Case report

“Preleukemic or smoldering” chronic myelogenous leukemia (CML): BCR-ABL1 positive: A brief case report

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A B S T R A C T

Chronic myelogenous leukemia (CML), in the Chronic Phase (CP), is often suspected as a result of a complete blood count (CBC), which shows increased granulocytes, mostly mature including a peak in myelocytes, increased basophils, and rarely blasts and/or promyelocytes. Morphologic dysplasia is not present. CML is confirmed by detecting the characteristic Philadelphia chromosome (Ph) [t(9;22)(q34;q11.2)] by routine cytogenetics or fluorescent in situ hybridization (FISH) or molecular studies (RT-PCR) for the bcr-abl fusion gene.

The most common feature of CML is an elevated WBC count, usually above $25 \times 10^3/\mu L$, and frequently above $100 \times 10^3/\mu L$. We report a case of confirmed Ph+ CML with a normal CBC detected because of the presence of rare myelocytes and 2% basophils [Fig. 1]. Previous leukocyte counts for the preceding eight years were normal with the exception of one done four months prior to his presentation that showed an abnormal differential with 1% basophils, 2% metamyelocytes and 2% myelocytes.

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1. Case Report

A 65-year-old man with a past medical history of morbid obesity, hypertension, paroxysmal atrial fibrillation, depression and arthritis developed substernal chest pressure and palpitations and presented to the emergency department in September 2013 for evaluation. The patient denied fever, night sweats, anorexia or unintentional weight loss. He denied tobacco or alcohol use. His family history was significant for renal cancer in his mother, breast cancer and lung cancer in his sisters, diffuse large B cell lymphoma in his brother, colon cancer in his maternal grandfather, head and neck cancer in his paternal grandmother, bladder cancer in his maternal uncle, and childhood leukemia in a nephew.

The general physical examination revealed an obese man with a heart rate of 140/minute but was otherwise unremarkable. The cardiac exam revealed an irregular rhythm. The abdominal exam revealed no tenderness or hepatosplenomegaly. A complete blood count (CBC) was performed and the results of the CBC are outlined in Table 1.

Table 1

| Laboratory data                      | September 2013 |
|--------------------------------------|----------------|
| WBC ($10^3/\mu L$)                   | 10.6           |
| RBC ($10^6/\mu L$)                   | 4.4            |
| Hemoglobin (g/dl)                    | 12.7           |
| HCT (%)                              | 40             |
| MCV (fl)                             | 91             |
| RDW (%)                              | 15.7           |
| Platelet count ($10^9/\mu L$)        | 254            |
| Differential                         |                |
| Neutrophils #                        | 8.1            |
| Lymphocytes #                        | 1.3            |
| Monocytes #                          | 0.4            |
| Eosinophils #                        | 0.2            |
| Basophils #                          | 0.3            |

Evaluation of the peripheral blood smear revealed a mild basophilia (2%) and myelocytes (1%) and meta myelocytes (1%). A hematology consultation was requested for evaluation. A bone marrow aspiration and biopsy was performed in October 2013. Examination of the marrow revealed a slightly hypercellular marrow with a granulocytic hyperplasia [Fig. 2]. Rare monoblasted megakaryocytes were present. Karyotype analysis revealed 46, XY, t(9;22) (q34,q11.2) in 20 cells analyzed and was the sole abnormality observed. FISH performed with the ABL1/BCR probe identified the...
fusion of the ABL on chromosome 9 with the BCR gene on chromosome 22 in 90.5% of the metaphases. Quantitative Reverse Transcriptase-Polymerase Chain Reaction analysis revealed the presence of the BCR-ABL transcript (p210 form) in 162/200 (81.0%) cells scored.

The patient was diagnosed with chronic phase CML. The initial hematology opinion recommended initiating tyrosine kinase inhibitor therapy, and the patient sought a second opinion. Considering his asymptomatic presentation and stable blood counts, the treating physicians supported a plan of active surveillance with periodic CBCs and differential and LDH. He was last seen in August 2014. He remains asymptomatic with essentially stable blood counts [Table 2].

2. Discussion

CML was the first malignancy to be linked to a clear genetic abnormality, the Philadelphia chromosome. This chromosomal abnormality is so named because of the city in which it was first discovered and described in 1960 by Peter Nowell and David Hungerford [1]. The fusion protein results in increased activity of a tyrosine kinase and several other signal transduction pathways with deregulation of the normal control mechanisms of granulopoiesis [2]. In most published series of consecutive patients diagnosed with CML the total leukocyte counts are elevated [3]. In one recent series [4], 245 patients were analyzed and 178 of these (72.6%) were in Chronic Phase. The mean total leukocyte count was 168 $\times 10^9$/L (range: 35–959).

In 1972 Canellos and Whang-Peng [5] reported on a 43-year-old male with a leukocyte count of 8800/cmm but 6% metamyelocytes and 7% myelocytes. Examination was normal. The Ph was detected in 22% of the metaphases and the patient remained asymptomatic for five years without treatment before developing a blast crisis. A second case was reported more recently by Hudnall and coworkers from the University of Texas, Galveston. [6] Their case was complicated by the simultaneous presentation of Hodgkin lymphoma, Stage III, successfully treated. The total leukocyte count remained normal for 15 months after recognition of the BCR-ABL transcript.

The “containment” of these patients’ granulocyte proliferation remains a mystery.

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Author's contributions

JMB was the pathologist of record and drafted the manuscript. KGD wrote the case report. MP was responsible for the patient care aspects. KO'D served as initial consultant and contributed to the manuscript writing.

Conflict of interest

All authors have no conflict of interest to report.

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