



Relevance Of Ihc Markers With Emphasis On Biologically Aggressive Pituitary Adenomas

¹Dr. Kalla Amrit Raj, ²Dr. Tyagi Surabhi, ³Dr. Singh Kuldeep

^{1,2}M.D Pathology, ¹Assistant Professor, ²Prof. Neuropathology, ³3rd year Resident
Department of Pathology,

¹Dr. S.N Medical College, Jodhpur, Rajasthan

^{2,3}Mahatma Gandhi Medical College, Jaipur, Rajasthan

***Corresponding Author:**

Dr. Amrit Raj Kalla

N90 Ashiana Amarbagh, New Pali Road, Jodhpur (Rajasthan), India

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Abstract

Background – Pituitary adenomas comprise 10-25% of all primary brain tumors. Wide range of behaviour is exhibited by Pituitary adenomas. Using immunohistochemistry aggressive pituitary adenoma can be subtyped and can be further advised for close follow up.

Objective – Assess the hormonal profile of pituitary adenomas with emphasis on biologically aggressive pituitary adenomas.

Material & methods –This is a tertiary hospital based study of forty cases of pituitary adenoma. All specimens were fixed in 10 percent formalin and entire biopsy tissue was processed as per standard guidelines. IHC markers were done after H&E microscopy. IHC was done using primary antibody against the these antigens- ACTH, GH, LH, FSH, PRL, TSH and MIB1.

Results & Conclusion – Total of twenty two aggressive adenomas (55%) were seen in our study. Majority of them were gonadotrophs comprising 31.81% of all aggressive adenomas.

Keywords:

Introduction

Pituitary adenomas are third most common primary brain tumor.^[1] These tumors exhibit spectrum of clinical behaviour depending on their clinical activity and size. With the use of immunohistochemistry aggressive adenomas can be recognized by their hormonal profile and MIB-1 index.^[2] MIB-1 index is widely accepted marker of proliferation.

Material and Methods

This is a tertiary hospital based study. A total of forty cases of Pituitary adenomas who got IHC done were included in the study.

Institutional ethical committee approval was obtained prior to study.

Written and informed consent was obtained from participants.

IHC was done using primary antibody against the these antigens- ACTH, GH, LH, FSH, TSH and MIB1.

Results

Total 40 cases of Pituitary adenoma were evaluated for Hormonal profile and Proliferation index.

Table 1: Association Between MIB-1 and IHC Results (n = 40)

IHC Results	MIB-1 LI		
	≤2 %	>2 %	Total
Somatotroph	7 (26.9%)	3 (21.14%)	10 (25.0%)
Gonadotroph	3 (11.5%)	7 (50.0%)	10 (25.0%)
Corticotroph	8 (30.7%)	1 (7.1%)	9 (22.5%)
Lactotroph	3 (11.5%)	2 (14.2%)	5 (12.5%)
Plurihormonal	4 (15.3%)	0 (0.0%)	4 (10.0%)
Mammosomatotroph	1 (3.8%)	1 (7.1%)	2 (5.0%)
Total	26 (100.0%)	14 (100.0%)	40 (100.0%)

50% of cases subjects with MIB-1 LI >2% were gonadotrophs, 21.14% were somatotrophs, 14.2% were lactotroph and both Corticotroph and mammosomatotroph were 7.1%.

Table 2: Distribution of Biologically aggressive Pituitary adenomas

Interpretation	Frequency	Percentage
Lactotroph in Male	4	28.5%
Recurrent adenomas	4	28.5%
Plurihormonal adenoma	4	28.5%
Silent Corticotroph	2	14.3%
Total	14	100.0%

Two of the lactotrophs in males and all recurrent pituitary adenomas were biologically aggressive as well as had MIB-1 LI > 2.

Table 3: Association Between Aggressive adenomas (biologically aggressive & high proliferative index) and IHC Results (n=22)

Interpretation	Frequency	Percentage
Gonadotrophs	7	31.81%
Lactotrophs	4	18.18%
Plurihormonal adenoma	4	18.18%
Corticotroph	3	13.63%
Somatotroph	3	13.63%

Interpretation	Frequency	Percentage
Mammomatotroph	1	4.54%
Total	22	100.0%

Seven out of twenty-two aggressive adenoma were gonadotrophs including three of them being recurrent with high MIB-1 LI and other four had MIB-1 LI >2

Discussion

Out of total of twenty two aggressive adenomas (55%), fourteen cases were aggressive only on the basis of increased MIB-1 LI and fourteen cases were diagnosed as aggressive on the basis of immunohistochemistry as per WHO 2017 criteria. They were in the category of biologically aggressive adenomas. Of these biologically aggressive adenomas six cases also had increased MIB-1 LI- Two lactotrophs in males and four recurrent adenomas.

Certain pituitary adenomas are considered as biologically aggressive adenoma irrespective of MIB-1 LI on basis of gender, hormonal activity, histological and immunohistochemical findings such as Lactotrophs in males, Sparsely granulated somatotroph, silent corticotroph, Pit-1positive plurihormonal adenoma and recurrent adenoma.

Four recurrent pituitary adenomas (25%) were seen in our study. MIB-1 LI was found to be high in all of the four recurrent adenomas. Study by Manash Bora, Radhey Shyam Mittal *et al* yielded similar results.^[3]

In our study, MIB-1 LI was >2% in 40% of clinically non-functioning adenomas with one silent lactotroph having MIB-1 LI of 12-15%. Wolfsberger *et al*, considered MIB-1 LI as gold standard for relevance in post-operative management of clinically non-functioning adenoma.^[4] Ekramullah *et al* found that there was an inverse correlation of Ki-67 with tumor doubling time in regrowing non-functioning adenoma.^[5]

Conclusion

Pituitary adenoma are frequently encountered tumours, silent pituitary adenomas represent a challenging group of tumors.

MIB-1 LI is long considered as gold standard for assessing the cell proliferation and biological aggressiveness of the tumor.^[6] MIB-1 LI of >2 % is of prognostic significance.

Correlation of immunohistochemistry and proliferative index with clinical history may be important in further adjuvant therapies which may be needed in certain pituitary adenomas. Postoperative Radiotherapy is needed in tumors with high proliferative index.

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