A single-centre audit of treatment outcomes in a case series of 218 acromegaly patients

Khan S¹, Jabeen S³, Perez-Fernandez L¹, Mola L⁵, Vincent A¹, Cudlip S², Grossman A¹, Jafar-Mohammadi B¹, Pal A¹

1. Oxford Centre for Diabetes, Endocrinology and Metabolism, Churchill Hospital, Oxford University Hospitals NHS Foundation Trust
2. Department of Neurosurgery, John Radcliffe Hospital, Oxford University Hospitals NHS Foundation Trust
3. Department of Endocrinology, Agha Khan University, Karachi, Pakistan
4. Department of Endocrinology, 12 de Octubre Hospital, Madrid, Spain
5. Department of Endocrinology, Hospital Universitario de Castellón, Castellón de la Plana, Spain

Introduction

Acromegaly is an endocrine disorder characterized by growth hormone (GH) excess almost always from a pituitary adenoma leading to a syndrome of musculoskeletal and metabolic changes associated with significant morbidity and mortality (standardized mortality ratio [SMR]: 0.94–2.5) [1]. It is rare with a prevalence of 2.8-13.7 cases per 100,000 and an incidence of 0.2-1.1/100,000 people annually [2]. Treatment options for acromegaly include Trans Sphenoidal Adenohypophysectomy (TSA) as first line treatment in the vast majority of cases; recent published series [7-12] in the literature have reported cure rates (based on the 2010 consensus criteria [6]) of 63-100% in microadenomas and 40-72% in macroadenomas. Other treatment modalities include radiotherapy (RT) and pharmacotherapy (somatostatin analogues [SSA], dopamine agonists [DA] and pegvisomant). These treatments lead to biochemical and clinical control of acromegaly in the majority of patients and a normalised SMR [1].

Methods

We conducted a retrospective casenotes review to audit the management of patients attending our centre over the last 52 years (since 1966) for acromegaly management against the 2014 Endocrine Society Guidelines [3]. Patients were identified from the departmental database and clinics. Post-operative cure and disease control, were defined as normal age- and sex-adjusted IGF-1, and either a random serum GH<1μg/L or GH nadir<1 μg/L on OGTT as per the 2010 consensus criteria [6] and the 2014 endocrine society guidelines [3].

Results

218 patients (53% males) were included in this audit with a follow up ranging from 2 to 587 months (mean 136.8) between 1966-2018.

Diagnosis: The mean age at diagnosis was 45 years. The most common presenting features were increased hand and shoe size and acromegalic facies (graph1). IGFl level, random GH level and OGTT was done in 166/218 (76%), 188/218 (86%) and 180/218 (82%) patients at diagnosis respectively. 196/218 (90%) patients had imaging at diagnosis; magnetic resonance imaging (MRI) for 171 and computed tomography (CT) for 25. This revealed 69/195 (35%) microadenomas (<1 cm) and 126/195 (65%) macroadenomas (>1 cm). 72 (37%) patients had colonoscopy at diagnosis.

Graph 1: Symptoms at presentation

- Carpal Tunnel Syndrome: 12%
- Macroglossia: 12%
- Headaches: 22%
- Sweating: 38%
- Acromegalic facies: 51%
- Increased hand & shoe size: 70%

Pharmacotherapy: 135/218 (62%) patients either did not have surgery or remained uncontrolled after surgery. 108 (80%) of these patients were started on pharmacotherapy; SSA in 105 (98%), DA in 50 (46%) and Pegvisomant in 7 (6%), achieving remission in 81/108 (75%).

Radiotherapy: RT was done in 55/218 (25%) patients; of which 37/55 (67%) achieved remission.

TSA: 197/218 patients were treated with TSA over the last 5 decades by two different neurosurgeons (table 1); 48 (24%) of whom received preoperative SSAs.

Recurrence: Interestingly, 6.5% (6/93) of patients who were initially cured with TSA, developed a recurrence after a mean duration of 7 years.

Graph 2: Treatment modalities used in Controlled patients (total 108)

Overall remission

In 147/218 patients, we have recent biochemical data available (last 18 months). 21 (14%) have IGF-1/GH discordance; IGF-1 discordance in 18 and GH discordance in 3. In the remaining 126, 108 (86%) are in remission (see graph 2 for treatment modalities used to achieve remission) and 19 (15%) are not controlled (further treatment is being organised in majority).

Discussion

Our audit includes a large number of patients managed over more than 4 decades e.g. 98/218 patients in our series presented in the last century. Our surgical remission rates are comparable to other published series, while the 86% control achieved with multimodal therapy in patients (108/126) assessed within the last 18months compares favourably with other series. We find a recurrence rate of 6.5% at a mean duration of 7 years post remission which emphasises the importance of long term follow-up. It will be important to prioritise review of patients where acromegaly is not currently controlled to reassess if there is scope to escalate treatment.

References