Chronic Myelogenous Leukaemia with Additional Cytogenetic Abnormalities Transformation into Blastic Crisis

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Chronic Myelogenous Leukaemia (CML) is a myeloproliferative neoplasm (MPN) with clonal proliferation of all myeloid cell lines which originates in an abnormal pluripotent bone marrow stem cell. CML is characterized by the t(9;22)(q34;q11) translocation in Philadelphia (Ph) chromosome forming *BCR-ABL1* fusion gene. Additional cytogenetic abnormality in CML is associated with disease progression, resistance to tyrosine kinase inhibitors (TKI) and impact on prognosis of the illness. We report a case of a young male diagnosed in 2017 with CML with acquired additional t(3;21)(q26.2;q22) mutation. He developed resistance to treatment with first and second-generation TKI and progressed to blastic crisis early on. Patient was found to have *E255K BCR-ABL* kinase domain mutations. Apart from CML, *BCR-ABL* gene fusion caused by t(9;22) translocation can also be found in ALL and AML. Diseases caused by this fusion gene are depended on the breakpoint location on the *BCR* gene. The most common breakpoint location in CML is in the major cluster *M-BCR* that produces p210 protein. Breakpoint in the minor area *m-BCR* will produce p190 protein mostly related to ALL for cases with positive Philadelphia chromosome. Additional cytogenetics abnormalities are strongly associated with an early progression to blastic crisis, but their prognostic impact is yet to be defined. However, patients with *E255K* mutation have a poor prognosis, regardless of the stage of the disease at detection. Furthermore, the *E255K* mutation has been associated with imatinib and nilotinib resistance in patients with CML. Hence, cytogenetic and molecular screening is important not only during diagnosis of CML but also during management to improve patient's prognosis and survival rate.

Keywords: Chronic Myelogenous Leukaemia, t(9;22)(q34;q11), *E255K BCR-ABL* kinase domain mutation

Acknowledgements
We would like to extend our gratitude to the Director-General of Health Malaysia, Deputy Director General (Research & Technical Support) of Health Malaysia and Director of Institute for Medical Research, National Institute of Health for support and approval of this poster. We also thank the staff of Molecular Genetic Laboratory, IMR for performing the molecular laboratory procedures involved.

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