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

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Introduction

Acromegaly is a 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 Adenophysectomy (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

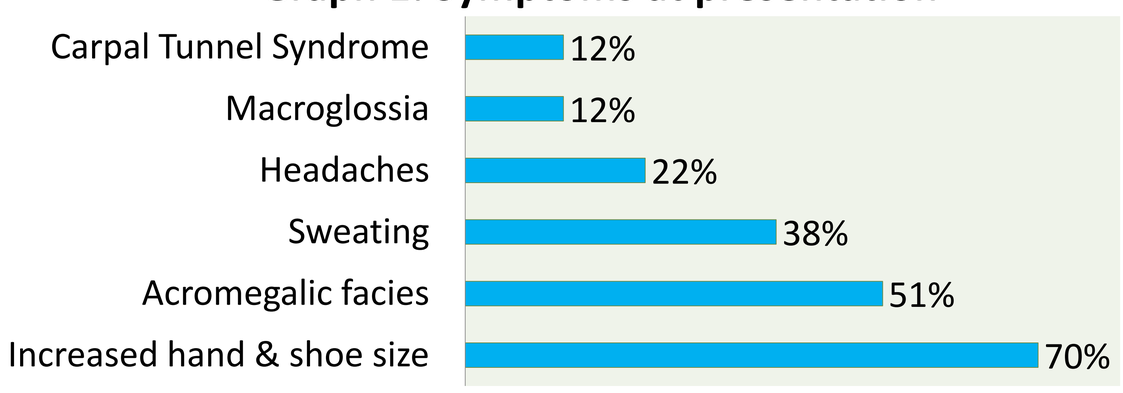
We conducted a retrospective casenotes review to audit the management of patients attending our centre over the last 52 years (since 1966) for acromegaly management against the 2014 Endocrine Society guidelines [3]. Patients were identified from the departmental database and clinics. Post-operative cure 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). IGF-1 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



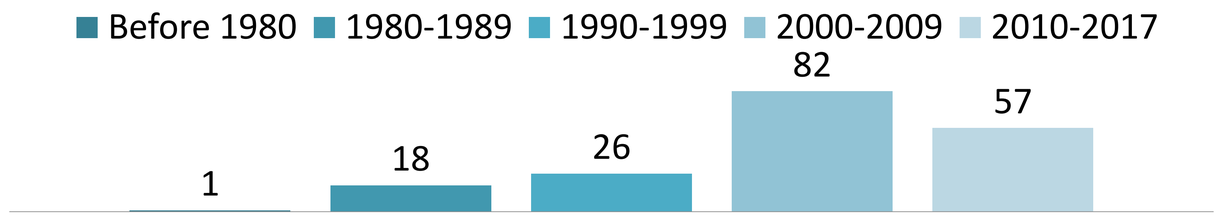
Pharmacotherapy: 135/218 (62%) patients either did not have surgery or remained uncontrolled after surgery. 108 (80%) of these patients were started on pharmacotherapy; SSA in 105 (98%), DA in 50 (46%) and Pegvisomant in 7 (6%), achieving remission in 81/108(75%).

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.

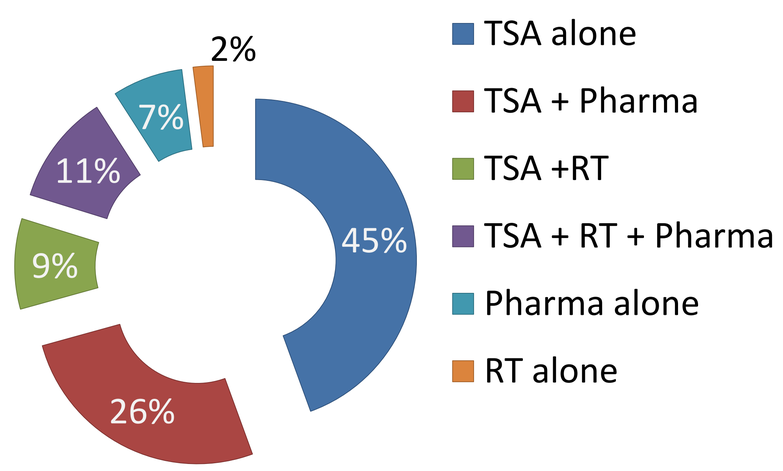
Table 1: TSAs done per decade



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).

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



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

1- Lavrentaki et al. Pituitary. 2016;20(1):4-9. JCEM ; 98: 626–635. **2-** Ntali et al. F1000Res. 2015;4:F1000 Faculty Rev-1426. Published 2015 Dec 11. **3-** Katznelson et al. J Clin Endocrinol Metab. 2014;99(11):3933–3951. **4-** Ludecke et al. Neuroendocrinology. 2006;83(3-4):230–239. **5-** Nomikos et al. Eur J Endocrinol. 2005;152(3):379–387. **6-** Giustina et al. J Clin Endocrinol Metab. 2010;95(7):3141-3148. **7-** Wang et al. Clin Endocrinol (Oxf). 2012;76(3):399–406. **8-** Jane et al. J Clin Endocrinol Metab. 2011;96(9):2732–2740. **9-** Starke et al. J Clin Endocrinol Metab. 2013;98(8):3190–3198. **10-** Sun et al. J Neurol Surg B Skull Base. 2014;75(1):47–52. **11-** Hazer et al. J Neurosurg. 2013;119(6):1467–1477. **12-** Gondim et al. Neurosurg Focus. 2010;29(4):E7. 13- Giustina et al. J Clin Endocrinol Metab. 2000;85(2):526–529.

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