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Symptomatic Hyperprolactinemia: A Six Years of Experience

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To determine the underlying etiologies among hyperprolactinemic cases, evaluate treatment options and patient compliance. Methods: We evaluated the data of 111 hyperporlactinemic patients, admitted to our clinic with hyperprolactinemia from 1999 through 2005 retrospectively. Results: One-hundred-six (95.5%) women, 5 (4.5%) men, mean age of 34.7 ± 11.0 years, were included. Magnetic resonance imaging (MRI) procedures revealed; adenoma in 78 (73.58%) patients; microadenoma in 65 (61.32%), macroadenoma in 13 (12.2%) and normal findings in 28 (26.4%). Microprolactinoma was most prevalent among women (n=68, 64.1%), whereas it was macroprolactinoma among men (n=3, 60%). Higher levels of prolactin were detected in macroadenomas ($p<0.05$). Cabergoline was the drug of choice for 78.7%, bromocriptine for 28.8 % of cases. Among 82 patients, who were consuming medicine, 57 (69.5%) were on regular follow-up; 23 ± 14 months. Although their tumor size decreased in varying degrees, there was no change among 25 (43.9%) cases, moreover, 10 subjects (17.5%) experienced an increase despite appropriate therapy. Conclusions: Our data was compatible with literature. However, the relatively higher number of cases who were resistant to therapy was a question of debate. We think that in such cases, it is necessary to recheck diagnostic procedures and the patient compliance cautiously.

Keywords: Hyperprolactinemia, prolactinoma, microadenoma, macroadenoma

Introduction

Prolactin is a pituitary-derived hormone that plays a pivotal role in a variety of reproductive functions. An excess of prolactin above a reference laboratory's upper limits or "biochemical hyperprolactinemia," can be identified in up to 10% of the population. Serum prolactin levels of women with oligomenorrhea, amenorrhea, galactorrhea or infertility, and men with hypogonadism, impotence or infertility must be determined. The prevalence of symptomatic hyperprolactinemia has been reported to range from 0.4% to 5% among a randomly selected healthy adult population at a family planning clinic. The rate is even higher among patients with amenorrhea; (9%), with galactorrhea; (25%) and as high as 70% among women with both amenorrhea and galactorrhea. Its prevalence is about 5% among men who present with impotence or infertility (1).

Lactotroph adenomas are predominantly responsible for the clinical symptoms of hyperprolactinemia and most of them respond to medical therapy (2). However, other causes of hyperprolactinemia need to be investigated thoroughly. Management of this clinical entity depends on the cause, clinical presentation and the expectations of the affected individual.

In this retrospective study, we aimed to analyse the clinical and laboratory findings of the patients who were admitted to our clinic with symptomatic hyperprolactinemia. We also inquired the response to medications and patient compliance to the therapy.

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Materials and Methods

The study was performed at the outpatient clinic of Division of Endocrinology and Metabolism of Baskent University School of Medicine. The medical records of 111 patients with symptomatic hyperprolactinemia, from 1999 through 2005, were supplied from hospital archives and were reevaluted. Symptoms and complaints, such as; oligoamenorrhea, hirsutismus, androgenic alopecia for women, loss of libido and empotence for men and galactorrhea and infertility for both sexes were recorded. Drug of choice, response to medical treatment and the time spent on regular follow-up were also noted.

Results

Of 111 patients; 106 were (95.5%) women, 5 (4.5%) were men with a mean age of 34.7 ± 11.0 years (17-72 years), (34.3 ± 10.0 years for women, 43.6 ± 22.0 years for men).

Magnetic resonance imaging (MRI) procedures revealed; adenoma in 78 (73.58%) patients; microadenoma in 65 (61.32%), macroadenoma in 13 (12.2%) and normal findings in 28 (26.4%) cases. We could not be able to reach the MRI reports of five remaining subjects. Microprolactinoma was the most prevalent cause among women (n=68, 64.1%), whereas it was predominantly macroprolactinoma among men (n=3, 60%).

On admission, mean prolactin values was 1716.73 ± 1227.01 mIU/L (normal limits 33.36-580.8 mIU/L). Higher levels of prolactin were detected in patients with macroadenomas than the ones with normal hypophyseal imaging findings ($p<0.05$). Mean prolactin levels regarding choice of treatment, tumor size and therapy outcome were shown in Table 1.

All hyperprolactinemic men reported empotence and loss of libido. Among women, a positive correlation was detected between galactorrhea and adenoma size ($r=0.74$, $p<0.05$). However, no correlation was found betweeen menstrual abnormalities and size. After correction for age, according to forty years old, a positive correlation appeared between menstruel abnormalities and the adenoma size for the premenapousal group ($r=0.73$, $p<0.05$).

Cabergoline was the first drug of choice for 78.7% and bromocriptine for 28.8 % of the cases. Among 16.2% of the subjects, cabergoline was prescribed after bromocriptine either due to the lack of improvement in prolactin levels or bromocriptine related adverse effects. Surgery was performed in 1.8% of the patients and 14.4% of all were on follow-up without medication. Treatment options served to the cases are shown in Figure 1.

Among 82 patients, who were using medicine, only 57 (69.5%) were on regular follow-up. Their mean time spent on follow-up was 23 ± 14

Table 1. Prolactin levels regarding choice of treatment, tumor size and therapy outcome

Mean prolactin levels of patients :	initial (mIU/L)	Post-treatment (mIU/L)
Whole group (n=111)	1716.73± 1227.01	518.43± 784.30
Bromocriptine group (n=32)	1697.99±1122.99	498.97±868.13
Cabergoline group (n=43)	1637.04±1129.36	536.71±939.55
Cabergoline after bromocriptine group (n=18)	2138.38±1621.16	381.76±334.26
Surgical treatment (n=3)	3420,00± 2127.74	173,87±228,07
Without treatment (n=15)	1367.96±1083.79	732.83±546.37
Patients with microadenoma (n=68)	1754.26±1339.77	471.99±764.09
Patients with macroadenoma (n=14)	2108.56±997.08	419.24±708.18
Patients with no adenoma on MRI (n=29)	1502.27±106.18	645.44±852.44
Post-treatment tumor size reduction by>50% (n=9)	1901.69±1078.68	519.93±277.45
Post-treatment tumor size reduction by 25-50% (n=10)	1889.01±886.52	615.85±785.87
Post-treatment tumor size reduction by <25% (n=3)	2236.67±1815.03	53.67±21.96
Post-treatment no tumor reduction (n=25)	2148.57±1920.05	545.55±1116.31
Post-treatment tumor enlargement (n=10)	1582.42±775.81	321.57±304.71

months. Althrough follow-up, 50 (87.7%) of the subjects became free of symptoms, 9 (15.8%) had their adenoma size reduced by 50%, 10 cases (17.5%) had tumor reduction by 25-50% and 3 patients had (5.3%) by < 25%. There was no change in tumor size among 25 (43.9%) of all, even further, 10 subjects (17.5%) experienced an increase in size despite of appropriate therapy.

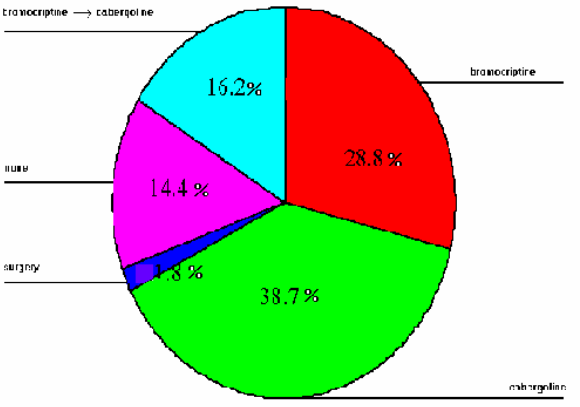

Figure 1. Distribution of patients regarding treatment options. Mean time spent on therapy is 23.09± 9.42 months (3-54)

Discussion

Symptomatic hyperprolactinemia usually represents itself with symptoms of hypogonadism. Galactorrhea is observed less commonly and can be identified among 50% of the cases (3). The most common cause of symptomatic hyperprolactinemia is prolactin releasing adenomas. There is a linear association between clinical findings and the size of the adenoma (4). In our group, in accordance with literature, most of the patients were women with microadenoma and had symptoms of hypogonadism (5). We detected a positive correlation between galactorrhea and adenoma size, however, similar relationship could not be established with hypogonadism among women on admission. After correction for age, an association was found for the premenapousal group.

Cabergoline is considered to be the drug of choice due to its high effectivity and low rates of adverse effects. In meta-analysis of large series, prolactin levels were normalized in 80% and adenom sizes reduced in varying degrees among 74% of the cases with cabergoline treatment. The rates mentioned above were more or less true for bromocriptine (6-15). In our group, clinical cure rates were compatible with the literature, however, the magnitude of reduction in adenoma size was not as expected, since 61.4% of the patients did not exhibit a significant reduction in adenoma size. This finding might be attributed to drug resistance and/or patient incompliance and/or diagnostic errors. Considering the relatively low number of patients who had been on regular control for six years, patient incompliance seemed to be predominant reason.

In literature, drug resistance is defined as unresponsiveness at biochemical analyses and imaging methods despite three months of medical therapy at maximum doses, and can be observed among 10% of the patients (16). The number of resistant subjects in our group is much higher than that and brings the query of diagnostic errors. Besides, macroprolactinemia, stalk compression of a nonfunctioning adenoma, hypothalamic disorders and accompanying drugs are needed to be investigated again.

In conclusion, the data we obtained was compatible with literature. However, the relatively higher number of cases who were resistant to therapy was a question of debate. We think that in such cases, it is necessary to recheck diagnostic procedures and the patient compliance cautiously.

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