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Acromegaly as a Multisystem Disease – Analysis of Metabolic Complications. Review of Current Literature

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ABSTRACT

Introduction and purpose

Acromegaly is an endocrine disorder resulting from an excess of growth hormone (GH), most often caused by a pituitary adenoma. In addition to typical somatic symptoms, a key clinical aspect is its complications (particularly metabolic). Chronic exposure to GH and insulin - like growth factor (IGF-1) significantly affects lipid and carbohydrate metabolism. This paper presents the current state of knowledge on acromegaly, including the most common metabolic disorders occurring during its course.

The aim of this review is to deepen the understanding of acromegaly as a systemic disease, with particular emphasis on its metabolic complications.

Material and methods

The paper analyzes scientific publications on acromegaly and its metabolic complications published between 2008 and 2024. To gather relevant data, the literature available on PubMed was used, utilizing the following keywords: acromegaly, metabolic disorders, complications.

Results

The analysis of available scientific publications revealed the presence of metabolic disorders in the majority of patients with acromegaly. Lipid disturbances affect as many as 74% of patients. These individuals typically exhibit hypercholesterolemia, hypertriglyceridemia, and decreased HDL-C levels. Equally significant are disturbances in glucose metabolism, affecting more than 50% of patients. The data confirm that prolonged excess of GH and IGF-1 significantly disrupts the body's homeostasis, requiring monitoring and comprehensive treatment.

Conclusions

Acromegaly is a potentially fatal disease whose effects extend far beyond the endocrine system. Its complications significantly increase cardiovascular risk, worsen patient prognosis,

and negatively impact their quality of life (QoL). To improve treatment outcomes, a holistic approach to patient care, appropriate metabolic monitoring, and individualized treatment are essential.

Keywords: Acromegaly; metabolic disorders; complications

INTRODUCTION

Acromegaly is a rare, chronic, and progressive endocrine disorder. Its prevalence ranges from 2.8 to 13.7 per 100,000 people, and the average age at diagnosis is 50 years [1,2]. Acromegaly is caused by excessive production of growth hormone (GH), usually due to the presence of a pituitary adenoma. The excess GH leads to increased levels of insulin - like growth factor 1 (IGF-1), which is primarily produced by the liver. Elevated hormons levels cause abnormal growth of soft tissues, most noticeably in the face and extremities. However, changes in appearance are not the only manifestation of acromegaly. The disease also significantly affects metabolic regulation, leading to numerous complications and a marked decline in patients' quality of life. Early symptoms may go unnoticed or be mistaken for other conditions, resulting in delayed diagnosis - often by several years - which can postpone treatment by as much as 8 to 10 years [3].

ETIOLOGY

In 99% of individuals with acromegaly, the cause of the disease is the presence of a somatotropin - secreting pituitary adenoma that produces growth hormone (GH). In most cases, by the time the diagnosis is made, the tumor is a macroadenoma (diameter > 10 mm). This tumor is usually benign. Assessing the hormonal activity of the tumor is of key clinical importance. According to studies, surgical treatment of adenomas secreting both GH and prolactin (Prl) is less effective - remission occurs in 20% of such cases compared to 68% for tumors secreting only GH. However, it is important to note that the mere presence of an adenoma does not justify a diagnosis, as hormonally inactive tumors may be asymptomatic [1].

Acromegaly can also be associated with genetic disorders such as McCune-Albright syndrome (characterized by fibrous dysplasia of the bones, café-au-lait spots, and precocious puberty), Carney complex (adrenal micronodular hyperplasia – ACTH - independent

hypercortisolism, skin abnormalities, and benign tumors of the skin, heart, and pituitary), or MEN1 (multiple endocrine neoplasia type 1 - characterized by hyperparathyroidism, pancreatic neuroendocrine tumors, and pituitary adenomas) [4].

In a small proportion of patients (<1%), acromegaly is caused by ectopic tumors that secrete GHRH, GH, or both. These are most commonly neuroendocrine tumors (NETs) of the lungs and pancreas, but other tumors - such as pituitary gangliocytomas - may also be responsible. An ectopic source is usually suspected when pituitary imaging (MRI) does not reveal the presence of an adenoma. It should also be considered when atypical symptoms are present, such as cough or shortness of breath (suggestive of lung cancer). Further diagnostic evaluation is warranted if surgical treatment proves ineffective [5].

DIAGNOSIS

The diagnosis of acromegaly is based on the clinical presentation and must be confirmed by biochemical testing [4]. According to the recommendations of the Fourteenth Acromegaly Consensus Conference (Italy, 2022), in a patient with characteristic symptoms, the disease is confirmed by an IGF-I level > 1.3 times the upper limit of normal (ULN) for the patient's age. Measurement of GH levels after an overnight fast is not required for diagnosis, but may be useful for prognostic purposes. In patients with borderline IGF-I results, it is recommended to repeat the test using the same validated assay.

Additionally, an oral glucose tolerance test (OGTT) may be helpful to assess GH suppression following glucose administration. In healthy individuals, GH levels significantly decrease after glucose intake, while in patients with acromegaly, levels may remain elevated or even increase. For the test, the patient should receive 75 g of glucose while fasting, and GH levels should be measured at 30, 60, 90, and 120 minutes to determine the lowest (nadir) value. Diagnostic cut - off values depend on the patient's BMI: < 0.4 µg/L for BMI < 25 kg/m² and < 0.2 µg/L for BMI ≥ 25 kg/m².

In all cases, the clinical picture must be taken into account, and an MRI scan of the pituitary gland is mandatory. In uncertain cases, the patient should be referred to a multidisciplinary center specializing in pituitary disorders [6].

CLINICAL PICTURE

Somatic Symptoms

Changes in the extremities and face of the patient are considered pathognomonic (seen in 80% of patients). There is noticeable enlargement of the hands and feet, along with widening and thickening of the fingers. Patients may report the need to wear larger rings and shoes. Typical features of the face include: thickening of facial features, enlarged ears, a prominent forehead, a thickened and widened nose, enlarged lips, and jaw enlargement with associated malocclusion and diastema (spacing of teeth). Skin thickening, due to the deposition of glycosaminoglycans in the tissues, is particularly visible on the face, hands, and feet. Due to hyperplasia and increased activity of sweat glands, the skin is moist. Additionally, excessive hair growth is often present [1,4,7].

Bones and Joints

Excessive GH and IGF-1 affect bone metabolism through various mechanisms, disrupting the balance between bone formation and resorption, and impairing the condition of the skeletal system. By altering the microstructure of bones, these hormones contribute to deformities and fractures. A prospective Korean study compared the risk of vertebral and hip fractures in 1,700 patients with acromegaly and 8,885 healthy individuals, matched for sex and age. It was shown that patients with acromegaly were significantly more likely to experience vertebral fractures (HR = 2.09) and hip fractures (HR = 2.52) compared to individuals in the control group [8]. In the spine, widening of the intervertebral spaces, enlargement of the vertebrae, osteophytes, thoracic kyphosis, and lumbar hyperlordosis can be observed. Deformities of the chest may also occur [4]. In acromegaly, overgrowth of soft tissues and cartilage occurs, and acromegalic arthropathy typically develops within 10 years of diagnosis. This condition is characterized by non - inflammatory joint pain, swelling, deformities, and either limited mobility or joint hyperlaxity. Large joints (e.g., the knees) are most commonly affected. These changes may be irreversible despite treatment [4,9].

Cardiovascular Symptoms

Cardiovascular disorders affect more than half of patients with acromegaly. These complications significantly increase the risk of hospitalization and lead to higher treatment costs [1]. It is suggested that the development of cardiovascular disease in acromegaly results from the coexistence of metabolic disorders, inflammatory processes, chronic oxidative stress, and endothelial dysfunction [10].

a) **Arterial Hypertension**

Arterial hypertension is a common complication of acromegaly, occurring in an average of 33.6% of patients (ranging from 11% to 54.7%). The pathogenesis is not fully understood, but a multifactorial basis is suggested. GH and IGF-1 contribute to increased sodium retention, which leads to expanded extracellular volume and promotes the development of hypertension [11,12]. Additionally, these hormones affect the endothelium by impairing the production of nitric oxide (NO). Carbohydrate and lipid metabolism disorders, as well as sleep apnea syndrome (SAS), which result from acromegaly, also play a key role in the pathogenesis. Sleep apnea may affect more than half of patients with acromegaly, typically taking the obstructive form due to anatomical changes such as enlargement of the jaw and maxilla, macroglossia, and hypertrophy of the mucosa and laryngeal cartilage [4,7,10]. According to studies, among 1,000 individuals with acral enlargement and symptoms of sleep apnea syndrome (SAS), acromegaly was confirmed in 1.35 cases [13]. The relationship between GH and IGF-1 and the renin – angiotensin - aldosterone system (RAAS) remains controversial, and authors emphasize the need for further research. Hypertension associated with acromegaly is characterized by higher diastolic blood pressure (DBP) and lower systolic blood pressure (SBP) compared to other patients. Additionally, a non - dipper blood pressure pattern - typical of secondary hypertension - has been observed in approximately 50% of cases, which increases cardiovascular risk [11,14].

b) **Acromegalic Cardiomyopathy**

Prolonged elevated levels of GH and IGF-1 lead to both morphological and functional changes in the heart [12]. Studies in rats have confirmed the direct hypertrophic effect of IGF-1 on cardiomyocytes. Acromegalic cardiomyopathy (affecting approximately 3% of patients) typically follows a three - stage progression. Initially, the hyperkinetic heart demonstrates increased efficiency, and cardiac output rises. Subsequently, due to ongoing inflammation, concentric biventricular hypertrophy and proliferation of fibrous tissue develop, leading to impaired diastolic and systolic function. In the final stage, significant chamber dilation occurs, resulting in the development of congestive heart failure [15].

Patients with acromegaly are also at increased risk for more frequent valve defects and arrhythmias, which may further impair their heart function. These issues are likely due to fibrotic changes, and the risk of their occurrence increases with the duration of the disease [4].

METABOLIC COMPLICATIONS

Metabolic disorders are particularly important in the care of patients with acromegaly, as they increase the risk of death from cardiovascular causes [16]. According to studies, metabolic disorders (hyperlipidemia, prediabetes, diabetes) were the most common complications of acromegaly [17] (Table 1).

Table 1. Main complications of Acromegaly

SYSTEM/AREA	COMPLICATIONS
Metabolic	- insulin resistance - diabetes mellitus - dyslipidemia - lipodystrophy
Cardiovascular	- arterial hypertension - cardiomyopathy - arrhythmias - increased cardiovascular mortality risk
Musculoskeletal	- arthropathy - joint and bone pain - fractures
Respiratory	- ventilatory disorders - sleep apnea syndrome
Skin and soft tissues	- hyperhidrosis - hypertrichosis - skin thickening

Others	- hypopituitarism - hypogonadism - sexual disorders - increased risk of cancers - carpal tunnel syndrome - headaches - visual disturbances - depression - decreased quality of life

Lipid Metabolis

Studies have shown that hyperlipidemia is the most common comorbidity in acromegaly, affecting up to 74% of patients. It was found that 44% of the subjects had hypercholesterolemia, 16% had isolated hypertriglyceridemia, and 32% had both disorders [17]. GH inhibits lipogenesis by blocking lipoprotein lipase and reducing the expression of fatty acid synthase. It also has a lipolytic effect, leading to the release of free fatty acids (FFAs) into the bloodstream [18]. Additionally, individuals with acromegaly have lower levels of HDL-C, which results from reduced activity of LCAT (lecithin - cholesterol acyltransferase), involved in the esterification of free cholesterol to HDL. There is also a noticeable tendency for the presence of smaller and denser LDL-C particles compared to healthy individuals [19]. The above mechanisms accelerate the development of atherosclerosis and contribute to cardiovascular diseases.

Lipid metabolism disorders are associated with carbohydrate metabolism disorders [20]. Increased levels of released FFAs inhibit glucose transporters in adipose tissue, which reduces glucose uptake by insulin and promotes the development of insulin resistance [16]. Moreover, FFAs can be used as a substrate in the process of gluconeogenesis and can lead to the Randle effect (also known as substrate competition - an increased availability of FFAs for oxidation reduces glucose oxidation) [18,21].

The use of modern body composition analysis techniques has allowed for the characterization of GH - driven dysregulation of adipose tissue. Lipodystrophy in acromegaly is primarily associated with insulin resistance. It involves a reduction in total and visceral adipose tissue

(VAT), liver lipids, and impaired fat storage in subcutaneous tissue (SAT). As a result of lipid and carbohydrate disturbances, there is a redistribution of lipids and their abnormal deposition in muscles (IMAT) [18,22].

Proper treatment of acromegaly often leads to an improvement in the lipid profile. The best results are achieved with radical surgical treatment, while somatostatin analogs also contribute to the improvement of parameters. Additionally, after assessing cardiovascular risk, the initiation of lipid - lowering therapy should be considered [19].

Carbohydrate Metabolism

The frequency of complications related to carbohydrate metabolism disorders varies depending on the study. It is estimated that 16% to 46% of patients with acromegaly have impaired glucose tolerance (IGT), and 20% to 53% have diabetes mellitus (DM) [4,20]. Diabetes is secondary in nature and is classified as endocrinopathy - associated DM. It typically develops at a younger age compared to the general population [21]. The primary metabolic disorder is insulin resistance (IR), which, according to studies, is more pronounced in women than in men [18].

GH and IGF-1 play a crucial role in regulating carbohydrate metabolism, physiologically acting in a balanced manner. However, their prolonged excess leads to the development of disorders. GH has a pronounced diabetogenic effect – it induces gluconeogenesis, glycogenolysis, and lipolysis. Its chronically elevated levels cause hyperglycemia (excessive endogenous production and reduced utilization in muscles) and promote the development of IR (Figure 1). As its name suggests, IGF-1 increases insulin sensitivity. Under physiological conditions, IGF-1 - activated muscle receptors (IGF-1R) stimulate glucose transporters (GLUT4), leading to glucose uptake. IGF-1 also enhances the ability of adipose tissue and the liver to uptake free fatty acids (FFAs), which helps lower their levels in the blood [14,18,21].

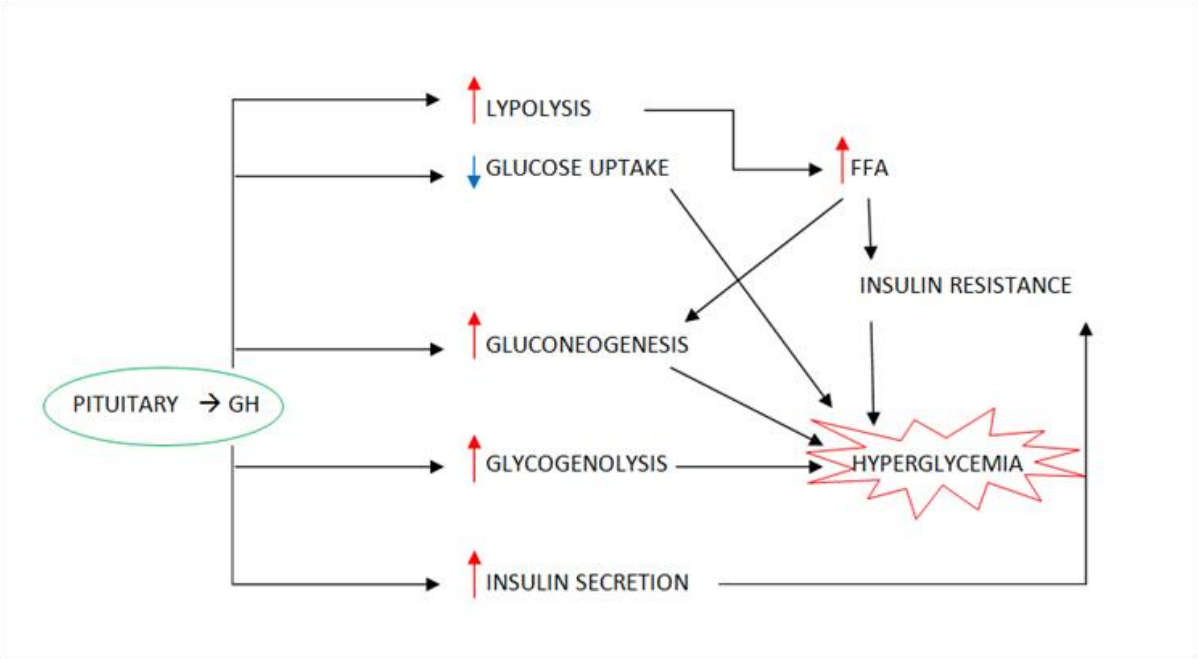

Figure 1. Impact of GH on glucose metabolism

It should be emphasized that in acromegaly, the diabetogenic effect of GH outweighs that of IGF-1 [12]. Initially, the body compensates for the IR caused by GH through increased insulin secretion from pancreatic β - cells. However, over time, these compensatory abilities become exhausted, leading to the development of IGT and DM in the patient. All antidiabetic medications can be used for hypoglycemic treatment in acromegaly [16,21].

An important aspect is that the treatment of acromegaly itself can affect glucose metabolism in various ways. Surgical resection of a pituitary adenoma typically improves carbohydrate metabolism. However, it is important to note that if pancreatic β - cells have been damaged, glucose disturbances may persist despite the surgery. Pharmacological treatments used in acromegaly also influence glucose metabolism. According to studies, pegvisomant (a GH receptor antagonist) has a beneficial effect in this regard, as it reduces lipolysis and glucose production. It appears to be the best choice for patients with acromegaly and poorly controlled diabetes, as it reduces the need for hypoglycemic medications. Dopamine agonists (DAs) also have a beneficial effect, particularly bromocriptine, which lowers HbA1c and insulin levels and improves glucose tolerance. When treating with first - generation somatostatin analogs (SSAs) - such as octreotide and lanreotide - monitoring blood glucose levels is recommended. According to meta - analyses, these drugs slightly worsen glucose metabolism, though without significant changes in HbA1c or fasting plasma glucose (FPG). The severity of the

disturbances depends on the state of glucose metabolism at the time of initiating SSAs therapy. Special caution is required when treating with pasireotide. Studies on the drug have shown that, although it provides more effective biochemical control of acromegaly compared to first - generation SSAs, side effects related to hyperglycemia are common. Pasireotide reduces insulin secretion and disrupts incretin release. If hyperglycemia occurs, the decision to continue pasireotide therapy should be made on an individual basis. Before initiating pasireotide treatment, glucose metabolism should be evaluated, and hypoglycemic therapy should be optimized in patients with diabetes mellitus. The results of many studies remain controversial, and authors emphasize the need for further research on this issue [18,21,23].

In the general population, IR is typically associated with obesity and reduced lean body mass (LBM), forming part of the metabolic syndrome. This condition is usually reversible through lifestyle modifications - such as physical activity and improved body composition (reducing excess fat and increasing LBM). Interestingly, individuals with active acromegaly present a unique combination of a lean phenotype with insulin resistance. This resistance is primarily due to uncontrolled lipolysis and is associated with impaired insulin signaling in muscle and adipose tissue. The exact molecular mechanisms are not yet fully understood. Notably, studies have shown that proper disease control improves insulin sensitivity despite an increase in fat mass and a decrease in LBM - contrary to what is observed in metabolic syndrome. The authors emphasize the importance of their findings in setting new therapeutic targets [24].

TREATMENT OF ACROMEGALY

The goals of acromegaly treatment are to reduce symptoms, normalize metabolic parameters, remove the pituitary tumor, prevent its recurrence, and improve long - term prognosis [3,4]. The availability of various therapeutic options allows for individualized treatment and enables effective disease control in 60 – 90% of patients [25].

Surgery

The first - line treatment for acromegaly is typically the surgical removal of the pituitary adenoma. This procedure is complex due to the challenging access to the pituitary gland and its close proximity to critical brain and vascular structures. The choice of surgical technique depends on the experience and preferences of the neurosurgeon. The majority of resections (>90 %) are performed via a transnasal approach through the sphenoidal sinus. The goal of the surgery is to remove as much of the tumor as possible while preserving normal pituitary function. The primary prognostic factor for achieving surgical remission is tumor size and

invasion of surrounding structures, particularly the cavernous sinus. Experienced medical centers report remission rates of 50 – 75% for macroadenomas and 80 – 90% for microadenomas. In cases of large tumors (> 4 cm) with invasive growth, these rates are significantly lower. According to studies, approximately 60% of patients achieve biochemical remission when it is defined as a nadir GH level <1 μg/L during the oral glucose tolerance test (OGTT). Using the criterion of GH <0.4 μg/L on the second day after surgery, remission is achieved in only about 40% of patients. In general, a successful surgical outcome is defined by normalization of IGF-1 levels within 12 weeks following the procedure. Reoperation should be considered in patients with significant residual tumor mass, in those who do not respond adequately to postoperative treatment, or in patients with a residual tumor after an unsuccessful initial surgery. If surgical intervention does not provide sufficient disease control, is not feasible, or is contraindicated, patients should be offered radiotherapy and/or pharmacological treatment [3,6,26].

Radiotherapy

To increase the effectiveness of therapy and minimize the risk of complications, radiotherapy should be conducted in experienced centers. The most common side effect is hypopituitarism. Other possible complications include visual deficits, cognitive impairments, vascular damage, and secondary intracranial tumors. To minimize side effects, stereotactic radiation (targeted at the tumor) is used [3,4,26].

Pharmacotherapy

The first - line drugs in acromegaly are first - generation somatostatin analogs - octreotide and lanreotide - administered by injection. By binding to somatostatin receptors on the pituitary adenoma cells, they inhibit GH secretion. The most common side effects are reactions at the injection site and gastrointestinal symptoms. The side effects and the parenteral route of administration may negatively impact the quality of life of patients and their adherence to treatment. Due to the variable bioavailability of octreotide after oral administration, the development of its oral form was challenging. In June 2020, the U.S. Food and Drug Administration (FDA) approved the developed oral octreotide capsules (OOC) for long - term maintenance treatment of acromegaly patients who have responded to octreotide or lanreotide therapy and have demonstrated good tolerance to it. This can significantly improve patient comfort and help achieve better compliance with treatment. Some patients require the use of alternative pharmacological treatments (e.g., in case of lack of efficacy of first - line therapy).

Examples of second - line drugs are pasireotide (a second - generation somatostatin analogue) and pegvisomant (a GH receptor antagonist). Combined therapy is also possible. In adjunctive treatment, dopamine agonists (bromocriptine, cabergoline) are used [3,4,27].

The greatest impact on the risk of death in individuals with acromegaly is the degree of disease control and the applied therapeutic strategy. Independent prognostic factors include advanced age, poor biochemical control, the presence of a malignant process, and previous radiotherapy. It was previously believed that acromegaly was associated with significantly higher mortality rates. However, recent studies suggest that with proper disease control, the risk of death significantly decreases. In studies published over the last decade, there has also been a shift in the leading cause of death among patients - from cardiovascular complications to malignant tumors (although no significant increase in cancer - related mortality has been observed) [14,25].

DISCUSSION

Acromegaly is a disease that affects almost all organs and tissues. Many of the mechanisms underlying the development of this pathology are not yet fully understood. The authors of the publication emphasize the need for further research, the results of which are often controversial.

When discussing the topic of acromegaly, it is also important to briefly mention other potential complications, aside from those described above. A significant clinical aspect in patients, particularly those with macroadenomas, may be the "mass effect." The pituitary tumor, by compressing adjacent anatomical structures, causes various disturbances. These may include vision disturbances, headaches, and symptoms of hypopituitarism. It is not uncommon for these to precede the diagnosis of acromegaly.

Scientific publications assess the impact of acromegaly on carcinogenesis. It is believed that excess GH and IGF-1 promote carcinogenesis by stimulating cell proliferation. Currently, this issue is a subject of much controversy, and research results are often contradictory. The latest meta - analysis results have shown a slightly increased risk of carcinogenesis, but a comparable mortality rate compared to the general population. In analyses, benign and malignant tumors of the colon and thyroid are most often evaluated. The risk of their development may increase with inadequate or untreated care, but the exact pathomechanism is

not fully understood. The authors unanimously recommend adherence to national screening programs (e.g., mammography, colonoscopy) [14,25,28].

An important aspect of patients' lives is sexual activity. The somatotropic axis is closely linked to the gonadotropic axis. A dysfunction in one of them can significantly affect the other. In patients with acromegaly, excess growth hormone (GH) may inhibit the release of gonadotropins (LH – luteinizing hormone and FSH – follicle - stimulating hormone). Moreover, the presence of an adenoma and pressure on the pituitary stalk may lead to hyperprolactinemia. It is also possible that the adenoma itself (in addition to GH) secretes prolactin. All of the mentioned factors (including surgical treatment and radiotherapy, as well as metabolic disorders) contribute to the development of hypogonadism, which affects 30 - 50% of patients. It manifests through, for example, menstrual irregularities, gynecomastia, erectile dysfunction, decreased libido, and reduced fertility. The perception of physical appearance in individuals with acromegaly also plays a significant role in negatively impacting physical intimacy. Researchers recommend paying attention to this aspect of the disease as well and regularly assessing total testosterone levels, sex hormone - binding globulin (SHBG), and prolactin [29].

The available literature emphasizes the aspect of quality of life (QoL) in patients. Advances in the treatment of acromegaly often allow for better control of the disease and its comorbidities. However, despite adequate biochemical control, some complications may persist (e.g., musculoskeletal complications, obstructive sleep apnea) and significantly reduce quality of life. In treatment decision - making, the importance of incorporating patient -reported outcome measures (PROMs) is increasingly highlighted. They may concern physical and psychological symptoms, functional problems, as well as more complex aspects. Disease - specific indicators for acromegaly include, for example, the AcroQoL questionnaire, the Patient - Assessed Acromegaly Symptom Questionnaire (PASQ), and the Leiden Bother and Needs Questionnaire for patients with pituitary disorders. Studies have shown that as many as 28% of patients with a pituitary tumor were not in paid employment, and 41% reported taking sick leave due to health - related reasons. Patients' families emphasize the negative impact of the disease on the psychosocial well - being of their loved ones. Studies show that up to 28% of patients suffer from depression, with a higher prevalence among women. Three out of 171 patients under observation died by suicide within a three - year period. The authors of the

publication highlight the important role of PROMs in the comprehensive assessment of disease control and recommend their annual evaluation [30,31].

CONCLUSIONS

Based on the analysis of available publications, it can be concluded that acromegaly is not limited to the endocrine system, but is a multisystemic disease. Excess growth hormone (GH) and insulin - like growth factor 1 (IGF-1) have a significant impact on virtually the entire body, including metabolic regulation. Abnormalities in carbohydrate and lipid metabolism (e.g., insulin resistance and dyslipidemia) affect the majority of individuals with acromegaly. These issues pose a clinical challenge and appear to play a key role in the pathophysiology of many complications, highlighting the need for regular metabolic monitoring.

Patients may report a wide range of symptoms. This is of practical importance, as the diagnostic process can be delayed by up to 10 years, leading to a late diagnosis. By that time, some of the resulting disorders may become irreversible, worsening both prognosis and quality of life. Efforts should focus on achieving earlier diagnosis. When multiple symptoms described in this review are present, physicians should be able to suspect the disease relatively quickly.

Due to the wide range of potential complications, acromegaly requires complex, multidisciplinary treatment. Management should be individualized for each patient and must take into account symptom control, hormonal and metabolic parameters, comorbidities, quality of life indicators, as well as potential treatment - related complications. With appropriate therapy, the life expectancy of patients can approach that of the general population.

There are still many conflicting study results, controversial observations, and unexplained mechanisms underlying the disease. This highlights the need for further research on acromegaly and its complications.

DISCLOSURES

Author’s contribution:

Conceptualization: DK, WF, PB, KD

Methodology: MS, JW, PK, IK, GP

Software: PF, PK

Check: DK, PB, WF

Formal analysis: MS, JW, IK

Investigation: GP, KD, PF

Resources: DK, PB, MS

Data curation: PF, WF

Writing-rough preparation: JW, KD

Writing-review and editing: DK, GP, IK

Visualization: PK, PB

Supervision: MS, WF

Project administration: GP, IK

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