Therapy-Related
Acute Myeloid Leukemia
Case 057

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Clinical History

- 39-year-old woman with pancytopenia
- 5 years before: fatigue, weight loss, severe hypertension and headache
- Findings:
  - Bence-Jones proteinuria
  - Renal failure (light chain cast nephropathy)
  - Plasma cell myeloma
- Dexamethasone, thalidomide, cytoxan, dialysis, plasma exchange: persistent disease
Clinical History

- Non-myeloablative marrow transplant and renal transplant 6m after dx (donor: patient’s brother)
- Renal disease recurred in one week
- Persistent myeloma, rx with velcade, decadron, melphalan, doxorubicin
- Engraftment successful; myeloma persisted
- 4 years post dx of myeloma, patient was pancytopenic.
- Marrow: RAEB-2 and persistent myeloma (paucicellular aspirate)
Clinical History

- Revlimid, Vidaza administered, but pancytopenia worsened over 6 months
- CBC:
  - WBC 2.2, Hct: 29, Plt 33
  - Differential: 16% polys, 55% lymphs, 19% monos, 10% blasts
- Bone marrow biopsy and aspirate performed (Case 057)
Bone Marrow, Additional Studies

- **Flow cytometry**
  - Blasts: CD33+, CD13+, CD117+, MPO+, CD14-, CD34+, HLA-DR+, CD4dim+, CD7dim+

- **Cytogenetics**
  - FISH: 100% of cells XY, consistent with donor origin of the leukemia
  - GTG-banding: 46XY
  - FISH on prior marrow: No 5q deletion
Case 057

DXZ1 Xp11.1-q11.1
DYZ1 Yq12
Diagnosis
Case 057

- Bone marrow biopsy and aspirate:
  - Acute myeloid leukemia, therapy-related, arising in cells of donor origin
  - Small population of clonal plasma cells, consistent with persistent plasma cell myeloma
- Panel diagnosis: agreed with this diagnosis
Follow-Up
Case 057

- Patient received mainly supportive therapy
- Worsening pancytopenia, with nosebleeds, ecchymoses, weight loss, lower extremity edema and ascites
- Died 4 months after dx of AML
- Brother (donor): alive and well, free of hematologic disease
Therapy-Related AML
Interesting Features

- Plasma cell myeloma occurring at an unusually young age (34 years old)
- AML, donor origin, most likely due to chemotherapy given after marrow transplant, resulting in damage to donor cells
  - Melphalan? Alkylating agent
  - Doxorubicin? Anthracycline
  - Donor: underlying genetic defect?
AML of Donor Origin
After Bone Marrow Transplant

- Literature review: Donor cell AML
  - Very rare
  - Case reports
  - Original disease: AML, ALL, CML, CLL, MDS, AA
  - Variable post-transplant interval (up to 11 years)
  - Most NOT clearly therapy-related
  - Other postulated mechanisms:
    - Abnormal immune surveillance
    - Altered marrow microenvironment
    - Residual chemotherapeutic agents
  - Donors: healthy


