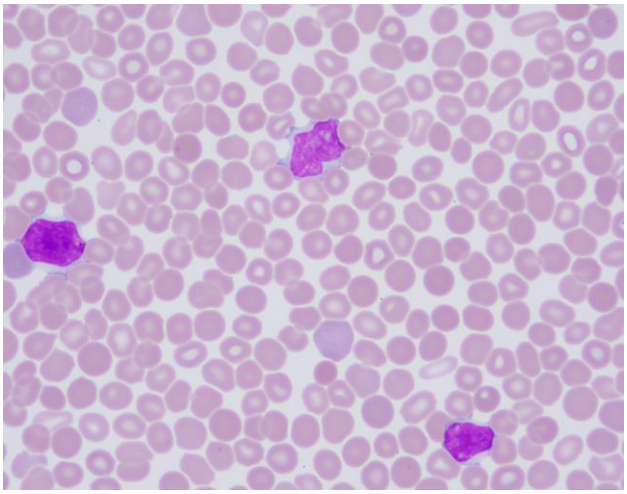
Mantle cell lymphoma

Specimen No 1207



Mantle cell lymphoma (MCL) is a mature B cell non-Hodgkins lymphoma. It comprises 3 – 10 % of non-Hodgkins lymphomas and its incidence increases with age with a median age of around 60. It has a significant male predominance of about 2:1 or greater. Most patients with MCL present with advanced stage disease, with lymphadenopathy, hepatosplenomegaly, and bone marrow involvement. Peripheral blood involvement is common and present in almost all patients by flow cytometry. Approximately 25% of patients present with symptoms from extranodal disease such as gastrointestinal tract (GI), breast, pleura, orbit and Waldeyers ring involvement.

The t(11;14)(q13;q32) translocation between IGH and CCND1 with the resultant overexpression of cyclin D1 is present in > 95% of cases of MCL. Although the t(11;14) translocation is found in most cases of MCL and is thought to be the primary genetic event it is not specific for MCL. In over half the cases of cyclin D1 negative MCL, translocations involving CCND2 and high levels of CCND2 mRNA can be detected, however immunostaining for CCND2 and CCND3 is also positive in other B-cell lymphomas. The SOX11 gene is a useful marker for MCL and has been found to be expressed in >90% of cases of MCL. In most of the cases of MCL that lack expression of Cyclin D1 or t(11:14), but have a gene expression profile suggesting a diagnosis of MCL, the SOX11 gene has found to be present.

A range of morphological variants are recognised in MCL. These include the aggressive variants; the blastoid and pleomorphic variants and the more indolent variants; small cell and marginal zone-like variants. In most cases of MCL the cells found are small to medium sized lymphoid cells, with a slightly irregular or 'notched' nuclei and inconspicuous nucleoli. The morphology of the cells in MCL however can range from small, more irregular lymphocytes to lymphoblast-like cells and even occasionally to mixtures of small and large cells or markedly atypical large cells. The cells in the blastoid variant of MCL can resemble lymphoblasts with dispersed chromatin and a high mitotic rate. The cells in the pleomorphic variant are as the name implies, pleomorphic, many of which are large cells with oval to irregular nuclear contours, mostly pale cytoplasm and often prominent nucleoli in at least some of the cells. Patients with blastoid/pleomorphic morphology have been reported to have a more aggressive clinical course and a poorer overall survival. The histological pattern of MCL growth in lymph nodes may be diffuse, nodular or mantle zone or a combination of all three.

The immunophenotype of the cells in MCL resemble the lymphocytes in the mantle zone of normal germinal follicles. The cells express high levels of surface IgM/IgD, more frequently with lambda light chain restriction than kappa restriction. They express pan B-cell markers (eg; CD19, CD20) CD5 and FMC7 and are negative for CD10 and CD23 is negative or weakly positive. Some cases however may be CD5 negative or CD23 positive. Nuclear staining for Cyclin D1 is present in >90% of cases of MCL, including those that are CD5 negative. Immunohistochemical staining for Ki67 can be useful to assess the proliferation index.

The clinical course of MCL is variable, moderately aggressive and is most often incurable. The median survival is 8-10 years with intensive therapies. Patients with a more indolent course, with a low stage, low risk disease, are being increasingly recognised. The most commonly used scoring systems to attempt to predict the course of disease in MCL are the International Prognostic Index (IPI), the Follicular Lymphoma International Prognostic Index (FLIPI) and the Mantle Cell Lymphoma International Prognostic Index (MIPI). MIPI incorporates patient age, performance status, lactate dehydrogenase and white blood cell count to identify patients as low, intermediate and high risk. Ki67 expression has also been incorporated into the MIPI score. Cases with <10% Ki67 positive cells have a more indolent course whereas cases with >30% Ki67 positive cells are associated with a poorer prognosis. Patients with *TP53* mutation or deletion have poor clinical outcomes, including shortened overall survival, following intensive chemotherapy.

Some patients with indolent disease may not require treatment initially, however the majority of patients with MCL will require treatment at diagnosis. Combination chemotherapy plus immunotherapy is the main treatment of choice. Rituximab is used successfully for several types of non-Hodgkin lymphoma, including MCL. Allogeneic stem cell transplant may be considered for patients with relapsed or refractory disease.

The patient in this case presented with 2-3 months of worsening fatigue, light headedness and lethargy. She had noted some easy bruising and night sweats. Her blood film revealed a pancytopenia with many abnormal lymphoid cells present. An abnormal complex t(11;14) clone was identified with evidence of clonal progression and loss of TP53. These are poor risk indicators. The patient was to be treated with Ibrutinib, Rituximab and Bendamustine with red cell and platelet support.

References:

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