Turkish Journal of Endocrinology and Metabolism, (2005) 3 : 103-106 **CASE REPORT**

Myelodysplastic Syndrome in an Acromegaly Patient: A Case Report

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Acromegaly patients have higher incidence of neoplasia than the general population, especially for colonic carcinoma. Recently, various hematological malignancies have been reported in patients with acromegaly. However, myelodysplastic syndrome has not been reported in acromegaly previously. In this paper, we reported a unique patient with acromegaly and concomitant pancytopenia and myelodysplastic syndrome.

Keywords: Myelodysplastic syndrome, acromegaly

Introduction

In adults, growth hormone (GH) excess leads to acromegaly, the syndrome characterized by local overgrowth of bone, particularly of the skull and mandible. In acromegaly, GH secretion is increased and its dynamic control is abnormal. Most of the deleterious effects of chronic GH hypersecretion are caused by its stimulation of excessive amounts of insulin-like-growth factor (IGF)-1, and plasma levels of this compound are increased in acromegaly. The growth-promoting effects of IGF-1 lead to characteristic proliferation of bone, cartilage, and soft tissues and increase in size of other organs to produce the classic clinical manifestations of acromegaly (1,2).

Acromegaly reduces life expectancy and leads to 3.5-fold increase in mortality. The main causes are cardiovascular, pulmonary and enhanced prevalence of deaths from malignancy. Successful therapy ought to normalize GH, IGF-1 secretion, remove adenoma mass and its local pressure effects and preserve pituitary function to improve systemic morbidity and normalize mortality (1-3).

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Acromegaly is a rare disease with an estimated incidence of three per million people per year. Acromegaly patients have higher incidence of neoplasia than the general population, especially for colonic carcinoma (4-8). Recently, thyroid, brain, renal, bone neoplasias have been reported in patients with acromegaly (4,9-11). There are few reports of hematological malignancy in acromegaly patients in the literature (12-15).

Myelodyslastic syndrome (MDS) has been used to describe patients with refractory cytopenias whose, bone marrows showed morphologic evidence of dysplastic changes in at least two of the three hematopoietic cell lines and in whom the disease showed a propensity to undergo transformation into acute myeloid leukemia (15). We did not encounter any reports in the literature about MDS in acromegaly. In this paper, we report a patient who had myelodysplastic syndrome and acromegaly.

Case Report

A 65-year-old male was admitted to our department with enlargement of the hands and feet and coarsening of the facial features. Physical examination revealed that his blood pressure was 130/80 mmHg, pulse was 86/minutes and body temperature was 36.4°C. Prognathism, enlargement of nose, macroglossia and widely spaced teeth was detected. On thyroid examination,

multiple bilateral mobile and solid nodules (diameter 3 x 2 cm in maximum, in the right lobe) were found. On respiratory system examination, prolonged expirium was found. The 2/6 systolic murmur was heard on cardiac apex. Abdominal examination revealed a tender, 4 cm hepatomegaly with regular face. Enlargement of hands and feet was found on extremities examination.

Plasma prolactin, GH, testosterone, luteinizing hormone (LH), follicle-stimulating hormone (FSH), thyroid-stimulating hormone (TSH), free T3, free T4, cortisol were determined by electrochemiluminescence immunoassay "ECLIA" method (Roche Elecsys 1010/2010 Analyzer). Plasma adrenocorticotropic hormone (ACTH) was determined by two-site immunoradiometric assay (IRMA) method. Plasma IGF-1 was determined by radioimmunoassay method (BioSource IGF-1-D-RIA-CT Kit). On hormonal examination, plasma GH level [34.5 ng/mL (0.06-5.0)] was increased. Plasma prolactin [11.6 ng/mL (2.5-17)], testosterone [989.7 ng/dL (normal: 212-1511)], LH [3.52 mIU/mL (normal: 1.4-7.7)], FSH [7.02 mIU/mL (normal: 1.5-14)], TSH [1.03 mIU/mL (normal: 0.4-4.0)], free T3 [3.99 pg/mL (1.57-4.71)], free T4 [1.2 ng/dL (0.85-1.78)], ACTH [23.2 pg/mL (normal: 0-46)], and cortisol levels [13.6 μg/dL (normal: 5-25)] were normal. Other laboratory examination; hemoglobin (8.6 g/dL), hematocrit (31%), leukocyte: 3100 /uL, platelet: 111000 /uL each were below the normal limit. Corrected reticulocyte was lower (<1%). Mean corpuscular volume (86 fL), plasma iron (46 ug/dL), ferritin (220 μg/L), folat (11.6 ng/ml), vitamin B12 (284 pg/ml) were found in normal limitis. Erytrocyte sedimentation rate was 9 mm/h. Plasma glucose (79 mg/dL), sodium (145 mmol/L), potassium (4.5 mmol/L), creatinine (0.6 mg/dL), alanine aminotransferase (10 U/L), aspartate aminotransferase (21 U/l), Lactate dehydrogenase (319 U/L) were within normal range. Plasma IGF-1 was increased [370 ng/ml, (normal value: 70-150)].

On peripheral blood smear examination, anisocytosis, poikilocytosis was seen. Bone marrow biopsy revealed that marrow/fat ratio was 90/10 and his marrow was hypercelular. This hypercellularity was derived from three cell lineage. Megakaryocytes were small and maturation (nucleus/cytoplasm ratio) was abnormal. Erythroid cell line was lower. Maturation of granulocyte cell line was normal. As a result, dysmegakaryopoiesis and dyserythropoiesis were noticed, especially in imprint preparation (Figure 1). Cytogenetic exa*mination could not be evaluated because of unavailability.

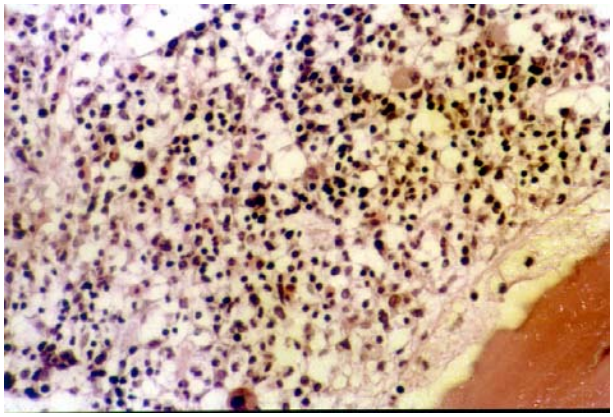
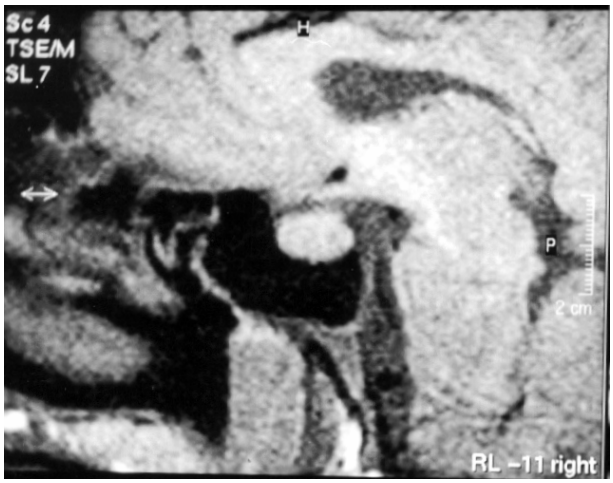


Figure 1.

After hospitalization we performed 100 gr glucose suppression test. Plasma GH was not suppressed after the oral glucose ingestion (GH levels; baseline: 21.7 ng/mL, 15. minutes: >40 ng/mL, 30. minutes: 34.5 ng/mL, 60. minutes: 18.8 ng/mL, 90. minutes:16.5 ng/mL, 120. minutes: 18.0 ng/mL). Macroadenoma (diameter 1.5 x 1 cm) was detected on pituitary magnetic resonance imaging (Figure 2). Visual loss was not detected.



Figute 2.

Ultrasonographic examination of thyroid, right and left thyroid sizes were measured as 2.9 x 3.0 x 6.6 and 3.1 x 2.7 x 5.7 cm, respectively. With thyroid

ultrasonographical and scintigraphical findings, a case was finally diagnosed as euthyroid multinodular goiter. Benign cytological findings and colloidal goiter was detected on thyroid fine needle aspiration examination. Spleen size 13.5 cm and liver size 16.5 cm, grade 1 hepatosteatosis were detected by abdominal ultrasonography. Expanded left atrium and ventricle, left ventricle hypertrophy, mitral and aortic insufficiency were found on echocardiographical examination. Ejection fraction was 50% and pulmonary arterial pressure was 37.5 mmHg.

Discussion

When GH hypersecretion is present for many years, late complications occur. In addition, the morbidity and mortality rate is increased; after the age of 45 years, the death rate in acromegaly from cardiovascular and cerebrovascular atherosclerosis, respiratory diseases, and malignancy is two to four times that of the healthy population (1-3).

An increased cancer of incidence has been reported in acromegaly patients, especially those with persistently raised GH and IGF-1 levels. This is probably related to the positive effect of GH and IGF-1 on cellular proliferation. The role of GH in carcinogenesis is unclear, but it raises serum concentrations of IGF-1, which is mitogenic and antiapoptotic. Results of in vitro and animal studies suggest that growth hormone might raise the risk of hyperplasia, dysplasia, and malignancy (1,2,16, 17). The increase in cancer rate is most significant with colonic carcinoma and screening programmes have been proposed. Endoscopical examination of gastrointestinal system was normal in our patient.

There are few reports on hematological malignancy in acromegaly patients (12-14). One study reported two cases of leukemia among 220 patients who had an overall threefold increased cancer risk (7). The observation of Au and coworkers (14) have suggested that acromegaly patients might have an increased leukemic risk, by at least one order of magnitude. The occurrence of leukemia in acromegaly patients may be relevant, as a clustering of cases has also been observed in children receiving GH therapy. In children receiving GH therapy, thirty-four cases have been reported, including mostly acute lymphoblastic leukemia and acute myeloid leukemia (AML), and, less commonly, chronic myeloid leukemia and MDS (18).

MDS generally presents as a refractory cytopenia, predominantly in the elderly, with >80% of the patients being older than 60 years of age. MDS provides a clinical model for evaluating the evolution of a relatively benign clonal myeloid hemopathy into a frankly malignant neoplasm, a form of AML (15). Progressive pancytopenia was determined in our patient. We detected mor-phologic evidence of dyserythropoiesis and dysmegakaryopoiesis.

Both structural and numerical chromosomal changes may be found in MDS. Cytogenetic abnormalities in the marrow cells of patients with de novo MDS are found in 40-60% at diagnosis, whereas >80% of patients with secondary MDS have abnormal karyotypes (15). Cytogenetic examination could not be evaluated because of unavailability in our patient.

In most patients with primary MDS the disease develops de novo. However, an increasing number of patients who had previously been treated with chemotherapy or chemotherapy plus radiation therapy for other malignancies, or who had been extensively exposed to a variety of marrow toxins, are developing a secondary form of MDS (15). Our patient had not received any chemotherapy and radiotherapy.

In this paper, we reported MDS in a patient with acromegaly which is not reported previously.

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