A NOVEL IGH TRANSLOCATION RESULTING FROM A t(9;14)(p24;q32) IN DIFFUSE LARGE B-CELL LYMPHOMA: A CASE REPORT
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Introduction
- Diffuse large B-cell lymphomas (DLBCLs) are a clinically diverse group within non-Hodgkins lymphoma
- DLBCLs often exhibit rearrangements involving IGH at 14q32
- Most common oncogenic partners for IGH are BCL at 3q27 (15-25%) and BCL2 at 18q21 (15-25%)
- IGH rearrangements result in a promoter exchange wherein the immunoglobulin gene controls the expression of the partner gene
- To date IGH rearrangements have been identified with 33 different genes in leukemia and lymphoma

Clinical History
- 85-yr old female admitted with altered mental status and labored breathing
- CT scan revealed large intra-abdominal mass
- Obtained four needle core bx. with one bx (0.6 cm) submitted for cytogenetic studies
- Patient expired 3 weeks later from multi-system organ failure

Surgical Pathology Results
- Morphologic findings
  Sections showing intermediate to large sized lymphoid cells with large nuclei. Differential included large cell or Burkitt-like lymphoma
- Immunophenotypic findings
  • Cellular antigens (Indicating cell lineage)
  - CD20+ (B-cell)
  - CD3- (T-cell)
- BCL6+ (+ results seen in a high % of DLBCL)
- BCL2- (+ results associated with poorer prognosis in DLBCL)
- High proliferation fraction: Ki-67 80% (High proliferative rate has been associated with worse survival)

Initial Cytogenetic Results
- Main clone:
  47,XX,+2,i(7)(q10),add(10)(p13),add(14)(q32)[17]
- Subclone:
  47,idem,-i(7)(q10),+add(7)(p12)[3]

Final Results
- Final diagnosis: Diffuse Large B-cell lymphoma
- Final karyotype: 47,XX,+2,i(7)(q10),add(10)(p13),add(14)(q32)[17]/47,idem,i(7)(q10),+der(7)t(7;15)(p12;q21.3)[3]

Discussion
- t(9;14)(p24.1;q32.3) represents a unique translocation involving IGH in DLBCL
- 9p24.1 breakpoint localized to an approximate 3Mb region at the 3’ end of JAK-2
- JAK-2 dysregulation reported in various neoplasms including B-cell lymphoma
- No other genes within 9p24.1 have been associated with DLBCL
- Significance of this translocation is currently unknown, however, given the heterogeneity of DLBCL all novel IGH rearrangements should be explored

FISH Results
- LSI BCL6 and C-MYC breakapart probe: Negative
- M-FISH: Revealed der(7)t(7;15) and der(10)t(X;10)
- LSI IgH dual-color breakapart probe Revealed translocation with 9p24
- LSI 9ptel (SG) / LSI 9qtel (SO) Confirmed reciprocal translocation with 14q32
- Homebrew JAK2 dual-color breakapart probe Placed 9p breakpoint proximal to JAK2 gene region

Gene Description
- JAK2: Encodes a protein tyrosine kinase involved in subset of cytokine receptor signaling pathways
- PDCD1LG2: Programmed cell death 1 ligand 2
- UHRF2: Encodes a protein involved in cell cycle regulation
- JMJD2C: Chromosomal aberrations and increased expression associated with esophageal squamous cell CA
- PTPRD: Encodes a protein involved in a variety of cellular processes including cell growth, differentiation, mitotic cycle and oncogenic transformation

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