Age-dependent differences in acromegaly at diagnosis

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Introduction

Age at diagnosis (AaD) and disease duration are among the factors affecting the disease outcome in acromegaly. Etiopathogenesis and clinical management of acromegaly may vary according to the age at diagnosis. We identified the distinctive demographic, clinical and biochemical features of patients with acromegaly according to AaD.

Methods

In this retrospective, single-center study, Hacettepe University (a tertiary clinic in Ankara, Turkey) electronic database was screened to determine the patients with acromegaly. Three hundred eighty-four patients with acromegaly who had relevant clinical and biochemical data were included for final analysis. Patients were divided into three groups based on the AaD (group 1, 20-40; group 2, 41-60; group 3, >60 years). Data regarding the demographic and clinical features, pre-operative hormone levels, radiological and pathological characteristics of adenoma, treatment modalities, and comorbidities were retrieved.

Results

Groups consisted of 194 (88F/106M), 167 (84F/83M), and 23 (13F/10M) patients, respectively. Gender distribution was similar. Pre-operative GH and prolactin levels were significantly higher in group 1 compared to patients in groups 2 and 3 ($p<0.001$ and $p=0.002$, respectively). Pre-operative IGF-1 levels were lowest in group 3. The maximum tumor diameter was highest in group 1 patients [20 mm (14-27) vs. 13 mm (9-20) vs. 10.5 mm (9-15), $p<0.001$]. Macroadenoma was detected in 139 (71.7%) of group 1 patients, 92 (55.1%) of group 2 patients, and 13 (56.5%) of group 3 patients ($p<0.001$). Suprasellar extension and cavernous sinus invasion were more common in group 1 ($p=0.005$ and $p=0.003$, respectively). Ki-67 index was > 3% in 7.2% and 2.4% of patients in groups 1 and 2, respectively. In contrast, none of the patients in group 3 showed Ki-67 index > 2%. There was a significant difference between groups regarding the use of somatostatin receptor ligands (68.6% vs. 55.1% vs. 47.8%, $p=0.011$) and dopamine agonist (20.6% vs. 10.8% vs. 0%, $p=0.004$). The distribution of patients who received radiotherapy was also significantly different between groups ($p=0.002$). Hypopituitarism was present in 53 (27.3%) and 32 (19.2%) patients in groups 1 and 2, respectively whereas none of the patients in group 3 had hypopituitarism ($p=0.006$). When patient groups were evaluated according to comorbidities; hypertension, diabetes mellitus, hyperlipidemia, and coronary artery disease were found to be less common in group 1 patients, Table 1.

Conclusion

Younger patients with acromegaly had higher hormone levels, and larger and more aggressive tumors. Clinicians should be aware of age-related differences in patients with acromegaly.

Table 1. Comparison of the demographic, clinical and biochemical parameters according to age at diagnosis in patients with acromegaly

	Group 1 (n: 194)	Group 2 (n: 167)	Group 3 (n: 23)	p
Gender (F/M)	88/106	84/83	13/10	0.459
Age at diagnosis (years)	32 (27-36)	49 (45-54)	64 (62-68)	**<0.001**
Duration of symptoms before diagnosis (years)	2 (0-5)	2 (0-5)	4 (0-6)	0.220
Pre-operative GH (ng/mL)	17.8 (7-39.7)	7.9 (4.2-20.9)	6.7 (4.2-13.4)	**<0.001**
Pre-operative IGF-1 (ng/mL)	893 (587.3-1078)	864 (602-1100)	692 (442.3-862)	0.068
Pre-operative PRL (ng/mL)	20.3 (11.2-55.7)	14.1 (9.9-27.2)	11.7 (8.2-20.7)	**0.002**
Pituitary tumor max diameter (mm)	20 (14-27)	13 (9-20)	10.5 (9-15)	**<0.001**
Macroadenoma (n, %)	139 (71.7%)	92 (55.1%)	13 (56.5%)	**<0.001**
Suprasellar extension (n, %)	41 (21.1%)	25 (15%)	3 (13%)	**0.005**
Cavernous sinus invasion (n, %)	31 (16%)	26 (15.6%)	0 (0%)	**0.003**
Immunohistochemistry (n, %)				0.959
GH (+)	60 (30.9%)	61 (36.5%)	10 (43.5%)	
GH+PRL (+)	60 (30.9%)	54 (32.3%)	7 (30.4%)	
Plurihormonal (+)	24 (12.4%)	24 (14.4%)	3 (13%)	
Ki 67 index (n, %)				**0.012**
<%1	33 (17%)	47 (28.1%)	12 (52.2%)	
%1-2	23 (11.9%)	20 (12%)	3 (13%)	
%2-3	11 (5.7%)	17 (10.2%)	0 (0%)	
>%3	14 (7.2%)	4 (2.4%)	0 (0%)	
Treatment (n, %)				
Surgery				**0.013**
Not operated	4 (2.1%)	7 (4.2%)	2 (8.7%)	
Transsphenoidal	173 (89.2%)	155 (92.8%)	20 (87%)	
Transcranial	16 (8.3%)	3 (1.8%)	0 (0%)	
Medical treatment				
SRL	133 (68.6%)	92 (55.1%)	11 (47.8%)	**0.011**
Dopamine agonist	40 (20.6%)	18 (10.8%)	0 (0%)	**0.004**
Pegvisomant	9 (4.6%)	4 (2.4%)	0 (0%)	0.456
Radiotherapy	52 (26.8%)	28 (16.8%)	0 (0%)	**0.002**
Re-operation (n, %)	64 (33%)	23 (13.8%)	0 (0%)	**<0.001**
Residue tumor (n, %)	116 (59.8%)	69 (41.3%)	5 (21.7%)	**0.001**
Hypopituitarism (n, %)	53 (27.3%)	32 (19.2%)	0 (0%)	**0.006**
Hypertension (n, %)	34 (17.5%)	78 (46.7%)	16 (69.6%)	**<0.001**
Diabetes mellitus (n, %)	36 (18.5%)	82 (49.1%)	10 (43.5%)	**<0.001**
Hyperlipidemia (n, %)	81 (41.8%)	97 (58.1%)	15 (65.2%)	**0.010**
Coronary artery disease (n, %)	6 (3.1%)	18 (10.8%)	2 (8.7%)	**0.009**
Malignancy (n, %)	23 (11.9%)	28 (16.8%)	6 (26.1%)	0.125