

# A Rare Case of Chronic Myeloid Leukemia At a Patient with Achondroplasia

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**Abstract** The coincidence of chronic myeloid leukemia (CML) and achondroplastic dwarfism is very rare. A 40-year old man with achondroplastic dwarfism was diagnosed with chronic myeloid leukemia in blastic phase with a Sokal index of 1.34. Standard dose imatinib treatment was immediately started after the diagnosis.

**Keywords:** chronic myeloid leukemia, achondroplasia, CML, achondroplastic dwarfism

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## 1. Introduction

Achondroplasia is the most frequent type of genetic dwarfism, with a prevalence between 0.1 and 1.5 per 10,000 births. Disproportionate short stature and other skeletal anomalies resulting from a defect in the maturation of the chondrocytes in the growth plate of cartilage are the characteristics of the disease [1].

Chronic myeloid leukemia is a myeloproliferative disease characterized by the improper production and uncontrolled proliferation of mature and maturing granulocytes with considerably normal differentiation. Its peak incidence is observed at the age of 53 and men are more commonly involved, compared to women [2]. CML is associated with the fusion of two genes: BCR (on chromosome 22) and ABL1 (on chromosome 9) that results in the BCR-ABL1 fusion gene. This abnormal fusion typically originates from a reciprocal translocation between chromosomes 9 and 22, t(9; 22)(q34; q11), that leads to an abnormal chromosome 22 usually called as the Philadelphia (Ph) chromosome. This newly-formed chromosome 22 carries the BCR-ABL1 fusion gene [3].

The main clinical feature of CML is the uncontrolled production of mature and maturing granulocytes, mainly neutrophils, besides basophils and eosinophils. The natural course of CML has three phases: chronic, accelerated, and blast phases. The majority of the patients present in the chronic phase, around 10% present in the accelerated phase, and another 10% in the blast phase. Without treatment, CML progresses from a chronic phase to an accelerated phase and even to a terminal blast crisis. Sometimes it goes from chronic phase directly to blast crisis, especially when lymphoid cells are observed in the blast phase [4].

## 2. Case Report

A 40-year old man with achondroplasia applied to the local hospital with the complaint of knee pain. He had been diagnosed with achondroplasia at the birth of his first child 10 years ago. At routine laboratory examination, complete blood count revealed a haemoglobin of 11.2 g/dL, total leucocyte count of  $26.600 \times \mu\text{L}$ , and a platelet count of  $99.000 \times \mu\text{L}$  and he was referred to our center with prediagnosis of acute leukemia. At our initial examination, the patient had disproportionate short stature and splenic enlargement where the spleen extended 5 cm below the left costal margin (Figure 1). The peripheral smear showed 8% blasts, 5% lymphocytes, 5% myelocytes, 5% metamyelocytes, 5% promyelocytes, 72% neutrophils and stab forms. The prediagnosis was chronic myeloid leukemia and the patient was started on hydroxyurea and allopurinol. Twenty days later, he was admitted to the outpatient clinic again with complaints of knee pain, fever and nose bleeding. Chromosome analysis revealed no mutation for Janus kinase-2 but fluorescence in situ hybridization (FISH) analysis showed the bcr-abl fusion gene with a rate of 95%. The patient was diagnosed with chronic myeloid leukemia (CML) at chronic phase. The patient was started on 400 mg of imatinib. After three days of treatment, the patient stated that he could not tolerate the drug and he refused to use it. After he was discharged from the hospital, he was lost to follow up.

## 3. Discussion

At a study by Stoll and Feingold at 2004 about sporadic achondroplastic patients, maternal and paternal origins of neo-mutations in achondroplasia were discussed and the authors stated that chronic myeloid leukemia was observed at grandmothers and grandfathers of people with achondroplasia. According to the authors, in achondroplasia, the neo-mutations may have a paternal origin raising the hypothesis of the existence of a "mutator" gene acting in

male meiosis and in somatic, mitotic cells in both sexes and a mutator or susceptibility gene present in an individual could lead to a cancer in the ancestor and to a mutation in the germ cell of offspring of the ancestor. They found out that paternal grandfathers and grandmothers of people with achondroplasia had significantly more cancers than maternal grandfathers and grandmothers, and general population [5]. As for our

patient, none of the parents had achondroplasia and his two elderly brothers were healthy. The patient himself also had two healthy children. The patient admitted that he had a chromosomal analysis at the birth of his first child and diagnosed with achondroplastic dwarfism. This raises a question about the relationship between sporadic achondroplasia and malignancy.



**Figure 1.** The patient had disproportionate short stature

At a case report by Geromin et al. at 1997 [1], a 25-year old woman with achondroplastic dwarfism who had been

diagnosed with CML and undergone allogeneic bone marrow transplantation (alloBMT) was presented.

Recombinant interferon was started and hematological response was obtained but there was no karyotypic response and so the patient was submitted to an alloBMT. This is the only case we could find that reports the coincidence of CML and achondroplastic dwarfism at literature. With the introduction of tyrosine kinase inhibitors (TKIs), the best treatment option for CML has now changed from conventional treatment regimens to molecularly targeted therapies. Although alloBMT is still an option for the treatment of CML, first and second generation TKIs are now preferred as the first treatment option [6].

#### 4. Conclusion

The number of patients with achondroplasia who were reported to have CML is very scarce at literature. This is the reason why we wished to present this interesting case. We believe that the relationship between sporadic achondroplasia and malignancy needs further investigation.

#### References

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