Outcome in acromegaly: A retrospective analysis

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ABSTRACT

Introduction: Many of the treatment modalities recommended for acromegaly are either too expensive or not available in large parts of India. There is a dearth of treatment and outcome data in Indian patients. Aims and Objectives: The purpose of this study was to analyze the treatment modalities used and the respective outcomes which include remission, recurrence, hypopituitarism, other complications, and mortality. Materials and Methods: This is a retrospective data analysis of 15 acromegaly patients treated at a tertiary care hospital in eastern India. A remission criteria of nadir growth hormone level <1 µg/dl after Oral Glucose tolerance test (OGTT) and normal age related IGF-1 levels was used. Results: All patients (100%) had macroadenomas. Surgery could not be done in five (33%); three (19.8%) refused, two (13.2%) had comorbidities. Transsphenoidal surgery (TSS) achieved remission in four out of ten (40%). Conventional radiotherapy (CRT) failed in all five patients and caused hypopituitarism in three (60%). Cabergoline (CAB) either alone or following surgery achieved remission in one out of four (25%) though symptomatic relief and tolerability were remarkable. One patient (7%) had pituitary apoplexy with remission, two patients (14.3%) died due to CVA. Conclusions: TSS remains the treatment of choice in acromegaly, though in macroadenomas the success is limited. A sizeable proportion of patients refuse or are unfit for surgery. As most of the recommended options are very costly or unavailable, alternative treatment options generally used are CRT or CAB which have limited efficacy. Incidence of hypopituitarism, following CRT is very high.

Key words: Acromegaly, cabergoline, radiotherapy, transsphenoidal surgery

INTRODUCTION

Many of the recommended treatment modalities for acromegaly like somatostatin analogues (octreotide and lanreotide) and growth hormone (GH) receptor antagonist (pegvisomant) are either too expensive or sparsely available in India. Stereotactic surgery is available in only selected centers. There is a dearth of treatment and outcome data in acromegaly patients in India. The purpose of the present study was to analyze the treatment modalities used in our part of the country and the respective outcomes.
Where surgery was not possible, conventional radiotherapy (CRT) and/or medical therapy was considered. The rest underwent transsphenoidal surgery (TSS).

All patients underwent pretreatment lab assessment of free T4, TSH, PRL, LH, FSH, testosterone/estradiol and short synacthen test.

Remission criteria was nadir GH level <1 µg/dl after OGTT and normal age related IGF-1 levels. GH and IGF-1 were measured by chemilumenescent immunoassay. Alternative therapy was considered when surgery failed. Pitutary functions were repeated post-surgery and long term after CRT.

Cabergoline (CAB) was used at the dose of 1.0-3.0 mg weekly for a minimum of 6 months. CRT was given in a total dose of 4500 rad split into 25 fractions of 180 rad each.

RESULTS

One patient refused surgery and was lost to follow up. Two patients could not be operated due to cardiomyopathy and respiratory morbidity respectively; one was put on CAB, the other had pituitary apoplexy during an episode of CVA and went into remission but with coincident hypopituitarism. Two more patients refused surgery; one was put on CAB and one was given CRT. In total, surgery could not be done in five patients (33%) either due to coexistent morbidities or due to patient refusal.

Outcome of transsphenoidal surgery

All fifteen patients (100%) had macroadenomas. Ten went for TSS from different centers; four underwent surgery at our center. TSS achieved remission in only four patients (40%); two were from our center. No recurrence was noted. Visual impairment occurred in one. The six patients with failed surgery were put on alternative modalities as add-ons. Four went for CRT; other two who refused CRT went for CAB.

Outcome of conventional radiotherapy

The patient who received CRT as primary therapy developed hypopituitarism within 9 years without normalization of GH levels. Post-surgery CRT failed in all four patients. Two of them expired within 3 years due to CVA. Rest developed hypopituitarism at a mean follow up of 8.5 years. Thus CRT was ineffective in all in achieving remission and overall incidence of hypopituitarism post-radiotherapy (post-surgery/primary therapy) was 60%.

Outcome of dopamine agonist cabergoline

CAB as primary therapy, did not achieve remission in the two patients. One of two patients achieved remission on add-on. Thus CAB post-surgery/primary therapy achieved remission in only 25% though symptomatic relief and tolerability were remarkable. GH decreased by an average of 24% at 1 year.

Mortality

The mortality in this case series was two out of fourteen (14.3%). Both died due to CVA following CRT after failed surgery.

DISCUSSION

In contrast to 70-80% incidence of macrodenomas reported in most series our incidence was 100%, probably due to late presentation in the overtly symptomatic stage. TSS is the treatment of choice in acromegaly. However, fewer than 50% of patients with macroadenomas undergo biochemical remission following TSS. We report a similar remission of 40%. The low recurrence rate in our subjects was in concordance with other similar studies.

CRT was used in our patients. Barkan et al.[3] reported post-irradiation IGF-1 normalization in less than 5% over 7 years. CRT achieved remission in none of our patients, 60% developed hypopituitarism. More than 50% of patients receiving radiation therapy develop pituitary failure.[1]

Regarding medical therapy, somatostatin analogues, and pegvisomant are largely unaffordable. Of the dopamine agonists, only CAB has any efficacy in acromegaly,[1] though mono-therapy is effective in less than 10% of patients.[4] We report 25% efficacy of CAB (alone/add-on) in achieving remission. The merits of CAB were its oral administration, excellent tolerability and a modest reduction (24%) of GH.

Recent studies report a 32% increased risk for all-cause mortality.[1] We report two (14.3%) deaths from CVA, in patients who were uncontrolled after CRT. CRT may increase risk of CVA due to radiation vasculopathy.[1]

The limitation of our study is the small number of cases. However, in the background of limited Indian data, the study is relevant in depicting the true picture of follow up of acromegaly patients in eastern India.

In conclusion, TSS remains the treatment of choice, though in macroadenomas, found in majority, the success is limited. Sizeable number of patients refuse or are unfit for surgery. As most of the recommended options are costly and sparsely available, alternative treatment

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options used are CRT or CAB which have limited efficacy. Incidence of hypopituitarism following CRT is very high. Optimal treatment needs to be individualized depending on the efficacy, availability and affordability of treatment modalities.

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