

Particular aspects concerning acromegaly amid pandemic

Mara CARȘOTE^{1,2}, Florica SANDRU^{2,3}, Diana Elena RENTEĂ¹, Stefania ZUGRAVU¹,
Claudia MEHEDINTU^{2,4}, Anda DUMITRĂȘCU¹, Mihai Cristian DUMITRĂȘCU^{2,5}

¹ "C.I. Parhon" National Institute of Endocrinology, Bucharest, Romania

² "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania

³ Elias Emergency Hospital, Bucharest, Romania

⁴ "Nicolae Malaxa" Clinical Hospital, Bucharest, Romania

⁵ University Emergency Hospital, Bucharest, Romania

ABSTRACT

Acromegaly embraces typical complications of a pituitary tumor as well as GH (growth hormone) and IGF1 (insulin-like growth factor) excess-related cardio-metabolic and oncologic conditions; and associated medical, surgical treatment or even radiotherapy issues. We point out a few particular aspects concerning acromegaly issues amid COVID-19 pandemic. The review includes only full length, English published papers. One of the most important complications of long standing, untreated or un-responsive to therapy acromegaly is related to respiratory and otorhinolaryngology issues like sleep apnea; this becomes an important aspect causing pulmonary complications in patients with active coronavirus infection. In subjects who are not going through a COVID-19 infection, but they had a prior diagnostic of acromegaly, two main aspects of medical and surgical practice were noted: a massive reduction of surgical volume during the first year of pandemic, mostly during peak months of high infection rate in general population and the introduction of tele (digital) health care systems, of different protocols and various platforms mostly depending of medical center, rather than country or even continent related protocols. Associated central adrenal insufficiency requires a particular attention if COVID-19 positive. The data directly targeting the endocrinologists amid pandemic are very limited. ACROCOVID is a 2021 study that was internationally conducted based on a questionnaire that was applied to 84 endocrinologists (67% of them in Europe); 33% of acromegalic individuals had a delay on procedure because of insufficient COVID-19 assays and 54% of them due to inefficient provision for neurosurgery. Secondary diabetes mellitus (with a potential worsening in some patients due to pasireotide LAR) is at high risk for COVID-19 infection; the level of glycated hemoglobin A1c seems a good predictor at onset of infectious disease. Acromegaly might associate osteoporosis; coronavirus infection aggravates bone loss due to oxidative stress, inflammatory status, cytokine release, immobilization, glucocorticoid use. Acromegaly field concerning pandemic changes represents a complex, still ongoing matter involving both patients and multidisciplinary practitioners.

Keywords: acromegaly, pituitary tumor, neurosurgery, COVID-19, coronavirus, pandemic

INTRODUCTION

Acromegaly, a rare endocrine tumor related endocrine condition, embraces typical complications of a pituitary tumor as well as GH (growth hormone) and

IGF1 (insulin-like growth factor) excess in terms of cardio-metabolic and even oncologic conditions; but, moreover, of associated medical, surgical treatment or even radiotherapy issues (1-10).

Corresponding author:

Florica Sandru

E-mail: florysandru@yahoo.com

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METHOD

We point out a few particular aspects concerning acromegaly issues amid COVID-19 pandemic. The review included only full length, English published papers, the search words are “acromegaly” or “pituitary tumor” or “neurosurgery” and “COVID-19” or “pandemic” or “coronavirus”. We also included collateral aspects amid pandemic in relationship to acromegaly related complications like diabetes mellitus, osteoporosis, sleep apnea etc. Several short sub-sections are included in terms of COVID-19 infection in patients with a prior diagnostic of acromegaly or pandemic regulations on endocrine practice.

SLEEP APNEA

One of the most important complications of long standing, untreated or non-responsive to therapy acromegaly is related to respiratory and otorhinolaryngology issues like sleep apnea; this becomes an important aspect causing pulmonary complications in patients with active coronavirus infection, as also reported in patients with prior respiratory co-morbidities like chronic obstructive bronchitis, lung neoplasia (11-19). We mention a case published in 2021, an adult female patient who was admitted for a severe form of coronavirus infection complicated with lung events who was diagnosed with acromegaly starting from these pulmonary complications; therapy with somatostatin analogue octreotide was immediately started (20).

VOLUME OF MEDICAL CARE

In subjects who are not going through a COVID-19 infection, but they had a prior diagnostic of acromegaly, two main aspects of medical and surgical practice were noted: a massive reduction of surgical volume during the first year of pandemic, mostly during peak months of high infection rate in general population and the introduction of tele (digital) health care systems, of different protocols and various platforms mostly depending of medical center, rather than country or even continent related protocols (21-29). These aspects are not specific for individuals with somatotropinomas (30). However, virtual visits are required to follow-up the medical therapy with somatostatin analogues, dopamine agonists and GH blockers and potential side effects (31-34). A study on telemedicine – associated pitfalls in 78 people (median age of 63 years) with acromegaly (more than half were women) showed: 91% - satisfaction over new practice in addition to time – and money – saving aspects versus pre-pandemic visits; the adherence to therapy was sustained for 84% of individuals; 13% of patients were identified as COVID-19 positive

at some point; the adherence to digital medicine dropped within the following 6 months suggesting that perhaps the best time frame to use virtual visits in these patients is for maximum 6 months (35). A web-based, single center, cross-sectional study on 217 patients with acromegaly versus 127 subjects with Cushing disease versus healthy control versus patients infected with coronavirus (without pituitary tumors) showed that anxiety elements were statistically significant higher in infected patients versus the others categories; it seems that discontinuity rate of treatment was higher in acromegaly versus Cushing’ disease (36).

COVID-19-RELATED HYPOPITUITARISM

Angiotensin-converting enzyme 2 (ACE2) receptor is found in pituitary gland, thus in infected patients (with or without previous pituitary tumors) it was identified a process of hypophysitis with consecutive hypopituitarism requiring prompt glucocorticoids replacement (37-40). Also, acromegalic people with associated central adrenal insufficiency require a particular attention if they become COVID-19 positive; they need to double the substitution dose from the very beginning even in mild forms or switching to intravenous glucocorticoids (as in cases with primary adrenal insufficiency) or within the days following vaccination against COVID-19 “sick days” rule should be applied (41-46).

EXPERTS’ OPINION

While the level of statistical evidence is still low (as revealed by some authors), some experts’ opinions have been released pointing out the particular pandemic aspects of patients with pituitary tumors, also including (in addition to somatotropinomas) prolactinomas, Cushing disease, non-functioning adenomas, *etc.*; the key-messages involve multidisciplinary teams, tele-adjustment, and fragile subpopulations facing the infection like those with adrenal insufficiency or diabetes mellitus as complications of pituitary masses (47-51).

ACROCOVID STUDY

The data directly targeting the endocrinologists amid pandemic are very limited. ACROCOVID is a 2021 study that was internationally conducted based on a questionnaire that was applied to 84 endocrinologists (67% of them in Europe) and 58% of them were female practitioners (52). 52% of physicians were from a specialized team on pituitary disorders; 47% of them had more than 50 acromegalic patients to take care (52). Concerning acromegaly: first line therapy was neurosurgery 84% (33% with a delay on procedure because

of insufficient COVID-19 assays and 54% due to inefficient provision for neurosurgery), medical therapy 14% (52).

DIABETES MELLITUS

GH/IGF-1 act as aggravating circumstances for secondary diabetes mellitus (with a potential worsening in some patients due to pasireotide LAR); a multitude of scientific information clearly pointed the condition (of different etiologies) as high risk for COVID-19 infection; the level of glycated hemoglobin A1c seems a good predictor at onset of infectious disease; the switch to insulin therapy is mandatory in severe infections (53-59).

HIGH BLOOD PRESSURE

Arterial hypertension, also of secondary cause, is correlated with severe coronavirus infection and a higher mortality (60,61). Clinical trials from 2021 showed that additional risk factors are early age at onset, nighttime arterial pressure, associated coronary heart disease; medication with blockers of renin-angiotensin system does not seem a high risk factor; older subjects should be treated based on individual management (advanced age is a general high risk factor) (62).

METABOLIC BONE DISEASE

Acromegaly might associate osteoporosis with a particular pattern (high bone mineral density) and prevalent vertebral fractures on one third of subjects; COVID-19 infection aggravates bone loss due to oxidative stress, inflammatory status, cytokine release, immobilization, glucocorticoid use etc.; while hypovitaminosis D has a high prevalence in general and acromegalic population, especially in menopausal women, with particular interest in immune-modulation concerning coronavirus effects at human body (63-70).

DISCUSSIONS

The topic of acromegaly should be expanded to associated tumors of endocrine and non-endocrine patterns, the umbrella phenotype in syndromes like multiple endocrine neoplasia type 1, McCune-Albright syndrome, Carney syndrome, neurofibromatosis type 1 etc. (71-75).

CONCLUSION

Acromegaly field concerning pandemic changes represents a complex, still ongoing matter involving both patients and practitioners.

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