Efficacy of early postoperative radiotherapy for nonfunctioning null cell or silent pituitary macroadenomas

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INTRODUCTION

The high voltage radiotherapy (RT) after surgery for nonfunctioning pituitary macroadenomas (NFMA) is still controversial, subjected to rapid technical and medical progress.

AIM

To appreciate the best period of time for RT in patients with pituitary macroadenomas with residual tumor after surgery.

SUBJECTS AND METHODS

We studied 97 patients with residual NFMAs to identify factors affecting tumor control such as the time of RT and tumor immunopathology. Partial pituitary surgery was performed either by trans frontal (35 patients) or transspenoidal (62 patients) approach. High voltage RT (mean total dose 50.5 Gy) was given to 41/97 patients. Twenty out of 41 patients had RT within the first year after surgery (Group A) and 21/41 had RT after 1 year (Group B). Fifty six out of 97 patients with surgery, without RT, represent the control group (Group C) (Fig.1). The increase of the postoperative remnant was defined as a minimum 25% increase of any diameter (either transversal or vertical) by serial imaging studies. The immunoperoxidase analysis (avidin biotin technique) for the anterior pituitary hormones and the final immunopathological classification of the NFMAs revealed: 44 null cell adenomas (a) (immunostaining was negative for all hormones), 23 gonadotropinomas (b) (positive immunostaining for LHB and FSHb) and 30 plurihormonal (immunostaining positive for more pituitary hormones different from gonadotropins) or unihormonal silent adenomas (c) (immunostaining positive for ACTH, GH or PRL), (Table1).

RESULTS

Table 2. The rate of the residual tumor regrowth in relation to the high voltage radiotherapy (RT)

<table>
<thead>
<tr>
<th>No. of regrowth after surgery without RT</th>
<th>No. of regrowth after RT according to immunohistochemestry</th>
<th>Null cell adenoma</th>
<th>Silent hormone adenoma</th>
<th>RT (&lt;1yr)</th>
<th>RT (+1yr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 (2%) vs 22* (39%)</td>
<td>7 (16%) vs 15* (28%)</td>
<td>44 (45%)</td>
<td>53 (55%)</td>
<td>2</td>
<td>5</td>
</tr>
</tbody>
</table>

Patients without RT (control group C) have a significant higher regrowth rate of residual tumor versus patients with RT (p = 0.025), at 5 years. Only 2/20 patients with immediate RT (group A) have regrowth at 5 years and 5/21 patients from group B, see Table 2, Fig.2. The chance for the remnant regrowth is decreased in group A vs group B (OR = 0.35).

It is important to emphasize that patients from group A vs patients from control group, without RT, have had more tumors with cavernous sinus invasion (p = 0.038), with high postoperative remnant (p = 0.001) and with size more than 2 cm (p = 0.001) and with residual mass outside the sella (p = 0.003). Patients from group B vs control, group C, showed also statistically significant higher postoperative remnant (p=0.047) and residual mass with suprasellar extension (p=0.023), (Table 1).

Figure 2. The regrowth up to 5 years of the postoperative remnant of the null cell and silent uni/plurihormonal pituitary macro adenomas

CONCLUSIONS

It is tempting to suggest as an optimal time for radiotherapy is the first year post partial surgery of nonfunctioning pituitary macro adenomas. Special attention should be given for uni/plurihormonal silent adenomas (as shown by immunohistochemistry).

Figure 1. Types of treatment.

Table 1. General characteristics of patients

<table>
<thead>
<tr>
<th>Control Group</th>
<th>Patients with radiotherapy after surgery (N = 41)</th>
<th>Group A (N = 20)</th>
<th>Group B (N = 21)</th>
<th>Mean age of diagnostic (yrs)</th>
<th>Sex ratio (M/F) n</th>
<th>Mean size (range) postoperative remnant (cm)</th>
<th>Patients with remnant grater 2 cm in size (n, %)</th>
<th>Patients with supersellar remnant (n, %)</th>
<th>Mean (range) time of RT after surgery (mo)</th>
<th>Cavernous sinus invasion (n, %)</th>
<th>Visual field deficits</th>
<th>IHC a/b/c</th>
<th>No. of regrowth after surgery without RT</th>
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<tbody>
<tr>
<td>50 ± 12.92</td>
<td>10/10</td>
<td>18/3</td>
<td>28/28</td>
<td>2.70 (0.90 - 4.70)*</td>
<td>1.94 (0.66 – 4.50)*</td>
<td>1.63 (0.50 – 5.50)*</td>
<td>15/20 (75%)*</td>
<td>15/20 (75%)*</td>
<td>6 (2-12)</td>
<td>13/20 (65%)*</td>
<td>14/20 (70%)*</td>
<td>73/10</td>
<td>0.05 vs patients with RT</td>
</tr>
<tr>
<td></td>
<td>*p=0.05, Group A vs Group C and Group B vs Group C</td>
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</table>

In the control group C, without RT, the patients with silent hormone adenomas have a regrowth rate more frequently than patients with null cell adenomas (p=0.060, CI 90%), (Table 2).

In the groups A and B, we observed by contrast that postoperative RT is associated with lower risk of residual tumor regrowth for these type of tumors expressing hormones vs null cell adenomas (OR = 0.16) (Fig 2).

*All p values have been adjusted for multiple comparisons using Bonferroni correction. OR: Odds Ratio; CI: Confidence Interval.