NOTE

Acute Promyelocytic Leukemia in the Course of Acromegaly: 
A Case Report

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Abstract. Acromegaly is an uncommon disease due to excessive amounts of growth hormone. Benign and malignant tumors have been reported in acromegalic patients. A 41-year-old female patient who had been followed up because of acromegaly by the endocrinology department for two years, was admitted to the hematology department for the evaluation of pancytopenia and the related signs and symptoms. Dopamine agonists were being used till a diagnosis of ‘acute promyelocytic leukemia’ was made. Occurrence of ‘acute promyelocytic leukemia’ in the course of acromegaly may have been caused by excessive endogenous GH or may be a coincidental situation.

Key words: Acromegaly, Acute promyelocytic leukemia

ACROMEGALY is a rare disorder with a defined prevalence of 40 cases per million of the population [2, 17]. It is a clinical entity due to a pituitary adenoma secreting excessive amounts of GH or, rarely, with the stimulation of GH by ectopic production of growth hormone releasing factor [2]. Patients with acromegaly have reduced life expectancy and various authors have reported that malignancies may increase the overall mortality of acromegalic patients [1, 5, 6, 9-15, 18, 20, 23, 24, 26].

In this case report, we are reporting a patient who developed acute promyelocytic leukemia in the course of acromegaly and are reviewing the literature about acromegaly and leukemia association.

Case Report

A 41-year-old female patient was admitted to the hematology department due to weakness, fa-
there was anisocytosis; macrocytes and rare tear drop cells were observed. Thrombocytes were solitary, and no piles were seen. For etiological evaluation, a bone marrow aspiration was attempted, but because it was not successful, a bone marrow needle biopsy was done. 'Infiltration with hypergranular blasts, promyelocytes with several Auer bodies (faggot cells)' were determined in the biopsy imprint (Fig. 1). 'Infiltration of atypical myeloid cell within bone trabeculas' was observed on bone marrow needle biopsy. Altogether the findings were commented on as 'acute promyelocytic leukemia'. Immunophenotyping and genetic investigation could not be done due to leukopenia and failure of bone marrow aspiration. Doxorubicin 40 mg/m², intravenously, 5–7 days + cytosine arabinoside 100 mg/m² two times daily, intravenously, 7 days + 6-thioguanin 100 mg/m², per oral two times daily for 7 days were administered beginning on April 22, 1994. The patient was monitored for the risk of disseminated intravascular coagulopathy with partial thromboplastin time, fibrin degradation products, platelet count and peripheral blood smear in this period. But no laboratory and clinical changes requiring any intervention were observed. The same induction chemotherapy was administered beginning on June 13, 1994 because of failure to begin remission. Hematological remission was obtained on July 22, 1994 and first consolidation therapy was begun again beginning as doxorubicin 40 mg/m², intravenously, 5 day + cytosine arabinoside 100 mg/m², two times daily, intravenously, for 5 days from July 25, 1994. Additionally, the same consolidation therapy was administered from September 15, 1994. 'Tissue loss in pituitary gland related to operation, and asymmetry (probably residual adenoma left in the gland which could not be differentiated from normal gland tissue), slightly right deviation in hypophiser infundibulum related to operation, minimal thickness in left anterior optic chiasma' was determined in hypophiser magnetic resonance imaging on September 5, 1994. FSH 4.4 mIU/ml (normal: N<15), LH 4.6 mIU/ml (N<25), PRL 12.4 ng/ml (N<15), GH 24.8 µU/ml (N<10), cortisol 10.1 µg/dl (N: 5–25), free T₃ 2.8 pg/ml (N: 2.2–4.7), free T₄ 1.4 ng/dl (N: 0.85–2.67) and thyroid stimulating hormone 2.6 µIU/ml (N<6.5) were measured on September 16, 1994. The patient was evaluated by the endocrinology department and lisuride therapy was begun. Gradually, the dose was increased and was finally maintained at a dose of 0.4 mg three times daily. The patient was hospitalized because of progressive headache which was augmented with head movements and decreased with resting, and visual loss in the right eye on November 23, 1994 during lisuride medication. Physical examination results were normal except for minimal palpable splenomegaly and the patient was found to have a white blood cell count of 142.4 x 10⁹/L, hemoglobin 10.0 g/dl, hematocrit 29.0% and thrombocyte 30 x 10⁹/L in peripheral blood. A blastic cell ratio of 93 percent was detected in the peripheral blood smear and dense infiltration with hypergranular blasts in bone marrow aspiration was found. CD 19 in 12.75%, CD 10 in 0.06%, CD 5 in 2.56%, CD 20 in 0.04%, CD 22 in 0.38%, CD 7 in 0.17%, CD 33 in 95.51%, CD 13 in 14.97% and HLA-DR in 1.89% were found to be positive in immunophenotyping. The patient was hydrated due to relapse and excessive tumor burden and preparations were made for leukopheresis and chemotherapy, but acutely in a few hours stupor progressed to a coma and the patient died within several hours after hospitalization.

**Discussion**

Acromegaly is a rare disorder due to excessive GH releasing. Related to cardiovascular, cere-
brovascular and respiratory diseases, the overall mortality rate is clearly increased in the course of acromegaly [2, 15, 17]. Especially in women, benign and malignant tumors are also increased in the course of acromegaly [1, 5, 6, 9–15, 18, 20, 23, 24, 26].

Firstly, the cause/result association with GH and tumor development is defined because of the effects of GH on hypophisectomized and healthy animals. GH, which was administered to female rats in studies by Moon and coworkers, caused neoplastic changes in various organs [9]. Leukemia development in the course of GH therapy was first reported from Japan in 1987 [23]. To date approximately 40 cases have been reported associated with the development of leukemia due to GH therapy [3, 4, 10, 13, 20, 22–26]. But, no leukemia case during the course of acromegaly has been reported so far.

The effects of GH on hematopoietic cells have been studied in detail in vitro. GH induces proliferation of human lymphocytes and lymphocyte blastogenesis [24]. Human granulopoiesis is stimulated by growth hormone and insulin-like growth factor I (IGF-I) [16]. GH increased the proliferation of leukemic T lymphocytes, T-lymphoblasts and erythroleukemic cells [24]. IGF-I receptors were found on leukemic cells of myeloid and B-cell origin [7, 19, 21]. GH and IGF-I also increased the proliferation of myeloid and lymphoid leukemic cell lines and blasts from acute lymphoblastic and acute myeloblastic leukemia patients [8, 21, 27].

No primary hematological disorder or predisposing leukemic factor such as myelodysplastic syndrome or ionizing radiation have been detected in our case with in retrospective evaluation. Acromegaly and acute promyelocytic leukemia association may be coincidental. But, we considered that development of acute promyelocytic leukemia in the course of acromegaly in our case has been induced by excessive GH endogenously, in relation with the results of in vitro studies associated with GH and IGF-I. Development of acute leukemia is the result of exogenous GH administration in all of the defined cases in literature. If it is accepted that acute leukemia was induced in the course of acromegaly in our case, this suggests that endogenous excessive GH may also induce acute leukemia. It may be considered that high doses of somatostatin and lisuride have been used for acromegaly therapy in our case and administration of dopamin agonists in vivo may control GH levels. Nevertheless, they may not control leukemic proliferation by endogenous GH. 24 h GH and the serum IGF-I concentrations could not be measured because of technical insufficieny. It is therefore not known whether the acromegaly was controlled or not, despite administration of high doses of dopamin agonists. The hypothesis that dopamin agonists could not control leukemic proliferation may therefore be misleading. If it is suggested that dopamine agonists may induce leukemic proliferation, side effects of this kind due to dopamine agonists have not yet been reported, either.

In conclusion, if our case is considered with similar reports in the literature, it may be suggested that endogenous or exogenous excess GH may induce leukemic proliferation. Based on in vivo observations, in vitro investigations associated with GH may shed light to the understanding of the biology of leukemia.

References


