

Pedro Bettencourt Medeiros
Centro Hospitalar de São João, Porto, Portugal

Triple-hit B cell lymphoma

Clinical presentation

- ⊙ 46-year old female
- ⊙ Previously healthy – ECOG 0
- ⊙ November/2015: abdominal pain + spontaneous bruising + petechiae
- ⊙ Initial blood counts:
 - Hb 9.7 g/dl, MCV 84 fl
 - WBC 22,45 x 10⁹/l, 26% blasts
 - Platelets 20 x 10⁹/l
 - LDH 2239 U/l, uric acid 11.7 mg/dl, beta-2 microglobulin 3861 µg/ml
- ⊙ CTAP CT: cervical (10 x 5mm), mediastinal (14x4 mm), bilateral axillary (17 x 18 mm), retroperitoneal, para-renal (bulky conglomerate), mesentery and pelvic adenopathies; splenomegaly ~ 16 cm
- ⊙ BM and PB smears: immature cells, with elevated N/C ratio, lax chromatin, basophilic cytoplasm, without granules, some with vacuoles + mature small lymphocytes

Clinical presentation

- ◉ BM flow cytometry
 - 2 monoclonal B cell populations: both lambda-restricted, CD19+, CD5-, CD11c+, CD20+, CD22+, CD79b+, CD103-;
 - the largest population (60%), CD10+, CD23-, CD38++, CD43+, IgM+;
 - the smallest population (40%), CD10+/-, CD23+/-, CD38-het., CD43-, IgM+/--het.
- ◉ BM karyotype:
47,XX,add(3)(q27);t(8;14)(q24;q32);t(8;15)(q24;q22),t(14;18)(q32;q21)[26];46 XX[4]
- ◉ BM trephine biopsy: morphological and immunohistochemical aspects of high grade peripheral B cell lymphoma, intermediate between DLBCL and Burkitt's lymphoma
- ◉ BM FISH:
 - 75% t(8;14)(q24;q32) – *MYC* and *IGH* rearrangement
 - *BCL2* gene rearrangements
 - 5' deletion of the *BCL6* gene due to rearrangement of this gene, with loss of one of the translocation derivatives

Diagnosis

B-cell lymphoma, unclassifiable, with features intermediate between DLBCL and Burkitt's lymphoma, stage IV-AXS, with bone marrow / leukemic expression

Triple-hit lymphoma, with *MYC*, *BCL2* and *BCL6* rearrangements

Treatment

- ⊙ R-HyperCVAD / MTX-AraC + autologous stem cell transplant
 - CR criteria after the 3rd cycle
 - Failed stem cell mobilization at completion of the 5th cycle
 - PD after the 6th cycle:
 - BM flow cytometry: 57% monoclonal cells, identical malignant phenotype
 - CT scan and MRI: intracanalicular soft tissue mass, C5-D12, with spinal cord compression.

- ⊙ Salvage treatment (with allogeneic stem cell transplant planning)
 - Emergent radiotherapy 30 Gy (daily 3Gy x10)
 - FLAG-IDA
 - PD after 1st cycle: 93% PB blasts, diffuse BM infiltration by malignant cells

- ⊙ Palliative chemotherapy: cytarabine + etoposide – outpatient

- ⊙ Death (January/2017) due to Gram-negative bacteremia with septic shock and MOD