinically and radiologically. None of the patients had clinical recurrence but 20% of patients had residual radiological lesion. Two patients had small radiological recurrence. Results of the present study were comparable to the study done by Van Lindert et al.\(^7\) In both these studies visual disturbances were the common mode of presentation. Headache was common among the patients in the present study. Nearly 30% of patients had hypopituitarism in both studies. Clinical improvement, minor complications, residual tumor on imaging and mortality, all were comparable in both studies. The present study is also comparable to the study by Symon et al.\(^8\) However the recurrence rate in the present study is 8% compared to 7% in the Symon et al. In the present study radiological recurrence is 8% compared to 5-10% in studies by Faria et al\(^9\) and E.R. Laws et al\(^10\) with maximum period of follow up of 2 years. In the study by Edward R. Laws,\(^10\) 91% had eventful recovery 1% had meningitis and 3% had transient diabetes insipidus. The high preponderance of pituitary adenomas in females in this study is similar to the studies by Kovacs et al\(^1\) and Mc Comb et al.\(^11\) Pituitary adenomas is seen in young adults. In this study 72% of patients were seen is the third and fourth decades of life with a mean age of 39 years. In the study by Yamada et al,\(^12\) Minderman et al\(^5\) and Kovacs et al\(^1\) the highest incidence was between third and sixth decades of life.

Pathologically 64% of adenomas in the present study were nonfunctional type whereas 36% were functional type compared to 40% nonfunctional types in study by Katznelson et al\(^13\) and 44% nonfunctional in the study by Ebersold et al.\(^14\) The clinical outcome, complications and recurrence rate in the present study was comparable with other international studies.

**CONCLUSION:** Pituitary adenomas are benign intracranial tumors which can attain large size. Presentation usually occurs with visual disturbances, headache and endocrine disturbances. Incidence of these tumors is most common between third and fourth decades of life. It is preponderant in females 60% compared to males 36%. Majority of this tumor are nonfunctioning with most of them having suprasellar or parasellar extension at the time of diagnosis. Transcranial intradural approach was an effective method for large tumors with suprasellar and parasellar extensions. Near total resection was done in majority of the patients and those with residual disease received adjuvant radiotherapy or medical therapy. Overall symptomatic and endocrine improvement was achieved in 90% of patients.
RESULTS:

| Age     | No. of Cases | Percentage (%) |
|---------|--------------|----------------|
| 21 – 30 | 5            | 20             |
| 31 – 40 | 12           | 48             |
| 41 – 50 | 6            | 24             |
| 51 – 60 | 2            | 8              |

Table I: Distribution of Cases according to Age

| Sex     | No. of Cases | Percentage (%) |
|---------|--------------|----------------|
| Male    | 9            | 36             |
| Female  | 16           | 60             |

Table II: Distribution of Cases according to Sex

| Clinical Presentation      | No. of Cases | Percentage (%) |
|----------------------------|--------------|----------------|
| Headache                   | 17           | 68             |
| Visual Disturbances        | 24           | 96             |
| Menstrual irregularity     | 3            | 12             |
| Acromegalic changes        | 4            | 16             |

Table III: Distribution of Cases According to Clinical Presentation

| Endocrine Function                  | Nos. | Total No.s |
|-------------------------------------|------|------------|
| Non Functional Tumors              |      | 16         |
| Functional Tumors                  |      |            |
| Acromegaly                          | 6    | 9          |
| Prolactin secreting tumors         | 3    |            |

Table IV: Distribution of Cases According to Endocrine Function of Tumors

| Extent of Imaging                        | No. of Cases |
|------------------------------------------|--------------|
| Sellar tumor with large suprasellar extension | 8            |
| Sellar tumor with suprasellar and parasellar extension | 18           |
| Carotid Encroachment                     | 6            |
| Extension to cavernous sinus             | 4            |

Table V: Distribution of Cases According to Imaging findings of patients

| Endocrine Function      | Total No. | Serum Hormone Levels | No. | % | % |
|-------------------------|-----------|----------------------|-----|---|---|
| Growth hormone          | 6         | >40mg/ml             | 2   | 33| 24|
|                         |           | <40mg/ml             | 4   | 66|   |
| Prolactin               | 4         | >200mg/ml            |     |   | 16|
| Hypopitutarism          | 7         |                      |     |   | 28|

Table VI: Distribution of Cases According to Endocrine Status of Patients
Tumor Resection | No. of Cases | Percentage (%) |
--- | --- | --- |
Near total resection | 20 | 80 |
Tumor decompression | 05 | 20 |

Table VII: Distribution of Cases According to Amount of Tumor resected

Imaging Findings | Residual Tumor | Percentage (%) |
--- | --- | --- |
Residual/Recurrent Tumor | 10 | 40 |
No Residual Tumor | 15 | 60 |

Table VIII: Distribution of Cases According to residual/recurrence of tumors on imaging at follow up

Clinical symptom | No. of cases | Improved | % |
--- | --- | --- | --- |
Visual disturbances | 24 | 18 | 75 |
Headache | 17 | 17 | 100 |
Acromegaly | 04 | 04 | 100 |
Galactorrhoea | 03 | 03 | 100 |

Table IX: Distribution of Cases According to clinical improvement immediately after surgery

Clinical symptom | No. of cases | Improved | % |
--- | --- | --- | --- |
Visual disturbances | 24 | 20 | 83 |
Headache | 17 | 17 | 100 |
Acromegaly | 04 | 04 | 100 |
Galactorrhoea | 03 | 03 | 100 |

Table X: Distribution of Cases According to Clinical Improvement after 1 month of surgery

Clinical symptom | No. of cases | Improved | % |
--- | --- | --- | --- |
Visual disturbances | 24 | 21 | 87 |
Headache | 17 | 17 | 100 |
Acromegaly | 04 | 04 | 100 |
Galactorrhoea | 03 | 03 | 100 |

Table XI: Distribution of Cases According to Clinical Improvement after 6 months of surgery
| Endocrine function | Total cases | Preop. Serum hormone levels | Post up serum hormone levels |
|--------------------|-------------|-----------------------------|-----------------------------|
| Growth hormone     | 6           | > 40mg/ml (2)               | < 10mg/ml (2)               |
|                    |             | < 40mg/ml (4)               | < 5mg/ml (4)                |
| Prolactin          | 4           | > 200mg/ml                  | <100mg/ml (4)               |

Table XII: Distribution of Cases According to Improvement in Endocrine status following surgery

| Postoperative period | No. of cases | Percentage (%) |
|----------------------|--------------|----------------|
| Meningitis           | 2            | 8              |
| Static vision        | 2            | 8              |
| Transient diabetes insipidus | 2 | 8 |
| Transient deterioration of vision | 2 | 8 |
| Radiological tumor recurrence in follow up | 2 | 8 |
| Deaths               | 1            |                |

Table XIII: Distribution of Cases According to Postoperative Complications

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