Society for Hematopathology/ European Association for Haematopathology 2013 WORKSHOP

Progress in Acute Myeloid Leukemia, Myelodysplastic Syndromes and Acute Lymphoblastic Leukemia:

Classification and Molecular Pathogenesis

October 24–26, 2013

Robert C. Hickey Auditorium · Floor 11, R. Lee Clark Clinic · 1515 Holcombe Boulevard

The University of Texas MD Anderson Cancer Center · Houston, Texas

Program Overview

Acute myeloid leukemia (AML), myelodysplastic syndromes (MDS) and acute lymphoblastic leukemia (ALL), represent a heterogeneous group of malignancies that present unique challenges to pathologists. AML can also arise from MDS or myeloproliferative neoplasms and the genetic mechanisms of transformation are largely unknown.. The advent of molecular diagnostics has heralded an explosion in new prognostic markers and many new entities were described in the recently published World Health Organization (WHO) classification of neoplasms of the hematopoietic system. Combined with sequencing and proteomic profiling, these technologies have helped identify new targets and signaling pathways, and may soon help to identify individual patients likely to benefit from specific therapies. Thus, this activity is designed to bring the spectrum of hematopoietic diseases to a forum for updating diagnostic criteria, pathophysiologic mechanisms and discussion. A unique aspect of this workshop is that we anticipate participation of expert hematopathologists, hematologists and oncologists from around the world.

2013 SH/EAHP WORKSHOP CASE

ISODERIVATIVE CHROMOSOME 20 IN A PATIENT WITH REFRACTORY CYTOPENIA WITH MULTILINEAGE DYSPLASIA

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Clinical history (including gender and approximate age):
85 year old man, presents with pancytopenia and mild kidney dysfunction.
CBC: Hb: 8.9 g/dL, Hct: 26.9, MCV: 98 fL, WBC: 2.7 x 103/µl [N:32%, L:61%, M:7%], PLT:112x 103/µl

Details of Biopsy (site, method of fixation, etc.) and gross/ microscopic pathology:
Bone marrow, aspirates and core (trephine) biopsy
Site: left posterior iliac crest
Method of fixation for trephine biopsy: Decalcification following by formalin fixation
Gross/microscopic pathology: Hypercellular marrow (75% cellularity);
M:E Ratio: 1:1
Myeloid series: complete maturation, few pseudo Pelger-Huet forms, no increase in blasts
Erythroid series: normoblastic and megaloblastoid maturation, binucleation, nuclear budding, cytoplasmic/ nuclear dyssynchrony
Megakaryocytes: number increased, hypolobated forms and micromegakaryocytes
No increase in lymphocytes and plasma cells

Immunohistochemistry/ Flow Cytometry:
IHC not performed
Special stains
Reticulin stain: demonstrated no fibrosis
Iron stain: demonstrated normal storage iron, no ringed sideroblasts
Flow cytometry
Slightly dyspoietic myeloid maturation, no increase in blasts

Molecular Analysis:
FISH analysis demonstrated deletion 20q

Cytogenetic findings:
Karyotype Analysis
46,XY,ider(20)(q10)del(20)(q11.2q13.3)[19]/46,XY[1]

Abnormal karyotype characterized by an isoderivative chromosome composed of a mirror image duplication of the deleted long arm of chromosome 20 (20q) in 19 of 20 cells analyzed. One normal 46, XY male cell was also observed.
CGH Array
arr 20p13->p11.21::q11.22->q13.32(9993->25610059::31582338->57426889)x1;
20q11.21::q13.32->q13.33(29540343->30590729::57561657->62141109)x3
Array CGH analysis was performed on this patient's DNA sample referenced to a normal female control DNA sample. This test is comprised of 3519 BAC clones corresponding to genomic loci encompassing the 22 autosomes and the sex chromosomes including loci targeted to genomic regions known to be clinically significant in hematological malignancies. This analysis showed a single copy number loss of 83 loci on chromosome 20, including the entire short (p) arm and a large region on the long (q) arm from q11.2 to q13.3 and a gain of 13 loci on chromosome 20, including the q11.2 and q13.3 regions. An array profile consistent with a male sex chromosome complement was identified.

Interesting features of submitted case:
This case of myelodysplastic syndrome (MDS) is associated with a rare cytogenetic abnormality, i.e. ider(20q) which results in loss of the short arm and duplication of the deleted long arm of chromosome 20. This event leads to loss and gain of genetic material.

This cytogenetic finding has been reported in a limited number of hematological malignancies including myelodysplastic syndrome (MDS), acute myeloid leukemia (AML), chronic myelomonocytic leukemia (CMML), acute lymphoblastic leukemia, and in two cases with minimal bone marrow morphological changes.

Clinical significance of ider(20q) in MDS is yet unclear.

We have five additional cases of ider(20q) in our files. These cases are associated with both myeloid proliferative neoplasm (MPN) and acute myeloid leukemia (AML).
Proposed diagnosis: Refractory Cytopenia with Multilineage Dysplasia (RCMD)
Pictures: Karyogram, FISH of ider(20q)