Pituitary Macroadenoma: Association with Hydrocephalus

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Abstract:

Objectives: *To find out the relationship between pituitary macroadenoma and hydrocephalus.*

Material and Methods: *This study was performed from April 2006 to October 2007 in department of neurosurgery BSMMU, Bangladesh. It was a cross sectional study, sample size was 30. All patients who were diagnosed clinically and radiologically as pituitary macroadenoma irrespective of age and sex were included and Pituitary macroadenomas without suprasellar extension and Suprasellar mass other than pituitary macroadenomas were excluded from this study.*

Results: *Analysis revealed that pituitary macroadenomas more than 4cm produce hydrocephalus with 95% confidence limit (p=<0.05).*

Abbreviations: *ACTH- Adrenocorticotropin hormone, ADH- Antidiuretic hormone, BSMMU- Bangabandhu Sheikh Mujib Medical University, CT- Computed Tomography, MRI- Magnetic Resonance Imaging, TH-Thyroid hormone, PRL- Prolactin, GH- Growth hormone, TSH-Thyroid stimulating hormone.*

Key words: *Pituitary macroadenoma, Hydrocephalus.*

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Introduction:

Pituitary adenomas are benign monoclonal tumors that arise from the cells comprising the anterior pituitary gland. They account for approximately 15%of all intracranial tumors. Adenomas are classified as a functioning or secretory adenoma and nonfunctioning or nonsecretory adenoma . Adenomas may be further subdivided into micro or macroadenomas based upon the size. Tumors less than 1 cm in diameter are considered micro adenoma and are predictably located solely within the sella turcica. Macroadenoma, by definition are tumors greater than 1 cm in diameter. They typically enlarge the sella turcica and frequently invade neighboring structures. Microadenoma usually are discovered because of an endocrinopathy; whereas macroadenoma present with compressive effects of the tumor; i.e. Bitemporal hemianopia , obstructive hydrocephalus as well as endocrinopathy.[1] Literature and textbook review show macroadenomas (>4 cm) produced obstructive hydrocephalus.

Hypothesis: There is a association between pituitary macroadenoma and obstructive hydrocephalus.

Objectives:

General objectives: To evaluate the effect of the size of the pituitary macroadenomas in relation to development of hydrocephalus.

Specific objectives:

To find out the size of the pituitary adenoma by imaging.

To find out the extent of hydrocephalus by imaging (CT & MRI).

To find out the association between suprasellar extension of pituitary macroadenoma and hydrocephalus.

Related Anatomical study:

The sella turcica, is a hollow at the cerebral surface of the body of the sphenoid bone, deepest part of which, the hypophyseal fossa lodges hypophysis cerebri. It is divided into anteriorly placed adenohypophysis and posteriorly placed neurohypophysis. Adenohypophysis further subdivided into pars anterior, pars intermedia, pars tuberalis.

Pathology :

Pituitary adenomas are the most common intrasellar pathology of the adult. Adenomas can be classified

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according to functional, anatomical/radiological, histological, immunohistochemical, ultrastuctural and clinicopathological criteria. Clinical and endocrinological classification broadly distinguishes tumors as functional or nonfunctional, based on their secretory activity in vivo. Functional adenomas are those that secrete prolactin (PRL), growth hormone (GH), thyroid stimulating hormone (TSH), or adrenocorticotropin hormone (ACTH), producing their respective clinical phenotypes of amenorrhea-galactorrhea syndrome, acromegaly or gigantism, secondary hyperthyroidism, and Cushing's disease or Nelson's syndrome. Tumors unassociated with a clinical hypersecretory state (i.e, gonadotroph adenomas, null cell adenomas, oncocytomas, and various silent adenomas) are collectively designated clinically as nonfunctional[2].

Prolactinomas are the most common of the hormone-secreting pituitary tumors. Most of them are microprolactinomas (< 1cm) and few are macroprolactinomas (> 1cm). The term giant prolactinoma is used for tumors larger than 4 cm in diameter. Clinical menifestations are attributed to marked hyperprolactinemia, gonadal failure, and neurological symptoms. The development of symptomatic hydrocephalus due to a pituitary adenoma is an exceptional event. Only a limited number of cases have been reported so far. The majority were nonfunctionig adenomas and only three were macroprolactinomas. Therapy with bromocriptine might be an effective medical approach to avoid ventriculo-peritoneal shunting in macroprolactinoma-induced symptomatic hydrocephalus.[3]

Measurment of hydrocephalus :

The size both temporal horn (TH) is >2mm in width (in the absence of hydrocephalus temporal horn should be barely visible) and the sylvian & interhemispheric fissures and cerebral sulci are not visible. OR

Both TH are >2mm and the ratio FH/ID>.05(where FH is the largest width of the frontal horn and ID is the internal diameter from inner table to inner table at this level).

Ballooning of frontal horns of lateral ventricles (Mickey Mouse ventricles) and 3rd ventricle.

Periventricular low density on CT, or periventricular high intensity signal on T2WI on MRI suggesting transependymal absorption or migration of CSF.

Used alone, the ratio FH/ID>50% suggests hydrocephalus.

Evan's ratio: ratio of FH to maximal biparietal diameter>30%[4]

Results:

Mean age of presentation were 39.06 years. The age ranges of the patients were 16 years to 65 years. The peak age group was 41 to 50 years. The male to female ratio was 2:1. Macroadenoma by types cited in table 3. Distribution of symptoms cited in table 4. Distribution of suprasellar extension cited in table 5. Distribution of hydrocephalus cited in table 6. Association between macroadenoma and hydrocephalus cited in table 7.

Table-I

Distribution of patients by sex.

Sex	Frequency	Percent
Male	20	66.67%
Female	10	33.33%
Total	30	100%

Table I shows the distribution of patients by sex. 66.67% of the patients were male and 33.33% of them were female. Male to female ratio was 2:1.

Table-II

Distribution of pituitary macroadenoma by types

Types	Frequency	Percent
GH secreting	4	13.33
Prolactinoma	10	33.34
Mixed (GH&PRL)	4	13.33
Nonfunctioning	12	40
Total	30	100

Table II shows distribution of types of pituitary macroadenomas. Of them 4(13.33%) were GH secreting tumors, 10(33.34%) were Prolactinomas, 4(13.33%) were mixed, 12(40%) were Nonfunctioning.

Table-III

Distribution of cases by presenting symptoms

Symptoms	Frequency	Percent
Headache	28	93.33
Visual disturbances (field defect)	22	73.33
Amenorrhea	4	13.33
Acromegaly	6	20
Impotence(decreased libido)	8	26.66
Vomiting	6	20
Decrease level of consciousness	2	6.67

Total was not corresponding to 100% because of multiple symptoms in same patient.

Table 4 shows the presenting symptoms among the patients with pituitary macroadenoma. More than 90% presented with the complaints of headache, 73.33% of the patients had history of visual disturbances, 20% had occasional vomiting, 13.33% had amenorrhea, 26.66% had impotence and 6.67% had decrease level of conscious level.

Table-IV

Suprasellar extension of pituitary macroadenomas.

Vertical diameter in cm	Frequency	Percent
≤4	24	80
>4	6	20
Total	30	100

Table IV shows the vertical diameter of the pituitary macroadenomas. 80% of the patients had vertical diameter below 4 cm and 20% had diameter above 4 cm.

Table-V

Distribution of hydrocephalus in pituitary macroadenomas.

Hydrocephalus	Frequency	Percent
Present	6	20
Absent	24	80
Total	30	100

Table 6 shows 6 (20%) patients had symptomatic hydrocephalus and 24 (80%) had no symptoms of hydrocephalus.

Table-VI

Association between vertical diameter of the pituitary macroadenoma and hydrocephalus.

		Hydrocephalus		Total
		Present	Absent	
Vertical	>4	4	2	6
diameter in cm	≤4	2	22	24
Total	6	24	30	

Pearson Chi-Sqaure (c^2) test value 6.68
df = 1
p value<0.01 (p value<.05 was considered significant in 95% confidence limit)

Table VI shows the association between vertical diameter of the pituitary macroadenoma and hydrocephalus. Pearson (c^2) test value was 6.68 with degree of freedom 1. p value was found <0.01, which was significant to establish the association between suprasellar extension of pituitary macroadenoma and hydrocephalus.

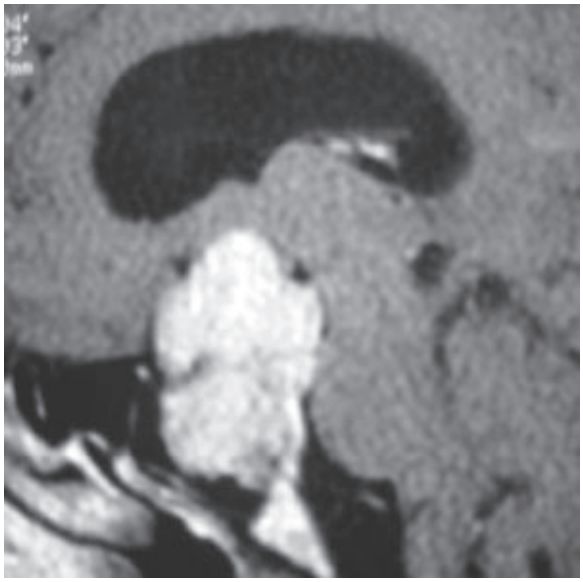

Fig.-1: *MRI of the brain sagittal view shows vertical extension of giant macroadenoma compressing the hypothalamus and third venticle*

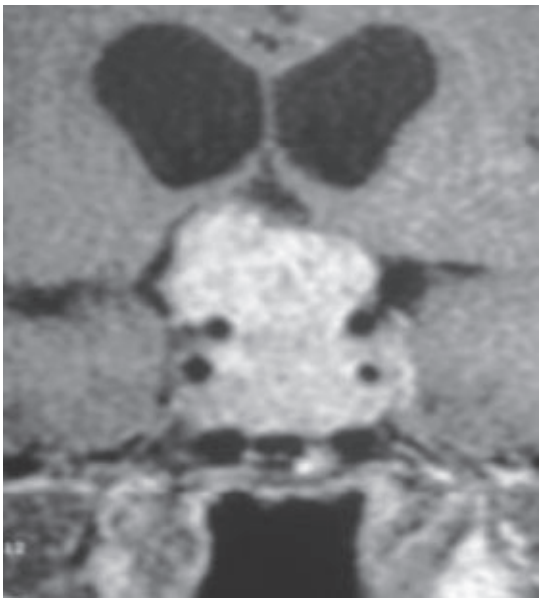

Fig.-2: *MRI of the brain coronal section shows giant macroadenoma compressing the third ventricle that produces obstructive hydrocephalus.*

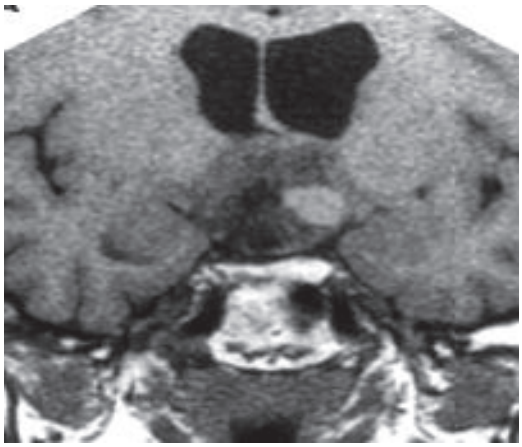

Fig.-3: *MRI of the brain coronal section shows pituitary apoplexy compressing the third ventricle that produces obstructive hydrocephalus.*

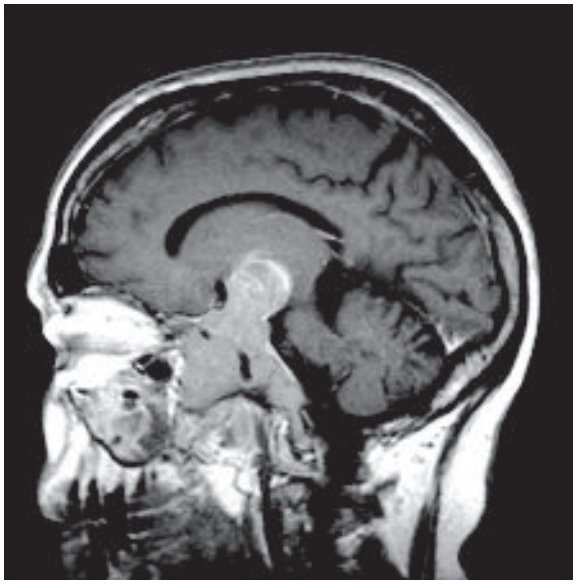

Fig.-4: *MRI of the brain sagittal view shows vertical extension of pituitary macroadenoma compressing the third ventricle and corpus callosum.*

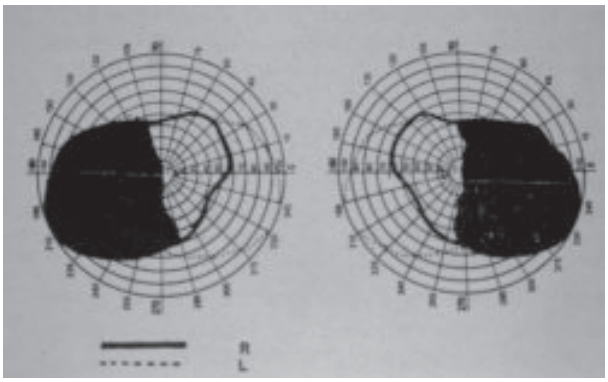

Fig.-5: *Bitemporal hemianopia in a patient of pituitary macroadenoma*

Discussion:

Our study was carried out in the department of neurosurgery, BSMMU, Dhaka during the period of April 2006 to October 2007 to know the association between suprasellar extension of pituitary macroadenoma and hydrocephalus.

The final study subjects were 30 patients with pituitary macroadenoma. The age range was between 16 years to 65 years. Mean age was 39.06 years. The highest incidence was in between 41-50 years. The male to female ratio (2:1).Headache, Visual disturbances, Acromegaly, Amenorrhea and impotence in the form of decreased libido are the most clinical presentation for pituitary macroadenoma. In our series more than 90% had complaints of headache, 73.33% of the patients presented with visual disturbances, 26.66% had impotence,20% had features of acromegaly and 13.33% presented with amenorrhea, which were almost similar to the study of Levy, 2004[5]. Among the pituitary adenomas prolactinomas, GH secreting adenomas and nonfunctioning adenomas are common. In our series 33.34% were prolactinomas, 13.33% were GH secreting, 13.33% were mixed (GH &PRL) and 40% were nonfunctioning. It is nearer to the study of Ramamurthi (2001)[6], in which prolactinomas were 27.0%, GH secreting adenomas were 14.0%, Mixed (GH&PRL) adenomas were 8.04% and nonfunctioning were 31.2%. Vertical diameter was measured from MRI scale. Vertical extension is a major factor that obstructs the foramen of Monro and leads to hydrocephalus. In our series vertical diameter more than 4cm in 6 (20%) cases, of them 4 cases (13.33%) presented as symptomatic hydrocephalus that was higher than the study of Mortini P et al. (2007)[7]. They found only three patients (3.2%) among 95 were present with symptomatic hydrocephalus.

Obstructive hydrocephalus occurs when flow of cerebrospinal fluid blocked within the ventricular system. One of the main causes of adult-onset obstructive hydrocephalus is a brain tumor located in the proximity of the intracranial ventricular system. Pituitary tumors are well recognized, although infrequent, cause of obstructive hydrocephalus.

In our study only four (13.34%) cases presented with the features of obstructive hydrocephalus, which was more than the study of Zikel et al. (1999)[8], they reported only three cases so far. This is due to fact that the patients were presented lately and took more time for confirmation of the diagnosis in our country.

Moreover CT Scan and MRI are not affordable by many patients.

Though very few studies have been done on association between suprasellar extension of pituitary macroadenoma and hydrocephalus. Zikel OM et al. 1999 reported only three cases of pituitary macroadenomas presented with symptomatic hydrocephalus. In this study we found that the vertical diameter more than 4cm of pituitary macroadenoma presented with symptomatic hydrocephalus. There was significant association (P = 0.001 in 95% confidence limit) between suprasellar extension of pituitary macroadenoma and hydrocephalus.

Summary:

Pituitary adenomas are benign monoclonal tumors that arising from the cells comprising the anterior pituitary gland and account for approximately 15% of all intracranial tumors classified as functioning and nonfunctioning. Very few numbers of patients presented with symptomatic hydrocephalus and vertical diameter of the pituitary macroadenoma is the key factor for the production of hydrocephalus. Our study was carried out in the department of neurosurgery, BSMMU, Dhaka during the period of April 2006 to October 2007 to elucidate the association between suprasellar extension of pituitary macroadenoma and hydrocephalus. For this purpose all consecutively admitted patients with compatible history, CT scan and MRI evidence of pituitary macroadenoma, fulfiling the selection criteria were included in the study. A total of 30 patients were included in the study and the variables that were analyzed included the vertical diameter of the tumor and presence or absence of hydrocephalus was evaluated. All data were analyzed by using statistical software package SPSS version 12.The age range of the patients was 16 years to 65 years. The most common age of presentation was 40 to 49 years (36.67%). Male to female ratio was 2:1. 73.33% of the patients had visual disturbances and 20% had features of raised ICP. 20% had vertical diameter more than 4 cm and 13.34% had features of hydrocephalus. In our study we found significant association between vertical extension of pituitary macroadenoma and hydrocephalus ($p < 0.01$).

Conclusion:

In our study we found that there is significant association between suprasellar extension of pituitary macroadenoma and hydrocephalus.

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