ACROMEGALY

DEFINITION AND EPIDEMIOLOGY

Acromegaly is a clinical syndrome, resulting from the increased secretion of growth hormone (GH). The prevalence of the disease is 60 per a million. The annual incidence of newly discovered cases is 3-4 per a million. Average age of diagnosis is 40-45 years.

ETIOLOGY

The most common cause (in over 95% of cases) are somatotrope adenomas in the pituitary gland (micro- or macroadenomas according to the size), sometimes with mixed secretion of prolactin. Less common causes include ectopic secretion of growth hormone releasing hormone (GHRH) or directly of GH.

CLINICS AND DIAGNOSIS

The excess of GH causes direct or mediated by the insulin-like growth factor-1 (IGF-1) the overgrowth of different tissues – skin, bones, cartilages, internal organs, as well as changes in metabolism – insulin resistance and diabetes, increased lipolysis and others. Due to the processes in the pituitary, common symptoms are headache, visual disturbances, hypopituitarism.

Changes appear slowly, first in the facial skull – overshot, undershot, teeth, thickening of the skin, growing of the wrists and feet, nose, lips, tongue, voice sinking, arthrosis and arthritis, tendinitis, increased sweating, fatigue, hypertension, predisposition to tumors in the thyroid, colon polyps, impaired sexual function – galactorrhoea, hypogonadism and others.

Diagnosis is based on the determination of the serum levels of IGF-1, serum GH and pituitary imaging. Additional tests include radiographs, scintigraphy, prolactin, visual status, blood glucose profile.

Differential diagnosis – rare hereditary syndromes, which may also lead to acromegaly include McCune-Albright syndrome, multiple endocrine neoplasia 1, familial acromegaly and Carney syndrome.

ESTABLISHED THERAPIES

Treatment is performed in three directions:

1. Surgical treatment
2. Medication
    - A. Inhibitors of GH secretion
        - Somatostatin analogues (*octreotide, COM 230 and others*)
        - Dopamine agonists (*cabergoline, bromocriptine*)
        - Mixed (*dopastatin*)
    - B. Blocker of GH receptors (pegvisomant)
3. Radiotherapy

Dopaminergic agonists have a paradoxical effect on the pituitary – in normal condition they stimulate the secretion of GH and vice versa, in pituitary increased function they push it down. They are effective in less than 15% of patients and are preferred in the presence of increased secretion of prolactin. In certain cases, they can be combined with the GH secretion blockers.

Somatostatin analogues inhibit the GH secretion. They are indicated in cases, when adequate surgery or radiotherapy can be done. There are forms with delayed release (*octreotide LAR*), applied once a month. Tracking these patients for 5-year period shows normalization of GH and IGF-1 levels, complete resolution of arrhythmias, reduced left ventricular hypertrophy, and significant improvement of lipid profile. This drug decreases the insulin resistance and glucose absorption in the intestine, as well as the triglycerides one. Monitoring of the effect of this therapy shows sustained reduction of the tumor mass by more than 50-87% and good control.

GH receptor blockers are applied in case of intolerance or resistance to somatostatin analogs.

Radiotherapy is an option in cases when the effect of the drug therapy is inefficient, the tumor size is increasing or there is some evidence of clinical activity.

Last but not least, ***symptomatic therapy*** is needed for clinical symptoms such as arthrosis and arthritis, accompanied by pain and immobility, which further aggravate the trend towards obesity in these patients, as well as conditions of tight tendon channels – carpal tunnel syndrome, which also proceeds with complaints of pain and sensory disorders. Thus, it gradually leads to contractures and impaired function. In this case, drugs are not always the best solution, especially if considering diabetes or poor status of heart and liver.

The ***physical therapy*** is a good alternative, which is without the side effects of the anti-inflammatory medication and it may be performed in all patients and repeated often enough to maintain the good status of the affected joints. Referring these patients to safer supportive treatments prolongs the survival and improves their quality of life.

Long-standing endocrine disorders as acromegaly may imply a degree of irreversibility of the pathological process and induce highly individualized affective responses. The physical and psychosocial impairment that is associated with incomplete remission from the endocrine illness suggests the need for an innovative approach to treatment, introducing in clinical endocrinology the concept of rehabilitation, which in other fields of medicine is already established. Indeed, **rehabilitation in acromegaly** may be indicated in the following cases: (a) delayed recovery after appropriate treatment; (b) discrepancy between endocrine status and current functioning; (c) presence of a decline in physical and social functioning; (d) persistence of important comorbidity, with psychiatric disturbances; (e) assessment of abnormal illness behavior; (f) problems with lifestyle and risk behavior, and (g) potential role of stress in acromegaly disturbances. The acromegaly rehabilitation team should ideally include a trained clinical endocrinologist, a physical therapist and a psychologist, with opportunities for other specialist consultations. The goal of such service would be to ensure education, support and specific interventions, helping the patient and his family to achieve optimal coping with the difficulties of the recovery process. Due to its comprehensive multidisciplinary characterization, this new approach would likely increase the chances of obtaining full recovery in a significant proportion of acromegaly patients and has the potential of being cost-effective.

REFERENCES

1. Guistna A, Barkan A, Casanueva F et al. Cruteria for cure of Acromegaly. A consensos statement. J Clin Endocrinol. Metab. 2000; 85: 526-529
2. Melmed S, Jackson I, Kleinberg D, Klibanski A, Current treatment guidelines for acromegaly. J Clin Endocrinol. Metab.1998; 83: 2646-52
3. Melmed S. Medical progress; acromegaly. 2006; 355: 2558-73
4. About Sandostatine Web site. Novartis core labelling, text March 16, 2009
5. Sonino N, Giovanni A. Fava. Rehabilitation in Endocrine Patients: A Novel Psychosomatic Approach. Psychother Psychosom 2007;76:319-324

To get further information on acromegaly, as well as on the opportunities for medical rehabilitation and patients' training, please contact Medical Centre "RareDis".

E-mail: medical@raredis.org
Postal address: *24, Landos Street, floor 1, 4000 Plovdiv, Bulgaria*
Phone: *(+359 32) 577 447*
Internet site: www.medical.raredis.org