

Does Trisomy 12 in Chronic Lymphocytic Leukemia Present in Advanced Stage?

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Objectives: Discuss the trisomy 12 cytogenetic abnormality of CLL and its presentation

Background:

Chronic lymphocytic leukemia (CLL), a mature B cell neoplasm predominantly affects older adults, median age at diagnosis approximately 72 years. Cytogenetic abnormalities play a major role in the pathogenesis, presentation, progression and survival. Literature is limited regarding the genetic factors associated with early disease onset and advanced presentation. We present a case of advanced CLL with trisomy 12 mutation presented relatively at an early age.

Case presentation:

A 56 year old gentleman without significant past medical history presented with constant, new onset right sided throbbing headache and fatigue for one month associated with progressive dyspnea on exertion and 5 pound weight loss in 2 weeks. No fever, chills, night sweats, or bruising. Exam showed conjunctival pallor, palpable posterior cervical lymph node, and palpable splenomegaly.

Labs were significant for severe normocytic anemia (Hgb, 2.9 g/dL), thrombocytopenia (PLT, 33 K/uL), leukocytosis (WBC, 278 K/uL), and smudge cells. Brain CT was unremarkable, chest CT showed numerous axillary lymph nodes, CT abdomen/pelvis showed splenomegaly and numerous bilateral inguinal lymph nodes. Flow cytometry identified CD5+ clonal B-cell population (97%) with a B-cell CLL/small lymphocytic lymphoma (CLL/SLL) immunophenotype. FISH for CLL detected trisomy 12 in 83% of nuclei. Patient was diagnosed with Rai stage IV and Binet stage C CLL.

The patient was transfused with 5 units of leukocyte reduced red blood cells. Upon discharge, he was started on Ibrutinib. His leukocyte (278-->139) and platelet (39-->121) counts started to improve within 2 weeks of therapy.

Conclusion:

Trisomy 12 chromosomal abnormality is detectable in 15-20% cases of CLL. It was previously reported to be associated with thrombocytopenia, Richter's transformation and intermediate prognosis. In one FISH based study, trisomy 12 was found to be associated with high proliferative activity and advanced disease. This might be through functional upregulation of integrin signaling in trisomy 12 CLL cells as described in the literature. The current case strongly emphasizes the trisomy 12 correlation with advanced disease presentation and the need for further studies about this genetic aberration at the molecular level.