Leukaemia Section
Mini Review

+6 or trisomy 6

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Clinics and pathology

Note
Trisomy 6 (+6) has been reported as the sole cytogenetics aberration in 14 cases of acute myeloid leukaemia (AML) and five cases of myelo-dysplastic syndrome. Three out of four AML patients with +6 in one series showed AML-M1 morphology and expression of stem cell antigen CD34 on the leukaemic blasts, suggesting that +6 may be associated with a more primitive form of AML. Nevertheless, other reported cases represent a broader spectrum of AML and it is therefore premature to draw conclusion as to whether special morphological and phenotypic features exist in AML with +6. Intriguingly, +6 as the sole cytogenetics abnormality have been reported in 12 cases of haematology-cal disorders characterized by peripheral blood cytopenia and hypoplastic bone marrow. Among the 12 cases, eight cases showed dysplastic change in the haemopoietic cells, whereas four did not. In two cases of aplastic anaemia with dyserythro-poiesis and +6, FISH showed +6 in erythroid as well as myeloid cells, suggesting involvement of an early haemopoietic progenitor cell. The overall survival ranges from 9-48 months. In all cases, normal cells without +6 are present, and the percentage of metaphases with +6 ranges from 6.9% to 85%. It is questionable whether such cases should be classified as hypoplastic MDS, based on clonal cytogenetic change of +6, or aplastic anaemia. The pathogenesis of aplastic anaemia is heterogeneous. While an immunological basis for this disorder is established based on response to immunosuppressive therapy, there is also evidence for clonal nature resulting from damage to the haemopoietic stem cell compartment. Indeed clonal chromosomal abnormalities are reported in other-wise typical aplastic anaemia. Furthermore, aplastic anaemia evolving into acute leukaemia is well documented. This is exemplified by the develop-ment of AML in a case of aplastic anaemia with +6 and no dysplasia 15 months after initial diagnosis. Although patients with +6 and marrow aplasia were uniformly non-responsive to treatments by steroids and anti-thymocyte globulin (ATG), clinical response to cyclosporine was seen in two cases. There was improvement of platelet count in one case and complete clinical response in another. Taken together, it is plausible that +6 defines a distinctive subtype of aplastic anaemia with mild dysplastic changes, poor response to steroids and ATG therapy, and a propensity for AML transformation. Rare instances of +6 may be encountered in childhood acute mixed lineage leukaemia, lymphoblastic transformation of chronic myeloid leukaemia, and chronic myeloproliferative disorder.

Phenotype/cell stem origin
Three out of four AML patients with +6 in one series showed AML-M1 morphology and expres-sion of stem cell antigen CD34 on the leukaemic blasts, suggesting that +6 may be associated with a more primitive form of AML.

Evolution
A case of aplastic anaemia with +6 and no dysplasia showed transformation into AML at 15 months after initial diagnosis.

Prognosis
Trisomy 6 may define a distinctive subtype of aplastic anaemia with mild dysplastic changes, poor response to steroids and ATG therapy, and a propensity for AML transformation. More cases need to be collected to substantiate this contention.
Cytogenetics

Complete karyotype showing 47,XY,+6. G-banding with trypsin/Giemsa. The patient is an 81-year old Chinese man who was admitted for myocardial infarction and was found to be anaemic. Physical examination was unremarkable. Blood counts showed: haemoglobin 8.6 g/dL, white cell count 3.2 X 10^9/L, and platelet count 174 X 10^9/L. Bone marrow morphology, cytochemistry and immunophenotyping results were consistent with a diagnosis of acute myeloid leukaemia. Chromosome analysis on bone marrow cells showed: 47,XY,+6[2]/46,XY[5].

References


This article should be referenced as such: