Indian J Hematol Blood Transfus (June 2016) 32 (Suppl 1):S80–S81
DOI 10.1007/s12288-015-0523-4

CORRESPONDENCE

Development of Acute Promyelocytic Leukemia in a Patient With Gouty Arthritis on Long Term Colchicine

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Received: 30 December 2014 / Accepted: 3 March 2015 / Published online: 9 April 2015

Abstract Colchicine is a frequently used drug in rheumatological diseases. Acute promyelocytic leukemia developed in a patient who used colchicine for gouty arthritis since 10 years is presented and the possible relation between the long term use of colchicine and hematological malignancies is discussed.

Keywords Colchicine · Genotoxicity · Acute promyelocytic leukemia

Dear Editor,

Numerous factors, as individual genetic characteristics, drugs and environmental factors, can affect cells to develop malign process. It is known that autoimmune and chronic inflammatory conditions can develop into malignant, leukemia or lymphoproliferative diseases [1–3]. Ozdogu et al. [1] were the first to describe an association between colchicine use and development of acute promyelocytic leukemia (APL). They reported APL development upon long-term use of colchicine to treat Behcet's disease, and suggested that a cytotoxic effect of the drug contributed to chromosomal rearrangement associated with development of leukemia. Gouty arthritis is another recurrent inflammatory disease caused by uric acid crystal deposition. In this report, we describe a second case of APL in a patient who had a history of long-term use of colchicine to treat gouty arthritis.

A 44-year old male patient has suffered from of general weakness and spontaneous ecchymosis present since 1 month. He has gouty arthritis for 15 years and coronary heart disease for 5 years in his medical background. He was receiving colchicine (Colchicum dispert, Dr F. Frig Inc., Istanbul, Turkey) for the last 10 years, and clopidogrel, metoprolol, acetylsalicylic acid for few years. On physical examination multiple ecchymosis was detected. The initial hemogram showed pancytopenia, coagulation tests were in normal ranges except D-dimer (very high). Bone marrow smear was revealed maturation arrest at promyelocytic level with diminished erythroid elements. Most of the cells contained abundant large granules and Auer rods (Fig. 1). These cells were positive for CD13, CD33, CD123, and negative for CD34 and HLA DR in the immunophenotyping analysis. The conventional cytogenetic indicated t (15; 17) in all 20 metaphase cells. Although due to lack of additional cytogenetic abnormalities, distinction of de novo or secondary leukemia couldn't be detected according to cytogenetic report.

The patient was diagnosed with APL. He was treated AIDA protocol with supported blood and blood product if necessary. Before initiation of maintenance therapy, the patient achieved hematological and molecular remission.

Colchicine is often used to treat gout, gouty arthritis, familial Mediterranean fever, and Behcet's syndrome [1, 3]. The questions are: does an association exist between development of APL and inflammatory disease or the association is linked to chronicle use of colchicine? We know

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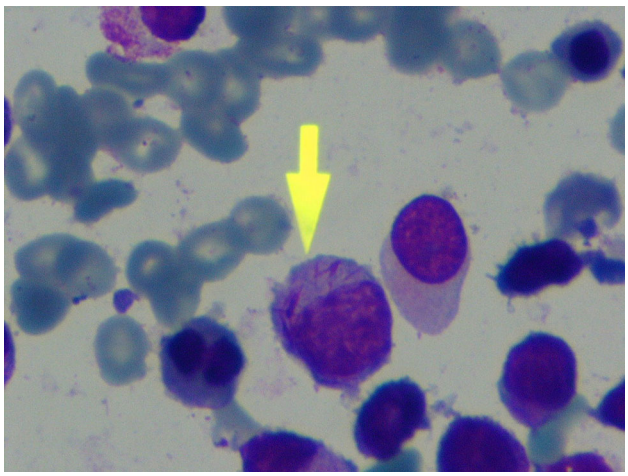

Fig. 1 Bone marrow smear is showing promyelocyte with Auer rods (Wright–Giemsa staining, 100× magnification)

that gouty arthritis is associated with increased risk of cancer but the data shown this association with mostly solid cancers [2]. Also the data from comprehensive population based study shown association between autoimmune disease and acute myeloid leukemia (subtype mostly APL), there is no data about gouty arthritis [3]. APL is a particular subtype of AML often characterized by particular cytogenetic abnormalities [1, 3]. The actions of colchicine at the cellular level are not directly associated with DNA modification, but genotoxic and mutagenic effects of colchicine on many cell types have been reported [1, 5].

Colchicine is well-tolerated anti-inflammatory agent, and finds wide application worldwide. In the USA, it appears that physicians diagnosing gouty arthritis prefer to prescribe colchicine, to limit the use of corticosteroids and non-steroidal anti-inflammatory drugs [4]. We wish to suggest to the physician community that the possible leukemogenic effect of colchicine should be considered in every patient prescribed long-term colchicine therapy.

The inform consent was obtained from the patient for being in this text.

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