Clinical Characteristics and Early Outcomes for Pituitary Adenomas Using the WHO Criteria

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Introduction

An atypical adenoma classification was proposed by the WHO in 2004 to classify pituitary adenomas more likely to have aggressive features such as invasion or metastasis. Histological finding including Ki-67 labeling index > 3%, nuclear p53 reactivity, and the presence of mitotic figures were proposed as atypical criteria, but evidence remains limited regarding the independent clinical utility of these markers. The aim of this study were to assess the value of the WHO criteria and classification on measures of tumor aggressiveness and post-operative outcomes.

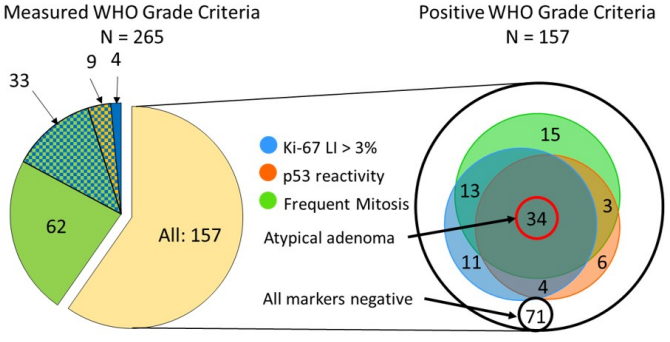
Methods

A retrospective analysis of 390 pituitary adenoma surgeries performed at a single institution between 2005 and 2012 identified 268 resections with adequate histological evaluation and follow-up for analysis.

Results

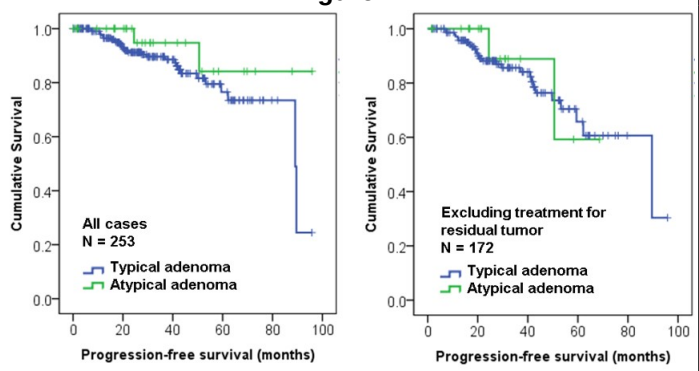
Three pituitary carcinoma cases were excluded from outcome analyses (2/36 atypical [5.6%] and 1/232 typical adenoma [0.4%]; Fisher's exact p=0.05). The distribution of the remaining 265 cases based on the measurement and positivity of WHO criteria is illustrated in Figure 1.

Figure 1



Distribution of non-excluded cases (N = 265) by measured WHO criteria (left). Venn diagram of cases with all three WHO criteria measured (N = 157) showing the distribution of positive criteria.

Figure 2



Kaplan-Meier plots illustrating progression / recurrence free survival (PFS / RFS).

Atypical adenomas (34/265 [12.8%]) were more likely to present as recurrent (odds-ratio [OR] 3.1, 95% confidence interval [CI] 1.4-6.6), undergo craniotomy (OR 6.4, 95% CI 2.2-18.6), and trended towards lower biochemical remission rate (9/13 cases [69.2%] v. 73/81 cases [90.1%]), Fisher's exact p=0.06, with no significant increase in tumor invasion on MRI (OR 1.6, 95% CI 0.8, 3.3) compared to typical adenomas. Typical adenoma cases with positivity in at least 1/3 WHO atypical criteria (52/265 [19.6%]) did not demonstrate these aggressive features; intriguingly, this category included 1/3 carcinoma cases (1/52 [1.9%]). No significant difference in extent of resection was noted between typical and atypical adenoma groups, Chi-squared (2, N=265) = 0.37, p=0.83. Kaplan-Meier analysis of cases that achieved biochemical remission (Figure 2, left) showed no difference in progression / recurrence-free survival (PFS/RFS) between typical and atypical adenoma cases (N=253, p=0.24, median follow-up 36.9 months). Kaplan-Meier analysis of cases treated with surgery only (i.e., no post-operative adjuvant therapy; Figure 2, right) also showed no difference in PFS/RFS between typical and atypical adenoma cases (N=172, p=0.72, median follow-up 35.4 months); however, atypical cases were more likley to receive post-operative adjuvant treatment (p=0.04). No progression/recurrence occurred after radiotherapy (0/75 cases) with a limited median follow-up of 27.1 months.

Conclusions

The atypical pituitary adenoma classification was more specifically associated with initial or presenting measures of tumor aggressiveness than typical adenoma with or without independent positivity in at least one WHO criteria, suggesting that the atypical designation carries some progrnositc significance. However, in early follow-up, survival analysis revealed no difference in PFS/RFS between typical and atypical adenoma, and no progression/recurrence occurred after radiotherapy. Taken together with prior reports on the clinical impact of extent of resection, our results suggest that aggressive surgery may be a more meaningful determinant of post-operative outcome than histology. Longer clinical follow-up would be useful in clarifying the value of this grading system.

Learning Objectives

By the conclusion of this session, participants should be able to 1) Describe the influence of the WHO criteria and grading system on measures of pituitary adenoma aggressiveness; and 2) Discuss, in small groups, the challenges of quantifying the relevance of tumor characteristics on poor post-operative course.

References

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