The importance of achieving disease control in Acromegaly: a retrospective single center analysis

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Introduction

- Growth hormone (GH) excess in acromegaly is associated with higher mortality and morbidity
- With improved treatment for acromegaly, many studies have demonstrated latest mortality rates to be improving and comparable to the general population (Schofl 2012 Eur J Endocrinol; Varadhan 2016 Pituitary)
- Though the SMR for acromegaly per se is improving with time, The mortality rates remain high largely due to cancers and circulatory disease (Esposito 2018 Eur J Endocrinol)
- Acromegaly is associated with significant morbidity (Dekkers 2008 J Clin Endocrinol Metab)
- There are not many studies that have looked at the predictors of morbidity associated with acromegaly
  - Development of comorbidities such as cardiovascular events and cancers are an important cause of mortality (Varadhan 2016 Pituitary)
  - A recent study used IgF1 as a marker but this may not be available in all patients who have been follow up for more than 2 decades (Jayasena 2011 Clin Endocrinol)
  - The duration of diabetes preceding the diagnosis of acromegaly is unaccounted for and could contribute to morbidity of acromegaly (Vallette 2013 Clin Endocrinol)
- The frequency of pituitary surgery to aim for cure for this condition has been progressively increasing (Esposito 2018 Eur J Endocrinol)
- Patients with acromegaly continue to have significant comorbidities, especially cancers, cardiovascular diseases, diabetes and hypopituitarism, which can account for a significant financial burden on health care system (Lesen 2017 Eur J Endocrinol)

Aim

The aim of the study was to assess the differences in mortality and morbidity associated with active acromegaly compared to patients in whom disease control was achieved

Methods

- Single centre study : Retrospective clinical observational study
- Data on all patients with acromegaly who had been treated since 1948
- 1948-2014 used for data collection
- All GH results were converted to mcg/L
- Divided into ‘control-achieved’ and ‘active disease group’ for calculations
- Data at baseline including proportion with macroadenomas, pituitary axes failures and cardiovascular events (diabetes, hypertension, strokes, MI and CCF) labelled as CVE, were collected
- Details regarding treatment modalities used: surgery, radiotherapy and medical treatment were counted and the number of times each was done was counted
  - Medical treatment included Somatostatin analogues, cabergoline/ bromocriptine or Pegvisomant
  - Each therapy was counted as a course if treatment sustained beyond 3 months continuously
  - Patients with repeated course of same therapy were counted as independent episodes
- Control was deemed achieved if latest GH consistently <1.5mcg/L.
- Data on mortality and CVE and duration to the events were calculated
- IgF-1 was not included in this analysis due to lack of sufficient data

Results

- N=167
- Control-achieved in 116 patients

	Control-achieved	Active Disease	p
N=	116	51	
At diagnosis			
Age	47.5 ± 13.3	53.9 ± 12.9	<0.005
GH(mcg/L)	16.6 ± 25.5	28.6 ± 36.3	<0.05
Patients with pit. Axes failure	9.5%	16%	NS
Macroadenomas	78.5%	82%	<0.001
At follow-up			
Duration follow up (months)	163 ± 118	102 ± 110	NS
Patients surgery done	65.5%	46.2%	<0.0005
Mean number of surgeries among operated	1.1 (1-3)	1.3 (1-3)	NS
Patients with medical Rx	98.3%	82.7%	NS
Mean no. of medical courses	1 (1-5)	0.8 (1-4)	NS
Total no. of treatment modalities	2.25	1.8	NS
New pituitary axes failure	38.2%	32%	NS
No. of total new failed axes	1.8 (1-3)	1.5 (1-4)	NS
New CVE	33.6%	36%	NS
Duration to CVE (months)	144 ± 112	69 ± 110	<0.05
Mortality	30.2%	64%	<0.0001

Discussion

- The initial GH at diagnosis and macroadenomas were significantly higher in the active disease group, suggesting more severe disease
- The proportion of patients operated was higher in the group were control achieved, again showing surgery as the most successful form of treatment
- The number of treatment modalities required to achieve control was higher compared to group where control not achieved, suggesting that a more aggressive approach may be helpful
- Though CVE was equal in both groups, the duration to achieve control was higher in patients where control achieved, again highlighting the benefit of curing acromegaly
- The mortality rates were higher in the active disease group
- Though the total number of treatment modalities was higher, the proportion suffering with further pituitary axes failure was comparable between the two groups

- ***<u>Limitations of our analysis</u>***
  - Retrospective analysis not allow for calculating incidence rates
  - Regression analysis could not performed as data on various other confounding factors for mortality and morbidity were not available
  - Data on cancer prevalence and cause of death was not available for this study

Conclusion

- Mortality rates from acromegaly were higher in patients with active disease
- Disease burden from acromegaly is significantly high in both ‘control-achieved’ as well as ‘active disease’ group; however the duration to develop these complications can be prolonged by achieving control
- The various available treatment options would need to be explored, with surgery being the preferred choice, to aim to achieve biochemical control of acromegaly to reduce the risk of complications