ACROMEGALY: A SEVERE NEUROENDOCRINE DISORDER WITH MULTISYSTEM MANIFESTATIONS

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Abstract. *Acromegaly is a severe neuroendocrine disorder caused by chronic hypersecretion of growth hormone (GH), leading to pathological periosteal bone growth, cartilage proliferation, soft tissue hypertrophy, and internal organ enlargement. It also affects the cardiovascular, pulmonary, and endocrine systems, leading to metabolic disturbances. The disease primarily manifests between the ages of 20 and 40, though it can occur after the age of 50. Epidemiological studies estimate a prevalence of 125–295 cases per million adults and an annual incidence of 3–4 new cases per million. However, true prevalence is likely higher. This review discusses the pathophysiology, clinical manifestations, complications, and diagnostic challenges of acromegaly, emphasizing the importance of early recognition and intervention.*

Key words: *acromegaly; somatotropinoma; growth hormone; insulin-like growth factor.*

АКРОМЕГАЛИЯ: ТЯЖЕЛОЕ НЕЙРОЭНДОКРИННОЕ РАССТРОЙСТВО С МУЛЬТИСИСТЕМНЫМИ ПРОЯВЛЕНИЯМИ

Аннотация. *Акромегалия — тяжелое нейроэндокринное расстройство, вызванное хронической гиперсекрецией гормона роста (ГР), приводящей к патологическому росту надкостницы, пролиферации хрящей, гипертрофии мягких тканей и увеличению внутренних органов. Оно также поражает сердечно-сосудистую, легочную и эндокринную системы, приводя к нарушениям обмена веществ. Заболевание в основном проявляется в возрасте от 20 до 40 лет, хотя может возникнуть и после 50 лет. Эпидемиологические исследования оценивают распространенность в 125–295 случаев на миллион взрослых и ежегодную заболеваемость в 3–4 новых случая на миллион. Однако истинная распространенность, вероятно, выше. В этом обзоре обсуждаются патофизиология, клинические проявления, осложнения и диагностические проблемы акромегалии, подчеркивая важность раннего распознавания и вмешательства.*

Ключевые слова: *акромегалия; соматотропинома; гормон роста; инсулиноподобный фактор роста.*

Introduction: Acromegaly results from excessive GH secretion, most commonly due to a somatotropinoma-a benign, monoclonal, GH-secreting pituitary adenoma.

Over 95% of cases are attributed to this etiology, which stimulates insulin-like growth factor 1 (IGF-1) secretion, promoting widespread tissue proliferation. Other causes include ectopic GH secretion, somatoliberin-secreting tumors, and genetic syndromes such as McCune-Albright syndrome, Wermer syndrome, Carney complex, familial isolated acromegaly, and X-linked acrogigantism. Recent genetic studies indicate that Gsα mutations are present in 40% of GH-secreting pituitary tumors, leading to G-protein dysfunction and impaired GTPase activity in somatotroph cells.

Clinical Features and Diagnostic Challenges

The progression of acromegaly is insidious, with a diagnostic delay ranging from 6.6 to 10.5 years. This delay contributes to organ complications and a four- to fivefold increase in mortality. Due to its broad clinical manifestations, patients often consult multiple specialists before receiving a correct diagnosis. Early recognition by primary care physicians is critical to improving outcomes.

Morphological and Systemic Changes:

- Skeletal and Soft Tissue Changes: Progressive enlargement of facial structures, including the nose, lips, tongue, supraorbital ridges, and zygomatic bones. Patients may exhibit diastema (widened interdental spaces), prognathism, and bite misalignment. Thickened vocal cords and sinus expansion result in a deep, coarse voice. Enlargement of hands, feet, and fingers is common.
- Skin and Soft Tissue Changes: Skin thickening, deepened scalp folds, interstitial edema due to increased mucopolysaccharides, hypertrichosis, hirsutism, seborrhea, and hyperpigmentation are frequent. Excessive sweating results from hypertrophy of sebaceous and sweat glands, often causing an unpleasant odor.
- Musculoskeletal Involvement: GH and IGF-1 influence bone and cartilage, causing hypertrophic osteoarthropathy characterized by severe pain exacerbated by physical activity. Spinal deformities such as kyphoscoliosis and osteoarthritis are prevalent, significantly impacting quality of life even after GH normalization.
- Visceral Organ Hypertrophy: Enlargement of internal organs, including the liver, kidneys, and spleen, is characteristic. Women frequently present with uterine fibroids (up to 70% prevalence), while men often develop benign prostatic hyperplasia.

Cardiovascular Complications

Cardiovascular disease is the leading cause of death in acromegaly, contributing to 60% of cases. Common complications include hypertension, cardiomegaly, concentric biventricular myocardial hypertrophy, arrhythmias, and systolic/diastolic dysfunction.

Hypertension affects 20–50% of patients, with a three- to fourfold increased prevalence compared to the general population. GH-induced myocardial hypertrophy progresses independently of hypertension, transitioning from concentric hypertrophy to dilated cardiomyopathy and heart failure. Increased risk of atrial fibrillation, supraventricular tachycardia, and ventricular arrhythmias is also noted.

Metabolic and Endocrine Disorders

- Glucose Metabolism: Insulin resistance and diabetes mellitus occur in 15–50% of acromegalic patients due to GH's counter-regulatory effects, promoting hepatic gluconeogenesis and peripheral insulin resistance. Acromegalic diabetes is notably resistant to conventional hypoglycemic therapies.
- Thyroid Dysfunction: Most patients exhibit thyroid gland enlargement with or without nodules, attributed to IGF-1 stimulation. While thyroid function is generally preserved, cases of hyperthyroidism and hypothyroidism exist. Secondary hypothyroidism can develop following pituitary adenoma surgery.
- Hypopituitarism and Hyperprolactinemia: Large somatotropinomas may impair anterior pituitary function, affecting gonadal, thyroidal, and adrenal hormone regulation. Women often experience menstrual irregularities and infertility, while both genders may develop hyperprolactinemia-induced galactorrhea.

Respiratory and Gastrointestinal Complications

- Sleep Apnea Syndrome: Affects 35–60% of patients, primarily in males. Airway obstruction results from facial bone deformities, macroglossia, and hypertrophy of pharyngeal tissues. Central apnea is linked to brainstem dysfunction and altered CO2 sensitivity.
- Pulmonary Dysfunction: Progressive lung changes include emphysema, pneumosclerosis, and restrictive pulmonary pathology due to musculoskeletal abnormalities. Mortality from respiratory failure in acromegaly is threefold higher than in the general population.
- Gastrointestinal Manifestations: Acromegalic patients have an increased prevalence of colonic polyps, dolichocolon, and diverticulosis. Studies indicate a higher risk of colorectal cancer, which normalizes with effective disease control.

Neurological and Ophthalmological Manifestations

- Carpal Tunnel Syndrome: Present in 25–51% of cases due to peripheral nerve compression by hypertrophic and edematous tissues. Symptoms include paresthesia and hand pain.
- Optic and Neurological Deficits: Pituitary adenomas extending beyond the sella turcica may compress the optic chiasm and cranial nerves, causing visual field deficits and ophthalmoplegia.

Large tumors may increase intracranial pressure, leading to persistent headaches.

Conclusion

Acromegaly is a debilitating disorder significantly impacting patient morbidity and mortality. Advances in neurosurgical techniques and pharmacological treatments have improved clinical outcomes, but early detection remains crucial. Clinical guidelines emphasize the need to screen patients presenting with at least two of the following symptoms:

- New-onset diabetes mellitus
- Chronic arthralgia
- Persistent fatigue
- Headaches
- Carpal tunnel syndrome
- Sleep apnea
- Excessive sweating
- Daytime sleepiness
- Treatment-resistant hypertension
- Biventricular hypertrophy or cardiac dysfunction
- Visual field narrowing
- Colonic polyps
- Progressive dental misalignment

Given its protean manifestations, acromegaly is often misdiagnosed under various somatic pathologies. Increased clinical awareness among healthcare professionals is essential for timely diagnosis and treatment, improving patient prognosis and quality of life.

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