Splenic Involvement in Mantle Cell Lymphoma

- Weisenburger *et al.* introduced the concept of mantle-zone lymphoma in 1982. This lymphoma appears to be arising from naive (somatically unmutated/pre-GC type of mature) B-cells and it typically shows expression of CD20 (high expression levels in contrast to CLL), surface Ig (high expression levels in contrast to CLL), CD43-positive, CD5-positive (often levels are less than in CLL and rare CD5-negative cases have been described), CD23-negative, cyclin D1-positive (cyclin D1-negative cases have been described), Bcl-6-negative, CD10-negative.

- Mantle cell lymphoma (MCL; previously called centrocytic lymphoma or lymphocytic lymphoma of intermediate differentiation) MCL represents 3-10% of non-Hodgkin's lymphomas and more frequently affecting middle-aged to older males (M>>F).

- MCL is generally regarded incurable; median survival of 3-4 years.

- MCL more often presents in stage III-IV with lymphadenopathy, hepatosplenomegaly, bone-marrow involvement, and leukemic spread.

- Typical morphologic features of MCL are monomorphic lymphoid proliferation of small and medium-sized cells with irregular nuclear contours in the tissue sections; typically, MCL is shows more variation in cytological features when circulating in the blood.

- Splenic enlargement occurs in nearly 40 percent of patients with MCL; splenic rupture is infrequent. However, spleen as primary site of involvement is rare at <1%. Hence, there is a difference between splenomegalic form of MCL and secondary involvement by primary nodal or extranodal MCL.

- Spleen involvement does not advance the stage of the disease in lymphoma but maybe a useful prognostic factor.

- Splenomegaly was found to be one of the factors associated with poor prognosis.

- MCL, nodal or extranodal, is frequently a disseminated disease, as stated above, this includes involving spleen. PET seems more sensitive than CT in about 10 to 20% of cases. Importantly, splenic involvement is most often diagnosed by imaging, not by splenic biopsy.

- Splenomegalic (no lymphadenopathy) form of MCL is a rare (<1%) biological variant, which presents like B-PLL and historically has been misdiagnosed as such. It is only after Catovski’s group in UK proposed that B-PLL with t(11;14) is a splenomegalic form of MCL with leukemic presentation rather than B-PLL, that this entity assumed its present designation.

- How is splenomegalic form of MCL different from B-PLL?
  - Younger age group (median 56 vs. 73)
  - MCL is more common in males and B-PLL without t(11;14) in female population
  - Has more pronounced anemia
  - Is much more often CD5+ and CD23-
  - Shows strong Ig surface expression
  - Post GC entity?
  - Has CCND1-IGH translocation
In the splenic forms of MCL, the neoplastic clone commonly shows an overt leukemic dissemination and BM involvement and harbors a mutated Ig repertoire with a higher frequency than nodal MCLs do.

Patients with mantle cell lymphoma tend to have bone marrow and spleen involvement more often than patients with other types of aggressive NHL.

Splenectomy may not be necessary for diagnosis of cases presented with primary spleen involvement:
- PB is involved and circulatory component, just like in other SL can by evaluated and definitive diagnosis made by flow cytometry
- Bone marrow biopsy usually helps in definitive diagnosis of splenic MCL, but it will also help in most cases of HSTL, LPL, and SMZL

CD5+ small B-cell lymphomas include atypical CLL, B-PLL, CD5+ SMZL, SL-u cases, CD5+ LPL, and rarely CD5+ DLBCL.

Cyclin D1+ B-cell lymphomas are not only MCL: cyclin D1+ DLBCL, HCL, plasma cell tumors, and CLL (in proliferation centers).

CCND1-IGH by FISH is required for diagnosis (very rare cases have rearrangements of other cyclins).

**Literature:**