

The influence of the tumoral cell proliferation rate in pituitary adenoma on expressing other factors with a prognostic role and therapeutic potential

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Abstract

Background: This article describes the growth rate of pituitary adenomas, their invasion and potential recurrence. Some of them grow rapidly while others remain in a dormant condition for a long time. The recurrence rate is also very hard to forecast. The pituitary adenomas that initially reduced their proliferation rate now acquire a rapid one, producing aggressive recurrences.

Materials and methods: Eighty two cases of pituitary adenomas were studied. The classification of human pituitary adenomas has been profoundly assisted by immunohistochemistry. Ki-67 antibody was used to assess the proliferative index of pituitary adenomas.

Results: Acidophil type adenomas or acidophil cells areas within mixed pituitary adenomas had the highest proliferation rate. Chromophobe pituitary adenomas were Ki67 negative in 90%, as well as the ones that presented the basophilic cells. The pituitary adenomas with a trabecular growth pattern had the lowest rate of proliferation, in about 50% of the cases being zero. The heterogeneity expression of growth factors and corresponding receptors is dependent on hormonal profile of pituitary adenomas.

Conclusion: The pituitary adenomas proliferation rate depends on the type of secreted hormone as well as on the hormonal associations met in some cases of pituitary adenomas.

Key words: pituitary adenoma, cell proliferation, Ki67.

Introduction

Pituitary adenomas are variable in growth rate, potential of invasion and recurrence. Some tumors grow fast; others remain in a dormant stage for a long time. The recurrence rate is also difficult to predict, the pituitary adenomas that initially reduced the proliferation rate acquire a fast proliferation rhythm and produce aggressive relapses. The ability to predict the proliferative potential of pituitary adenomas could have major implications for the clinical management of these tumors. Scientists have focused on identifying the predictive behaviour factors of pituitary adenomas. Ki67 proliferative index has been shown to be a useful tool in the measurement of tissue proliferation and for this reason, has been extensively studied.

Material and methods

Eighty two cases of pituitary adenomas were studied. The classification of human pituitary adenomas has been profoundly assisted by immunohistochemistry. Ki-67 antibody was used to assess the proliferative index of pituitary adenomas. Ki67 proliferation index was performed using Nikon Eclipse E600 microscope at 400X magnification assisted by a specialized cell counting computer program (NSI). The highest immunoreactivity areas were evaluated, an average of 1000 cells per case (about 3 microscopic fields taken as multimedia images) having been studied.

Results

Ki67 proliferation index in the pituitary adenomas was noted as being increased in cases with recurrences. There are no precise data on the pituitary hormones involvement in determining either the proliferation rate of pituitary adenomas or the growth factors. For this reason, the

aim of the present study was to identify the potential role of pituitary hormones and growth factors, GFAP and S100 protein in influencing the pituitary adenomas proliferation rate. Proliferating pituitary adenomas represent 73.33% of all cases included in the study. Ki-67 expression was nuclear restricted the reaction intensity being variable, in most cases moderate and intense. The proliferation rate was extremely heterogeneous within this group, ranging between 4/1000 and 49/1000 (Fig. 1 a, b).

The highest proliferation rate was recorded in the acidophil type adenomas or acidophil cells areas within mixed pituitary adenomas. Pituitary adenomas of the chromophobe type were Ki67negative in 90%, like basophilic cell adenomas.

According to the growth pattern, papillary type pituitary adenomas were proliferative, the proliferation rate in most cases being greater than 20/1000.

Pituitary adenomas with trabecular growth pattern showed the lowest proliferation rate, in about 50% of cases it is zero. Pituitary adenomas with compact growth pattern had an average index of proliferation, being located between the papillary and the trabecular types. The proliferation index of compact pituitary adenomas is middle, being located between the papillary and trabecular types.

Afterwards, we analysed the pituitary adenoma proliferation rate in respect of their hormonal status. In 50% of plurihormonal pituitary adenomas there was no proliferation, the index being denoted by 0. The remaining plurihormonal type adenomas had a high proliferation index, 83.33% of which ranges between 21-41/1000.

Pure pituitary adenomas, which immunohistochemically expressed only one hormonal type were proliferating at a rate of 59% of the cases, 41% were not proliferative. Approximately 80% of GH-secreting pituitary adenomas were proliferating at a rate of proliferation medium ranges be-

as prolactinoma [5] or ACTH-secreting adenomas [2, 6]. Some studies suggest that prolactinoma with increased proliferation index, besides the risk of recurrence, is pituitary carcinomas precursors [6].

The data given in literature indicate low levels of proliferation marker Ki 67 in both gonadotropic hormone-secreting adenomas, and non-secreting ones [1, 6, 7].

In addition to existing data, the present study has demonstrated that polyhormonal adenomas including co-expression of LH present a low proliferation index.

Conclusions

1. The heterogeneity expression of growth factors and corresponding receptors is dependent on hormonal profile of pituitary adenomas.

2. Secreting GH and PRL pituitary adenomas are the most active in terms of synthesis and release of growth factors.

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